Dossier zur Nutzenbewertung gemäß § 35a SGB V

Deutivacaftor/Tezacaftor/Vanzacaftor (Alyftrek®)

Vertex Pharmaceuticals (Ireland) Limited

Anhang 4-G

Behandlung der zystischen Fibrose bei Patienten ab 6 Jahren, die mindestens eine Nicht-Klasse-I-Mutation im CFTR-Gen aufweisen

Zusatzanalysen für das Nutzendossier

Stand: 30.06.2026

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Full Analysis Set

Duration of observation (weeks)	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Overall Study Observation Time		
n	202	196
Mean (SD)	50.85 (6.86)	51.03 (6.27)
Median	52.14	52.14
Min, Max	2.29, 58.86	7.00, 57.57
$ppFEV_1$ (percentage points)		
n	202	196
Mean (SD)	50.10 (7.59)	50.15 (7.77)
Median	52.14	52.14
Min, Max	2.00, 58.86	7.00, 57.57
BMI (kg/m^2)		
n	202	196
Mean (SD)	50.46 (7.34)	50.88 (6.67)
Median	52.14	52.14
Min, Max	2.00, 58.86	7.00, 57.57
BMI z-score		
n	40	32
Mean (SD)	46.91 (12.68)	47.48 (13.24)
Median	52.14	52.14
Min, Max	2.00, 58.86	7.57, 53.71
Sweat Chloride (mmol/L)		
n	202	195
Mean (SD)	49.86 (8.55)	49.32 (8.88)
Median	52.14	52.14
Min, Max	0.57, 53.86	3.43, 57.57

- Observation duration [weeks] is defined as (date of last observation - date of randomization +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results.

Table 1.1.1.1
Study VX20-121-102: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Weight (kg)		
n	202	196
Mean (SD)	50.79 (7.03)	50.96 (6.59)
Median	52.14	52.14
Min, Max	2.00, 58.86	7.00, 57.57
Pulmonary Exacerbation		
n	202	196
Mean (SD)	50.82 (6.84)	50.93 (6.23)
Median	52.14	52.14
Min, Max	2.29, 53.86	7.00, 57.57
CFQ-R		
n	201	196
Mean (SD)	50.78 (6.76)	50.68 (7.09)
Median	52.14	52.14
Min, Max	0.57, 53.86	7.00, 57.57
TSQM		
n	107	95
Mean (SD)	26.73 (25.88)	27.19 (25.70)
Median	42.43	47.43
Min, Max	0.00, 53.29	0.14, 57.57
CF-IQ		
n	202	196
Mean (SD)	49.64 (9.48)	49.81 (9.31)
Median	52.14	52.14
Min, Max	0.14, 53.29	3.43, 57.57

- Observation duration [weeks] is defined as (date of last observation - date of randomization +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results.

Table 1.1.1.1
Study VX20-121-102: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Safety		
n	202	196
Mean (SD)	49.85 (9.25)	50.54 (7.16)
Median	52.14	52.14
Min, Max	2.29, 56.71	5.29, 56.14

- Observation duration [weeks] is defined as (date of last observation - date of randomization +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results.

Zusatzanalysen zur Studie VX20-121-102

Table 1.1.2.1
Study VX20-121-102: Summary of Patients with Ongoing Antibiotic Medications at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline, N1	202	196
Subjects with 0 ongoing AB	79 (39.11)	74 (37.76)
Subjects with 1 ongoing AB	72 (35.64)	67 (34.18)
Subjects with ≥ 2 ongoing AB	51 (25.25)	55 (28.06)
Subjects with ≥ 1 ongoing IV AB	0	0
Week 52, N1	191	184
Subjects with 0 ongoing AB	74 (38.74)	72 (39.13)
Subjects with 1 ongoing AB	78 (40.84)	61 (33.15)
Subjects with ≥ 2 ongoing AB	39 (20.42)	51 (27.72)
Subjects with ≥ 1 ongoing IV AB	1 (0.52)	0

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- Ongoing antibiotic medications at baseline refer to those with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing antibiotic medications at Week 52 refer to those with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit, and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX20-121-102

Table 1.1.2.2
Study VX20-121-102: Summary of Patients with Antibiotic Medications during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
All subjects	202	196
Subjects with 0 AB	19 (9.41)	26 (13.27)
Subjects with 1-3 AB	83 (41.09)	79 (40.31)
Subjects with ≥ 4 AB	100 (49.50)	91 (46.43)
Subjects with 0 IV AB	152 (75.25)	172 (87.76)
Subjects with 1 IV AB	14 (6.93)	6 (3.06)
Subjects with ≥ 2 IV AB	36 (17.82)	18 (9.18)
Subjects with 0 ongoing antibiotic medications at baseline	79	74
Subjects with 0 AB	19 (24.05)	26 (35.14)
Subjects with 1-3 AB	37 (46.84)	27 (36.49)
Subjects with ≥ 4 AB	23 (29.11)	21 (28.38)
Subjects with 0 IV AB	61 (77.22)	62 (83.78)
Subjects with 1 IV AB	8 (10.13)	4 (5.41)
Subjects with ≥ 2 IV AB	10 (12.66)	8 (10.81)

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- Antibiotic medications during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX20-121-102

Table 1.1.3.1
Study VX20-121-102: Summary of Patients with Ongoing Physiotherapies at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline, N1	202	196
Subjects with 0 ongoing PT	119 (58.91)	112 (57.14)
Subjects with 1 ongoing PT	71 (35.15)	71 (36.22)
Subjects with ≥ 2 ongoing PT	12 (5.94)	13 (6.63)
Week 52, N1	191	184
Subjects with 0 ongoing PT	111 (58.12)	103 (55.98)
Subjects with 1 ongoing PT	68 (35.60)	68 (36.96)
Subjects with ≥ 2 ongoing PT	12 (6.28)	13 (7.07)

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- The ongoing physiotherapy at baseline is defined as a physiotherapy whose start date is prior to first dose date of study drug in the Treatment Period and the end date is ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing physiotherapy at Week 52 is defined as a physiotherapy whose start date is prior to Week 52 visit date and the end date is ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX20-121-102

Table 1.1.3.2
Study VX20-121-102: Summary of Patients with Physiotherapies during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
All subjects	202	196
Subjects with 0 PT	115 (56.93)	109 (55.61)
Subjects with 1 PT	72 (35.64)	73 (37.24)
Subjects with ≥ 2 PT	15 (7.43)	14 (7.14)
Subjects with 0 ongoing physiotherapies at baseline	119	112
Subjects with 0 PT	115 (96.64)	109 (97.32)
Subjects with 1 PT	4 (3.36)	3 (2.68)
Subjects with ≥ 2 PT	0	0

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- Physiotherapies during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX20-121-102

Table 1.1.4.1
Study VX20-121-102: Summary of Patients with Ongoing Inhaled Medications at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline, N1	202	196
Subjects with 0 ongoing IM	9 (4.46)	16 (8.16)
Subjects with 1 ongoing IM	21 (10.40)	12 (6.12)
Subjects with ≥ 2 ongoing IM	172 (85.15)	168 (85.71)
Week 52, N1	191	184
Subjects with 0 ongoing IM	10 (5.24)	14 (7.61)
Subjects with 1 ongoing IM	21 (10.99)	14 (7.61)
Subjects with ≥ 2 ongoing IM	160 (83.77)	156 (84.78)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 52 refer to those IMs with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX20-121-102

Table 1.1.4.2
Study VX20-121-102: Summary of Patients with Inhaled Medications during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
All subjects	202	196
Subjects with 0 IM	9 (4.46)	14 (7.14)
Subjects with 1 IM	19 (9.41)	12 (6.12)
Subjects with ≥ 2 IM	174 (86.14)	170 (86.73)
Subjects with 0 ongoing inhaled medications at baseline	9	16
Subjects with 0 IM	9 (100.00)	14 (87.50)
Subjects with 1 IM	0	0
Subjects with ≥ 2 IM	0	2 (12.50)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX20-121-102

Table 1.1.4.3
Study VX20-121-102: Summary of Patients with Ongoing Inhaled Medications for Mucolytics at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline, N1	202	196
Subjects with 0 ongoing IM	38 (18.81)	43 (21.94)
Subjects with 1 ongoing IM	56 (27.72)	58 (29.59)
Subjects with ≥ 2 ongoing IM	108 (53.47)	95 (48.47)
Week 52, N1	191	184
Subjects with 0 ongoing IM	41 (21.47)	40 (21.74)
Subjects with 1 ongoing IM	54 (28.27)	56 (30.43)
Subjects with ≥ 2 ongoing IM	96 (50.26)	88 (47.83)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 52 refer to those IMs with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX20-121-102

Table 1.1.4.4
Study VX20-121-102: Summary of Patients with Inhaled Medications for Mucolytics during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
All subjects	202	196
Subjects with 0 IM	36 (17.82)	40 (20.41)
Subjects with 1 IM	54 (26.73)	59 (30.10)
Subjects with ≥ 2 IM	112 (55.45)	97 (49.49)
Subjects with 0 ongoing inhaled medications at baseline	38	43
Subjects with 0 IM	36 (94.74)	40 (93.02)
Subjects with 1 IM	0	3 (6.98)
Subjects with ≥ 2 IM	2 (5.26)	0

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX20-121-102

Table 1.1.4.5
Study VX20-121-102: Summary of Patients with Ongoing Inhaled Medications for Obstructive Airway Disease at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline, N1	202	196
Subjects with 0 ongoing IM	25 (12.38)	24 (12.24)
Subjects with 1 ongoing IM	62 (30.69)	65 (33.16)
Subjects with ≥ 2 ongoing IM	115 (56.93)	107 (54.59)
Week 52, N1	191	184
Subjects with 0 ongoing IM	25 (13.09)	21 (11.41)
Subjects with 1 ongoing IM	56 (29.32)	60 (32.61)
Subjects with ≥ 2 ongoing IM	110 (57.59)	103 (55.98)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 52 refer to those IMs with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

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Table 1.1.4.6
Study VX20-121-102: Summary of Patients with Inhaled Medications for Obstructive Airway Disease during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
All subjects	202	196
Subjects with 0 IM	24 (11.88)	22 (11.22)
Subjects with 1 IM	57 (28.22)	58 (29.59)
Subjects with ≥ 2 IM	121 (59.90)	116 (59.18)
Subjects with 0 ongoing inhaled medications at baseline	25	24
Subjects with 0 IM	24 (96.00)	22 (91.67)
Subjects with 1 IM	0	1 (4.17)
Subjects with ≥ 2 IM	1 (4.00)	1 (4.17)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 1.1.5.1
Study VX20-121-102: Summary of Patients with Ongoing CF-related Medications at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline, N1	202	196
Subjects with 0 ongoing CF-related medications	2 (0.99)	2 (1.02)
Subjects with 1 ongoing CF-related medications	1 (0.50)	6 (3.06)
Subjects with 2 ongoing CF-related medications	6 (2.97)	8 (4.08)
Subjects with 3 ongoing CF-related medications	12 (5.94)	9 (4.59)
Subjects with 4 ongoing CF-related medications	22 (10.89)	19 (9.69)
Subjects with ≥5 ongoing CF-related medications	159 (78.71)	152 (77.55)
Week 52, N1	191	184
Subjects with 0 ongoing CF-related medications	1 (0.52)	3 (1.63)
Subjects with 1 ongoing CF-related medications	1 (0.52)	5 (2.72)
Subjects with 2 ongoing CF-related medications	4 (2.09)	7 (3.80)
Subjects with 3 ongoing CF-related medications	14 (7.33)	6 (3.26)
Subjects with 4 ongoing CF-related medications	19 (9.95)	17 (9.24)
Subjects with ≥5 ongoing CF-related medications	152 (79.58)	146 (79.35)

- CF-related medications: CF co-medications are defined as those medications with
o ATC level 2 names of "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES", "DIGESTIVES, INCL. ENZYMES", "ANTIBACTERIALS FOR SYSTEMIC USE", "DRUGS USED IN DIABETES", "BILE AND LIVER THERAPY", "GENERAL NUTRIENTS";
o or ATC level 3 names of "DRUGS FOR CONSTIPATION", "PROPULSIVES";
o or ATC level 4 names of "MUCOLYTICS".
In addition, the route of administration for "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES" and "MUCOLYTICS" requires to be "RESPIRATORY (INHALATION)" and the route for "ANTIBACTERIALS FOR SYSTEMIC USE" requires to be "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- The ongoing CF-related medications at baseline refer to those CF-related medications with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing CF-related medications at Week 52 refer to those CF-related medications with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

Table 1.1.6
Study VX20-121-102: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-102

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)	Total N = 31 n (%)
Subjects with any concomitant medications during the Treatment Period	11 (68.8)	11 (73.3)	22 (71.0)
RESPIRATORY SYSTEM	9 (56.3)	8 (53.3)	17 (54.8)
OTHER RESPIRATORY SYSTEM PRODUCTS	8 (50.0)	6 (40.0)	14 (45.2)
ELEXACAFTOR;IVACAFTOR;TEZACAFTOR	8 (50.0)	6 (40.0)	14 (45.2)
IVACAFTOR	3 (18.8)	4 (26.7)	7 (22.6)
NASAL PREPARATIONS	4 (25.0)	4 (26.7)	8 (25.8)
SODIUM CHLORIDE	3 (18.8)	1 (6.7)	4 (12.9)
DEXAMETHASONE	2 (12.5)	0	2 (6.5)
EPHEDRINE	1 (6.3)	0	1 (3.2)
EPINEPHRINE	0	1 (6.7)	1 (3.2)
MOMETASONE FUROATE	0	1 (6.7)	1 (3.2)
PREDNISOLONE	0	1 (6.7)	1 (3.2)
COUGH AND COLD PREPARATIONS	4 (25.0)	1 (6.7)	5 (16.1)
SODIUM CHLORIDE	3 (18.8)	1 (6.7)	4 (12.9)
DORNASE ALFA	1 (6.3)	0	1 (3.2)
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	2 (12.5)	2 (13.3)	4 (12.9)
DEXAMETHASONE	2 (12.5)	0	2 (6.5)
EPHEDRINE	1 (6.3)	0	1 (3.2)
EPINEPHRINE	0	1 (6.7)	1 (3.2)
MOMETASONE FUROATE	0	1 (6.7)	1 (3.2)
THROAT PREPARATIONS	4 (25.0)	0	4 (12.9)
IBUPROFEN	2 (12.5)	0	2 (6.5)
LIDOCAINE	1 (6.3)	0	1 (3.2)
LIDOCAINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
ANTIHISTAMINES FOR SYSTEMIC USE	2 (12.5)	1 (6.7)	3 (9.7)
CETIRIZINE HYDROCHLORIDE	0	1 (6.7)	1 (3.2)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 1.1.6
Study VX20-121-102: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-102

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)	Total N = 31 n (%)
DIPHENHYDRAMINE	1 (6.3)	0	1 (3.2)
DIPHENHYDRAMINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
ALIMENTARY TRACT AND METABOLISM	9 (56.3)	7 (46.7)	16 (51.6)
STOMATOLOGICAL PREPARATIONS	7 (43.8)	3 (20.0)	10 (32.3)
SODIUM CHLORIDE	3 (18.8)	1 (6.7)	4 (12.9)
DEXAMETHASONE	2 (12.5)	0	2 (6.5)
DOXYCYCLINE	1 (6.3)	0	1 (3.2)
EPINEPHRINE	0	1 (6.7)	1 (3.2)
LIDOCAINE	1 (6.3)	0	1 (3.2)
LIDOCAINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
MINOCYCLINE	1 (6.3)	0	1 (3.2)
NAPROXEN	1 (6.3)	0	1 (3.2)
PREDNISOLONE	0	1 (6.7)	1 (3.2)
ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	2 (12.5)	4 (26.7)	6 (19.4)
COLISTIMETHATE SODIUM	0	2 (13.3)	2 (6.5)
VANCOMYCIN	2 (12.5)	0	2 (6.5)
PREDNISOLONE	0	1 (6.7)	1 (3.2)
RIFAXIMIN	0	1 (6.7)	1 (3.2)
DRUGS FOR CONSTIPATION	5 (31.3)	1 (6.7)	6 (19.4)
SODIUM CHLORIDE	3 (18.8)	1 (6.7)	4 (12.9)
MACROGOL 3350;POTASSIUM CHLORIDE;SODIUM BICARBONATE;SODIUM CHLORIDE	2 (12.5)	0	2 (6.5)
DOCUSATE;SENNA ALEXANDRINA	1 (6.3)	0	1 (3.2)
MACROGOL 3350	1 (6.3)	0	1 (3.2)
POTASSIUM SORBATE;SORBITOL	1 (6.3)	0	1 (3.2)
MINERAL SUPPLEMENTS	3 (18.8)	3 (20.0)	6 (19.4)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 1.1.6
Study VX20-121-102: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-102

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)	Total N = 31 n (%)
SODIUM CHLORIDE	3 (18.8)	1 (6.7)	4 (12.9)
CALCIUM PHOSPHATE DIBASIC;FERROUS SUCCINATE;MAGNESIUM HYDROXIDE	0	1 (6.7)	1 (3.2)
POTASSIUM CHLORIDE	0	1 (6.7)	1 (3.2)
ANTIEMETICS AND ANTINAUSEANTS	5 (31.3)	0	5 (16.1)
ONDANSETRON	2 (12.5)	0	2 (6.5)
DIPHENHYDRAMINE	1 (6.3)	0	1 (3.2)
DIPHENHYDRAMINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
METOCLOPRAMIDE	1 (6.3)	0	1 (3.2)
DRUGS FOR ACID RELATED DISORDERS	4 (25.0)	1 (6.7)	5 (16.1)
PANTOPRAZOLE	2 (12.5)	0	2 (6.5)
ALUMINIUM HYDROXIDE;MAGNESIUM HYDROXIDE	1 (6.3)	0	1 (3.2)
ANTACIDS, OTHER COMBINATIONS	1 (6.3)	0	1 (3.2)
CALCIUM PHOSPHATE DIBASIC;FERROUS SUCCINATE;MAGNESIUM HYDROXIDE	0	1 (6.7)	1 (3.2)
MISOPROSTOL	1 (6.3)	0	1 (3.2)
BILE AND LIVER THERAPY	0	1 (6.7)	1 (3.2)
RIFAXIMIN	0	1 (6.7)	1 (3.2)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	1 (6.3)	0	1 (3.2)
METOCLOPRAMIDE	1 (6.3)	0	1 (3.2)
DERMATOLOGICALS	8 (50.0)	7 (46.7)	15 (48.4)
ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE	5 (31.3)	4 (26.7)	9 (29.0)
CIPROFLOXACIN	2 (12.5)	2 (13.3)	4 (12.9)
ACICLOVIR	1 (6.3)	0	1 (3.2)
CLARITHROMYCIN	0	1 (6.7)	1 (3.2)
DOXYCYCLINE	1 (6.3)	0	1 (3.2)
LEVOFLOXACIN	1 (6.3)	0	1 (3.2)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 1.1.6
Study VX20-121-102: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-102

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)	Total N = 31 n (%)
MINOCYCLINE	1 (6.3)	0	1 (3.2)
RIFAXIMIN	0	1 (6.7)	1 (3.2)
ANTI-ACNE PREPARATIONS	4 (25.0)	1 (6.7)	5 (16.1)
IBUPROFEN	2 (12.5)	0	2 (6.5)
AZITHROMYCIN	0	1 (6.7)	1 (3.2)
CLINDAMYCIN	1 (6.3)	0	1 (3.2)
DOXYCYCLINE	1 (6.3)	0	1 (3.2)
MINOCYCLINE	1 (6.3)	0	1 (3.2)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	4 (25.0)	1 (6.7)	5 (16.1)
CETIRIZINE HYDROCHLORIDE	0	1 (6.7)	1 (3.2)
DIPHENHYDRAMINE	1 (6.3)	0	1 (3.2)
DIPHENHYDRAMINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
LIDOCAINE	1 (6.3)	0	1 (3.2)
LIDOCAINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	2 (12.5)	2 (13.3)	4 (12.9)
DEXAMETHASONE	2 (12.5)	0	2 (6.5)
MOMETASONE FUROATE	0	1 (6.7)	1 (3.2)
PREDNISOLONE	0	1 (6.7)	1 (3.2)
MEDICATED DRESSINGS	3 (18.8)	1 (6.7)	4 (12.9)
SODIUM CHLORIDE	3 (18.8)	1 (6.7)	4 (12.9)
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS	3 (18.8)	1 (6.7)	4 (12.9)
SODIUM CHLORIDE	3 (18.8)	1 (6.7)	4 (12.9)
OTHER DERMATOLOGICAL PREPARATIONS	2 (12.5)	0	2 (6.5)
IBUPROFEN	2 (12.5)	0	2 (6.5)
ANTIINFECTIVES FOR SYSTEMIC USE	8 (50.0)	6 (40.0)	14 (45.2)
ANTIBACTERIALS FOR SYSTEMIC USE	8 (50.0)	6 (40.0)	14 (45.2)
CIPROFLOXACIN	2 (12.5)	2 (13.3)	4 (12.9)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 1.1.6
Study VX20-121-102: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)	Total N = 31 n (%)
TOBRAMYCIN	1 (6.3)	2 (13.3)	3 (9.7)
AMOXICILLIN;CLAVULANATE POTASSIUM	1 (6.3)	1 (6.7)	2 (6.5)
AMOXICILLIN;CLAVULANIC ACID	1 (6.3)	1 (6.7)	2 (6.5)
COLISTIMETHATE SODIUM	0	2 (13.3)	2 (6.5)
MEROPENEM	0	2 (13.3)	2 (6.5)
VANCOMYCIN	2 (12.5)	0	2 (6.5)
AZITHROMYCIN	0	1 (6.7)	1 (3.2)
CEFEPIME	1 (6.3)	0	1 (3.2)
CEFOTETAN	1 (6.3)	0	1 (3.2)
CEFTRIAXONE	1 (6.3)	0	1 (3.2)
CLARITHROMYCIN	0	1 (6.7)	1 (3.2)
CLINDAMYCIN	1 (6.3)	0	1 (3.2)
DOXYCYCLINE	1 (6.3)	0	1 (3.2)
LEVOFLOXACIN	1 (6.3)	0	1 (3.2)
LINEZOLID	0	1 (6.7)	1 (3.2)
MINOCYCLINE	1 (6.3)	0	1 (3.2)
PHENOXYMETHYLPENICILLIN	1 (6.3)	0	1 (3.2)
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 (6.3)	0	1 (3.2)
VACCINES	2 (12.5)	0	2 (6.5)
COVID-19 VACCINE	1 (6.3)	0	1 (3.2)
INFLUENZA VACCINE	1 (6.3)	0	1 (3.2)
MENINGOCOCCAL VACCINE B	1 (6.3)	0	1 (3.2)
MENINGOCOCCAL VACCINE CONJ	1 (6.3)	0	1 (3.2)
ANTIVIRALS FOR SYSTEMIC USE	1 (6.3)	0	1 (3.2)
ACICLOVIR	1 (6.3)	0	1 (3.2)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
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- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 1.1.6
Study VX20-121-102: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-102

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)	Total N = 31 n (%)
SENSORY ORGANS	8 (50.0)	6 (40.0)	14 (45.2)
OPHTHALMOLOGICALS	8 (50.0)	6 (40.0)	14 (45.2)
CIPROFLOXACIN	2 (12.5)	2 (13.3)	4 (12.9)
SODIUM CHLORIDE	3 (18.8)	1 (6.7)	4 (12.9)
TOBRAMYCIN	1 (6.3)	2 (13.3)	3 (9.7)
COLISTIMETHATE SODIUM	0	2 (13.3)	2 (6.5)
DEXAMETHASONE	2 (12.5)	0	2 (6.5)
VANCOMYCIN	2 (12.5)	0	2 (6.5)
ACICLOVIR	1 (6.3)	0	1 (3.2)
AZITHROMYCIN	0	1 (6.7)	1 (3.2)
BUPIVACAINE	1 (6.3)	0	1 (3.2)
CETIRIZINE HYDROCHLORIDE	0	1 (6.7)	1 (3.2)
EPHEDRINE	1 (6.3)	0	1 (3.2)
EPINEPHRINE	0	1 (6.7)	1 (3.2)
HEPARIN SODIUM	0	1 (6.7)	1 (3.2)
KETOROLAC TROMETHAMINE	1 (6.3)	0	1 (3.2)
LEVOFLOXACIN	1 (6.3)	0	1 (3.2)
LIDOCAINE	1 (6.3)	0	1 (3.2)
LIDOCAINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
NAPROXEN	1 (6.3)	0	1 (3.2)
POTASSIUM CHLORIDE	0	1 (6.7)	1 (3.2)
PREDNISOLONE	0	1 (6.7)	1 (3.2)
OTOLOGICALS	6 (37.5)	3 (20.0)	9 (29.0)
CIPROFLOXACIN	2 (12.5)	2 (13.3)	4 (12.9)
SODIUM CHLORIDE	3 (18.8)	1 (6.7)	4 (12.9)
DEXAMETHASONE	2 (12.5)	0	2 (6.5)
LEVOFLOXACIN	1 (6.3)	0	1 (3.2)
LIDOCAINE	1 (6.3)	0	1 (3.2)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 1.1.6
Study VX20-121-102: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-102

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)	Total N = 31 n (%)
LIDOCAINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
PREDNISOLONE	0	1 (6.7)	1 (3.2)
OPHTHALMOLOGICAL AND OTOLOGICAL PREPARATIONS	4 (25.0)	3 (20.0)	7 (22.6)
CIPROFLOXACIN	2 (12.5)	2 (13.3)	4 (12.9)
DEXAMETHASONE	2 (12.5)	0	2 (6.5)
LEVOFLOXACIN	1 (6.3)	0	1 (3.2)
PREDNISOLONE	0	1 (6.7)	1 (3.2)
NERVOUS SYSTEM	7 (43.8)	4 (26.7)	11 (35.5)
ANALGESICS	5 (31.3)	3 (20.0)	8 (25.8)
PARACETAMOL	2 (12.5)	2 (13.3)	4 (12.9)
MORPHINE	3 (18.8)	0	3 (9.7)
FENTANYL	1 (6.3)	0	1 (3.2)
FENTANYL CITRATE	1 (6.3)	0	1 (3.2)
HYDROCODONE;PARACETAMOL	1 (6.3)	0	1 (3.2)
HYDROMORPHONE	1 (6.3)	0	1 (3.2)
HYDROMORPHONE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
METAMIZOLE	1 (6.3)	0	1 (3.2)
OXYCODONE	1 (6.3)	0	1 (3.2)
TRAMADOL	0	1 (6.7)	1 (3.2)
PSYCHOLEPTICS	4 (25.0)	1 (6.7)	5 (16.1)
MELATONIN	1 (6.3)	1 (6.7)	2 (6.5)
MIDAZOLAM	2 (12.5)	0	2 (6.5)
ALPRAZOLAM	1 (6.3)	0	1 (3.2)
DIPHENHYDRAMINE	1 (6.3)	0	1 (3.2)
DIPHENHYDRAMINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
TEMAZEPAM	0	1 (6.7)	1 (3.2)
ANESTHETICS	4 (25.0)	0	4 (12.9)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
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- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 1.1.6
Study VX20-121-102: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
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- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-102

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)	Total N = 31 n (%)
BUPIVACAINE	1 (6.3)	0	1 (3.2)
FENTANYL	1 (6.3)	0	1 (3.2)
FENTANYL CITRATE	1 (6.3)	0	1 (3.2)
LIDOCAINE	1 (6.3)	0	1 (3.2)
LIDOCAINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
NITROUS OXIDE;OXYGEN	1 (6.3)	0	1 (3.2)
PROPOFOL	1 (6.3)	0	1 (3.2)
ANTI-PARKINSON DRUGS	2 (12.5)	0	2 (6.5)
DIPHENHYDRAMINE	1 (6.3)	0	1 (3.2)
DIPHENHYDRAMINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
ANTIEPILEPTICS	2 (12.5)	0	2 (6.5)
MIDAZOLAM	2 (12.5)	0	2 (6.5)
PSYCHOANALEPTICS	0	1 (6.7)	1 (3.2)
TRAZODONE	0	1 (6.7)	1 (3.2)
BLOOD AND BLOOD FORMING ORGANS	5 (31.3)	5 (33.3)	10 (32.3)
BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS	3 (18.8)	2 (13.3)	5 (16.1)
SODIUM CHLORIDE	3 (18.8)	1 (6.7)	4 (12.9)
CALCIUM CHLORIDE DIHYDRATE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	1 (6.3)	0	1 (3.2)
CALCIUM CHLORIDE;POTASSIUM CHLORIDE;SODIUM LACTATE	1 (6.3)	0	1 (3.2)
POTASSIUM CHLORIDE	0	1 (6.7)	1 (3.2)
ANTITHROMBOTIC AGENTS	1 (6.3)	2 (13.3)	3 (9.7)
ENOXAPARIN	1 (6.3)	1 (6.7)	2 (6.5)
HEPARIN SODIUM	0	1 (6.7)	1 (3.2)
ANTIANEMIC PREPARATIONS	0	1 (6.7)	1 (3.2)
CALCIUM PHOSPHATE DIBASIC;FERROUS SUCCINATE;MAGNESIUM HYDROXIDE	0	1 (6.7)	1 (3.2)

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- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 1.1.6
Study VX20-121-102: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-102

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)	Total N = 31 n (%)
ANTIHEMORRHAGICS	0	1 (6.7)	1 (3.2)
EPINEPHRINE	0	1 (6.7)	1 (3.2)
OTHER HEMATOLOGICAL AGENTS	1 (6.3)	0	1 (3.2)
DORNASE ALFA	1 (6.3)	0	1 (3.2)
GENITO URINARY SYSTEM AND SEX HORMONES	7 (43.8)	3 (20.0)	10 (32.3)
GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS	3 (18.8)	2 (13.3)	5 (16.1)
CIPROFLOXACIN	2 (12.5)	2 (13.3)	4 (12.9)
CLINDAMYCIN	1 (6.3)	0	1 (3.2)
OTHER GYNECOLOGICALS	3 (18.8)	0	3 (9.7)
IBUPROFEN	2 (12.5)	0	2 (6.5)
MISOPROSTOL	1 (6.3)	0	1 (3.2)
NAPROXEN	1 (6.3)	0	1 (3.2)
UROLOGICALS	2 (12.5)	1 (6.7)	3 (9.7)
CALCIUM PHOSPHATE DIBASIC;FERROUS SUCCINATE;MAGNESIUM HYDROXIDE	0	1 (6.7)	1 (3.2)
LIDOCAINE	1 (6.3)	0	1 (3.2)
LIDOCAINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	1 (6.3)	0	1 (3.2)
MIFEPRISTONE	1 (6.3)	0	1 (3.2)
CARDIOVASCULAR SYSTEM	5 (31.3)	3 (20.0)	8 (25.8)
CARDIAC THERAPY	4 (25.0)	1 (6.7)	5 (16.1)
IBUPROFEN	2 (12.5)	0	2 (6.5)
EPHEDRINE	1 (6.3)	0	1 (3.2)
EPINEPHRINE	0	1 (6.7)	1 (3.2)
LIDOCAINE	1 (6.3)	0	1 (3.2)
LIDOCAINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
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- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 1.1.6
Study VX20-121-102: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-102

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)	Total N = 31 n (%)
VASOPROTECTIVES	3 (18.8)	2 (13.3)	5 (16.1)
DEXAMETHASONE	2 (12.5)	0	2 (6.5)
HEPARIN SODIUM	0	1 (6.7)	1 (3.2)
LIDOCAINE	1 (6.3)	0	1 (3.2)
LIDOCAINE HYDROCHLORIDE	1 (6.3)	0	1 (3.2)
PREDNISOLONE	0	1 (6.7)	1 (3.2)
VARIOUS	3 (18.8)	3 (20.0)	6 (19.4)
HOMEOPATHIC PREPARATION	3 (18.8)	3 (20.0)	6 (19.4)
SODIUM CHLORIDE	3 (18.8)	1 (6.7)	4 (12.9)
EPINEPHRINE	0	1 (6.7)	1 (3.2)
POTASSIUM CHLORIDE	0	1 (6.7)	1 (3.2)
ALL OTHER NON-THERAPEUTIC PRODUCTS	3 (18.8)	1 (6.7)	4 (12.9)
SODIUM CHLORIDE	3 (18.8)	1 (6.7)	4 (12.9)
CONTRAST MEDIA	2 (12.5)	0	2 (6.5)
IOPAMIDOL	2 (12.5)	0	2 (6.5)
ALL OTHER THERAPEUTIC PRODUCTS	1 (6.3)	0	1 (3.2)
SUGAMMADEX	1 (6.3)	0	1 (3.2)
MUSCULO-SKELETAL SYSTEM	4 (25.0)	0	4 (12.9)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	3 (18.8)	0	3 (9.7)
IBUPROFEN	2 (12.5)	0	2 (6.5)
KETOROLAC TROMETHAMINE	1 (6.3)	0	1 (3.2)
NAPROXEN	1 (6.3)	0	1 (3.2)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	3 (18.8)	0	3 (9.7)
IBUPROFEN	2 (12.5)	0	2 (6.5)
KETOROLAC TROMETHAMINE	1 (6.3)	0	1 (3.2)
NAPROXEN	1 (6.3)	0	1 (3.2)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 1.1.6
Study VX20-121-102: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)	Total N = 31 n (%)
MUSCLE RELAXANTS	1 (6.3)	0	1 (3.2)
ROCURONIUM	1 (6.3)	0	1 (3.2)
SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS	2 (12.5)	1 (6.7)	3 (9.7)
CORTICOSTEROIDS FOR SYSTEMIC USE	2 (12.5)	1 (6.7)	3 (9.7)
DEXAMETHASONE	2 (12.5)	0	2 (6.5)
PREDNISOLONE	0	1 (6.7)	1 (3.2)
ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	0	1 (6.7)	1 (3.2)
ANTINEOPLASTIC AGENTS	0	1 (6.7)	1 (3.2)
PEMBROLIZUMAB	0	1 (6.7)	1 (3.2)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 1.2.1.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52
Full Analysis Set

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	201	193
Mean (SD)	67.22 (14.64)	67.03 (15.34)
Week 52		
n	184	177
Mean (SD)	67.04 (14.88)	67.05 (15.89)
Absolute Change at Week 52		
n	184	175
Mean (SD)	0.28 (5.31)	0.24 (5.51)
Absolute Change through Week 52 (MMRM)		
n	196	189
LS mean (SE)	0.36 (0.31)	0.48 (0.32)
95% CI of LS mean	(-0.26, 0.97)	(-0.15, 1.11)
P-value within Treatment	0.2508	0.1361
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-0.76, 1.00)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7918
Hedges' G (SE)		0.03 (0.10)
Hedges' 95% CI		(-0.17, 0.23)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Hedges' P-value		0.7917

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52
Full Analysis Set

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	202	195
Mean (SD)	23.03 (3.85)	22.71 (3.40)
Week 52		
n	189	183
Mean (SD)	23.19 (3.83)	23.05 (3.28)
Absolute Change at Week 52		
n	189	183
Mean (SD)	0.08 (1.39)	0.31 (1.24)
Absolute Change at Week 52 (MMRM)		
n	187	179
LS mean (SE)	0.08 (0.10)	0.30 (0.10)
95% CI of LS mean	(-0.11, 0.27)	(0.11, 0.49)
P-value within Treatment	0.4088	0.0023
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-0.05, 0.49)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1070
Hedges' G (SE)		0.17 (0.10)
Hedges' 95% CI		(-0.04, 0.37)
Hedges' P-value		0.1076

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52
for Subjects ≤20 Years at Baseline
Full Analysis Set

- N is the number of subjects in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 40	VNZ/TEZ/D-IVA N = 32
Baseline		
n	40	32
Mean (SD)	-0.14 (0.88)	-0.36 (1.09)
Week 52		
n	32	28
Mean (SD)	-0.14 (0.82)	-0.12 (0.95)
Absolute Change at Week 52		
n	32	28
Mean (SD)	-0.02 (0.53)	0.28 (0.48)
Absolute Change at Week 52 (MMRM)		
n	32	27
LS mean (SE)	-0.09 (0.09)	0.25 (0.10)
95% CI of LS mean	(-0.27, 0.09)	(0.05, 0.45)
P-value within Treatment	0.3266	0.0170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (0.07, 0.61)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0156
Hedges' G (SE)		0.64 (0.26)
Hedges' 95% CI		(0.11, 1.17)

- N is the number of subjects in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52
for Subjects ≤20 Years at Baseline
Full Analysis Set

	ELX/TEZ/IVA N = 40	VNZ/TEZ/D-IVA N = 32
Hedges' P-value		0.0181

- N is the number of subjects in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.4.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52
Full Analysis Set

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	201	194
Mean (SD)	54.27 (18.22)	53.55 (17.05)
Week 52		
n	186	171
Mean (SD)	53.43 (18.83)	46.54 (20.80)
Absolute Change at Week 52		
n	185	170
Mean (SD)	-0.97 (12.00)	-8.24 (12.61)
Absolute Change through Week 52 (MMRM)		
n	195	188
LS mean (SE)	0.53 (0.67)	-7.50 (0.69)
95% CI of LS mean	(-0.79, 1.84)	(-8.85, -6.15)
P-value within Treatment	0.4323	<0.0001
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.03 (-9.91, -6.14)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.86 (0.11)
Hedges' 95% CI		(-1.06, -0.65)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.1.4.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Hedges' P-value		<0.0001

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.1.4.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Non-missing value at Week 52, N1	186	171
Number of subjects with missing value at Week 52	16	25
SwCl <60 mmol/L at Week 52, n (%)	117 (57.92)	132 (67.35)
Relative Risk (RR) (95% CI)		1.1540 (1.0012, 1.3301)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0481*

- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- N/C: model does not converge.

Table 1.2.1.4.3
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Non-missing value at Week 52, N1	186	171
Number of subjects with missing value at Week 52	16	25
SwCl <30 mmol/L at Week 52, n (%)	25 (12.38)	41 (20.92)
Relative Risk (RR) (95% CI)		1.9597 (1.3197, 2.9101)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0009*

- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- N/C: model does not converge.

Table 1.2.1.5
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52
Full Analysis Set

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	202	195
Mean (SD)	64.54 (13.75)	65.08 (13.32)
Week 52		
n	189	183
Mean (SD)	65.40 (13.41)	66.52 (12.76)
Absolute Change at Week 52		
n	189	183
Mean (SD)	0.51 (4.11)	1.03 (3.72)
Absolute Change at Week 52 (MMRM)		
n	187	179
LS mean (SE)	0.50 (0.28)	1.01 (0.29)
95% CI of LS mean	(-0.05, 1.06)	(0.44, 1.57)
P-value within Treatment	0.0737	0.0005
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-0.29, 1.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2125
Hedges' G (SE)		0.13 (0.10)
Hedges' 95% CI		(-0.08, 0.34)
Hedges' P-value		0.2130

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.1.6.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	60 (29.7)	50 (25.5)
Subjects Censored	142 (70.3)	146 (74.5)
Event-free time (weeks)		
75 percent subjects	35.1429	42.8571
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9802 (0.9481, 0.9925)	0.9898 (0.9598, 0.9974)
4 Weeks	0.9653 (0.9285, 0.9833)	0.9796 (0.9465, 0.9923)
8 Weeks	0.9353 (0.8911, 0.9619)	0.9386 (0.8945, 0.9647)
12 Weeks	0.9001 (0.8494, 0.9344)	0.9130 (0.8638, 0.9450)
16 Weeks	0.8697 (0.8146, 0.9094)	0.8822 (0.8280, 0.9201)
24 Weeks	0.8192 (0.7583, 0.8661)	0.8199 (0.7583, 0.8672)
36 Weeks	0.7431 (0.6762, 0.7982)	0.7780 (0.7126, 0.8303)
52 Weeks	0.6955 (0.6258, 0.7547)	0.7408 (0.6727, 0.7968)
Hazard Ratio (95% CI)*	-	0.8413 (0.5777, 1.2253)
Two-sided P-value, superiority*	-	0.3677

-CI: Confidence interval.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
-*Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years).

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.1.7.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	17 (8.4)	8 (4.1)
Subjects Censored	185 (91.6)	188 (95.9)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9901 (0.9610, 0.9975)	0.9949 (0.9643, 0.9993)
4 Weeks	0.9901 (0.9610, 0.9975)	0.9949 (0.9643, 0.9993)
8 Weeks	0.9851 (0.9545, 0.9952)	0.9898 (0.9598, 0.9974)
12 Weeks	0.9750 (0.9411, 0.9895)	0.9847 (0.9532, 0.9950)
16 Weeks	0.9649 (0.9279, 0.9831)	0.9847 (0.9532, 0.9950)
24 Weeks	0.9599 (0.9214, 0.9797)	0.9743 (0.9394, 0.9892)
36 Weeks	0.9294 (0.8838, 0.9576)	0.9638 (0.9255, 0.9826)
52 Weeks	0.9139 (0.8652, 0.9456)	0.9584 (0.9186, 0.9790)
Hazard Ratio (95% CI)*	-	0.4863 (0.2098, 1.1271)
Two-sided P-value, superiority*	-	0.0928

-CI: Confidence interval.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-Subjects without any protocol-defined pulmonary exacerbation requiring hospitalization during the PEx analysis period were censored at the PEx analysis period end date.
-*Cox regression: time is the time-to-first pulmonary exacerbation requiring hospitalization or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years).

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.1.8.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	26 (12.9)	10 (5.1)
Subjects Censored	176 (87.1)	186 (94.9)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9901 (0.9610, 0.9975)	0.9949 (0.9643, 0.9993)
4 Weeks	0.9901 (0.9610, 0.9975)	0.9949 (0.9643, 0.9993)
8 Weeks	0.9851 (0.9545, 0.9952)	0.9898 (0.9598, 0.9974)
12 Weeks	0.9599 (0.9215, 0.9798)	0.9795 (0.9464, 0.9923)
16 Weeks	0.9498 (0.9088, 0.9727)	0.9795 (0.9464, 0.9923)
24 Weeks	0.9347 (0.8902, 0.9615)	0.9692 (0.9327, 0.9860)
36 Weeks	0.8840 (0.8306, 0.9214)	0.9534 (0.9123, 0.9755)
52 Weeks	0.8684 (0.8127, 0.9084)	0.9481 (0.9056, 0.9717)
Hazard Ratio (95% CI)*	-	0.3854 (0.1857, 0.7997)
Two-sided P-value, superiority*	-	0.0105

-CI: Confidence interval.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-Subjects without any protocol-defined pulmonary exacerbation requiring IV Antibiotics during the PEx analysis period were censored at the PEx analysis period end date.
-*Cox regression: time is the time-to-first pulmonary exacerbation requiring IV Antibiotics or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years).

Table 1.2.1.9.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	197	192
Mean (SD)	82.94 (15.68)	85.81 (14.75)
Week 8 (MMRM)		
n	196	188
LS mean (SE)	80.97 (1.21)	84.94 (1.23)
95% CI of LS mean	(78.59, 83.35)	(82.52, 87.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.97 (0.58, 7.37)
Absolute Change at Week 8 (MMRM)		
n	192	186
LS mean (SE)	-2.15 (1.21)	-0.82 (1.23)
95% CI of LS mean	(-4.54, 0.24)	(-3.24, 1.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.33 (-2.07, 4.74)
Week 16 (MMRM)		
n	196	189
LS mean (SE)	80.63 (1.22)	86.17 (1.25)
95% CI of LS mean	(78.22, 83.04)	(83.71, 88.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.54 (2.10, 8.98)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 16 (MMRM)		
n	192	186
LS mean (SE)	-2.18 (1.19)	0.79 (1.21)
95% CI of LS mean	(-4.53, 0.17)	(-1.60, 3.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.97 (-0.38, 6.32)
Week 24 (MMRM)		
n	196	187
LS mean (SE)	81.76 (1.22)	85.95 (1.25)
95% CI of LS mean	(79.36, 84.16)	(83.49, 88.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.19 (0.76, 7.63)
Absolute Change at Week 24 (MMRM)		
n	192	184
LS mean (SE)	-1.24 (1.24)	0.31 (1.26)
95% CI of LS mean	(-3.67, 1.20)	(-2.18, 2.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-1.93, 5.03)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 52		
n	192	184
Mean (SD)	81.84 (16.67)	87.12 (13.41)
Absolute Change at Week 52		
n	188	180
Mean (SD)	-1.23 (14.59)	1.51 (14.73)
Week 52 (MMRM)		
n	190	180
LS mean (SE)	81.75 (1.07)	87.13 (1.10)
95% CI of LS mean	(79.64, 83.86)	(84.97, 89.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.39 (2.37, 8.41)
Absolute Change at Week 52 (MMRM)		
n	186	177
LS mean (SE)	-1.36 (1.08)	1.33 (1.10)
95% CI of LS mean	(-3.49, 0.76)	(-0.85, 3.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.69 (-0.35, 5.73)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change through Week 52 (MMRM)		
n	192	186
LS mean (SE)	-1.60 (0.95)	0.81 (0.97)
95% CI of LS mean	(-3.47, 0.28)	(-1.10, 2.72)
P-value within Treatment	0.0954	0.4072
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.40 (-0.28, 5.08)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0788
Hedges' G (SE)		0.18 (0.10)
Hedges' 95% CI		(-0.02, 0.38)
Hedges' P-value		0.0793

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.1.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	197 (97.52)	192 (97.96)
Week 8	198 (98.02)	193 (98.47)
Absolute Change at Week 8	194 (96.04)	190 (96.94)
Week 16	198 (98.02)	194 (98.98)
Absolute Change at Week 16	194 (96.04)	190 (96.94)
Week 24	198 (98.02)	192 (97.96)
Absolute Change at Week 24	194 (96.04)	188 (95.92)
Week 52	192 (95.05)	184 (93.88)
Absolute Change at Week 52	188 (93.07)	180 (91.84)
Through Week 52	198 (98.02)	194 (98.98)
Absolute Change through Week 52	194 (96.04)	190 (96.94)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.1.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	197 (97.52)	192 (97.96)
Week 8	199 (98.51)	193 (98.47)
Absolute Change at Week 8	195 (96.53)	190 (96.94)
Week 16	198 (98.02)	194 (98.98)
Absolute Change at Week 16	194 (96.04)	190 (96.94)
Week 24	198 (98.02)	193 (98.47)
Absolute Change at Week 24	194 (96.04)	189 (96.43)
Week 52	193 (95.54)	184 (93.88)
Absolute Change at Week 52	189 (93.56)	180 (91.84)
Through Week 52	198 (98.02)	194 (98.98)
Absolute Change through Week 52	194 (96.04)	190 (96.94)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.1.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	197 (97.52)	191 (97.45)
Week 8	198 (98.02)	193 (98.47)
Absolute Change at Week 8	194 (96.04)	189 (96.43)
Week 16	198 (98.02)	194 (98.98)
Absolute Change at Week 16	194 (96.04)	189 (96.43)
Week 24	198 (98.02)	191 (97.45)
Absolute Change at Week 24	194 (96.04)	187 (95.41)
Week 52	192 (95.05)	184 (93.88)
Absolute Change at Week 52	188 (93.07)	179 (91.33)
Through Week 52	198 (98.02)	194 (98.98)
Absolute Change through Week 52	194 (96.04)	189 (96.43)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.1.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	197 (97.52)	192 (97.96)
Week 8	199 (98.51)	193 (98.47)
Absolute Change at Week 8	195 (96.53)	190 (96.94)
Week 16	198 (98.02)	194 (98.98)
Absolute Change at Week 16	194 (96.04)	190 (96.94)
Week 24	198 (98.02)	193 (98.47)
Absolute Change at Week 24	194 (96.04)	189 (96.43)
Week 52	193 (95.54)	184 (93.88)
Absolute Change at Week 52	189 (93.56)	180 (91.84)
Through Week 52	198 (98.02)	194 (98.98)
Absolute Change through Week 52	194 (96.04)	190 (96.94)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.1.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	197 (97.52)	192 (97.96)
Week 8	199 (98.51)	193 (98.47)
Absolute Change at Week 8	195 (96.53)	190 (96.94)
Week 16	198 (98.02)	194 (98.98)
Absolute Change at Week 16	194 (96.04)	190 (96.94)
Week 24	198 (98.02)	193 (98.47)
Absolute Change at Week 24	194 (96.04)	189 (96.43)
Week 52	193 (95.54)	184 (93.88)
Absolute Change at Week 52	189 (93.56)	180 (91.84)
Through Week 52	198 (98.02)	194 (98.98)
Absolute Change through Week 52	194 (96.04)	190 (96.94)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.1.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	197 (97.52)	192 (97.96)
Week 8	199 (98.51)	193 (98.47)
Absolute Change at Week 8	195 (96.53)	190 (96.94)
Week 16	198 (98.02)	194 (98.98)
Absolute Change at Week 16	194 (96.04)	190 (96.94)
Week 24	198 (98.02)	193 (98.47)
Absolute Change at Week 24	194 (96.04)	189 (96.43)
Week 52	193 (95.54)	184 (93.88)
Absolute Change at Week 52	189 (93.56)	180 (91.84)
Through Week 52	198 (98.02)	194 (98.98)
Absolute Change through Week 52	194 (96.04)	190 (96.94)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.1.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	197 (97.52)	192 (97.96)
Week 8	199 (98.51)	193 (98.47)
Absolute Change at Week 8	195 (96.53)	190 (96.94)
Week 16	198 (98.02)	194 (98.98)
Absolute Change at Week 16	194 (96.04)	190 (96.94)
Week 24	198 (98.02)	193 (98.47)
Absolute Change at Week 24	194 (96.04)	189 (96.43)
Week 52	193 (95.54)	184 (93.88)
Absolute Change at Week 52	189 (93.56)	180 (91.84)
Through Week 52	198 (98.02)	194 (98.98)
Absolute Change through Week 52	194 (96.04)	190 (96.94)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.1.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Baseline	197 (97.52)	192 (97.96)
Week 8	198 (98.02)	193 (98.47)
Absolute Change at Week 8	194 (96.04)	190 (96.94)
Week 16	198 (98.02)	194 (98.98)
Absolute Change at Week 16	194 (96.04)	190 (96.94)
Week 24	198 (98.02)	193 (98.47)
Absolute Change at Week 24	194 (96.04)	189 (96.43)
Week 52	193 (95.54)	184 (93.88)
Absolute Change at Week 52	189 (93.56)	180 (91.84)
Through Week 52	198 (98.02)	194 (98.98)
Absolute Change through Week 52	194 (96.04)	190 (96.94)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.1.2
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 192 n (%)	VNZ/TEZ/D-IVA N = 190 n (%)
Baseline	189 (98.44)	187 (98.42)
Week 8	191 (99.48)	188 (98.95)
Absolute Change at Week 8	188 (97.92)	185 (97.37)
Week 16	189 (98.44)	189 (99.47)
Absolute Change at Week 16	186 (96.88)	186 (97.89)
Week 24	189 (98.44)	188 (98.95)
Absolute Change at Week 24	186 (96.88)	185 (97.37)
Week 52	184 (95.83)	179 (94.21)
Absolute Change at Week 52	181 (94.27)	176 (92.63)
Through Week 52	189 (98.44)	189 (99.47)
Absolute Change through Week 52	186 (96.88)	186 (97.89)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.1.2
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 192 n (%)	VNZ/TEZ/D-IVA N = 190 n (%)
Baseline	189 (98.44)	186 (97.89)
Week 8	190 (98.96)	188 (98.95)
Absolute Change at Week 8	187 (97.40)	184 (96.84)
Week 16	189 (98.44)	189 (99.47)
Absolute Change at Week 16	186 (96.88)	185 (97.37)
Week 24	189 (98.44)	187 (98.42)
Absolute Change at Week 24	186 (96.88)	183 (96.32)
Week 52	183 (95.31)	179 (94.21)
Absolute Change at Week 52	180 (93.75)	175 (92.11)
Through Week 52	189 (98.44)	189 (99.47)
Absolute Change through Week 52	186 (96.88)	185 (97.37)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.1.2
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 192 n (%)	VNZ/TEZ/D-IVA N = 190 n (%)
Baseline	189 (98.44)	187 (98.42)
Week 8	191 (99.48)	188 (98.95)
Absolute Change at Week 8	188 (97.92)	185 (97.37)
Week 16	189 (98.44)	189 (99.47)
Absolute Change at Week 16	186 (96.88)	186 (97.89)
Week 24	189 (98.44)	188 (98.95)
Absolute Change at Week 24	186 (96.88)	185 (97.37)
Week 52	184 (95.83)	179 (94.21)
Absolute Change at Week 52	181 (94.27)	176 (92.63)
Through Week 52	189 (98.44)	189 (99.47)
Absolute Change through Week 52	186 (96.88)	186 (97.89)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.1.2
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 192 n (%)	VNZ/TEZ/D-IVA N = 190 n (%)
Baseline	189 (98.44)	187 (98.42)
Week 8	190 (98.96)	188 (98.95)
Absolute Change at Week 8	187 (97.40)	185 (97.37)
Week 16	189 (98.44)	189 (99.47)
Absolute Change at Week 16	186 (96.88)	186 (97.89)
Week 24	189 (98.44)	187 (98.42)
Absolute Change at Week 24	186 (96.88)	184 (96.84)
Week 52	183 (95.31)	179 (94.21)
Absolute Change at Week 52	180 (93.75)	176 (92.63)
Through Week 52	189 (98.44)	189 (99.47)
Absolute Change through Week 52	186 (96.88)	186 (97.89)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Baseline		
n	8	5
Mean (SD)	91.53 (11.47)	93.33 (6.67)
Week 8 (MMRM)		
n	8	5
LS mean (SE)	95.14 (5.09)	93.06 (6.37)
95% CI of LS mean	(83.75, 106.53)	(78.87, 107.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.08 (-20.60, 16.43)
Absolute Change at Week 8 (MMRM)		
n	7	5
LS mean (SE)	4.09 (3.88)	0.11 (4.76)
95% CI of LS mean	(-5.10, 13.28)	(-11.31, 11.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.98 (-18.87, 10.91)
Week 16 (MMRM)		
n	9	5
LS mean (SE)	89.16 (4.61)	90.75 (6.39)
95% CI of LS mean	(79.10, 99.23)	(76.91, 104.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.59 (-15.90, 19.07)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	8	4
LS mean (SE)	-3.12 (5.47)	3.15 (7.99)
95% CI of LS mean	(-15.31, 9.07)	(-14.57, 20.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.28 (-15.45, 28.00)
Week 24 (MMRM)		
n	9	5
LS mean (SE)	93.48 (3.18)	94.04 (4.56)
95% CI of LS mean	(86.52, 100.45)	(84.09, 103.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-12.21, 13.32)
Absolute Change at Week 24 (MMRM)		
n	8	4
LS mean (SE)	1.74 (4.33)	1.86 (6.41)
95% CI of LS mean	(-8.24, 11.72)	(-12.74, 16.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-17.90, 18.15)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Week 52		
n	9	5
Mean (SD)	90.12 (11.38)	97.78 (4.97)
Absolute Change at Week 52		
n	8	4
Mean (SD)	-2.64 (10.42)	8.33 (6.38)
Week 52 (MMRM)		
n	9	5
LS mean (SE)	91.02 (3.66)	96.85 (4.92)
95% CI of LS mean	(82.91, 99.12)	(86.14, 107.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.83 (-8.06, 19.73)
Absolute Change at Week 52 (MMRM)		
n	8	4
LS mean (SE)	-1.04 (3.07)	4.83 (4.62)
95% CI of LS mean	(-7.94, 5.87)	(-5.45, 15.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.87 (-6.93, 18.66)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	8	4
LS mean (SE)	-0.81 (3.79)	3.28 (5.66)
95% CI of LS mean	(-9.34, 7.73)	(-9.39, 15.95)
P-value within Treatment	0.8358	0.5752
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.09 (-11.54, 19.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5721
Hedges' G (SE)		0.35 (0.57)
Hedges' 95% CI		(-0.92, 1.62)
Hedges' P-value		0.5566

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.2.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers
Domain: Respiration

	ELX/TEZ/IVA N = 10 n (%)	VNZ/TEZ/D-IVA N = 6 n (%)
Baseline	8 (80.00)	5 (83.33)
Week 8	8 (80.00)	5 (83.33)
Absolute Change at Week 8	7 (70.00)	5 (83.33)
Week 16	9 (90.00)	5 (83.33)
Absolute Change at Week 16	8 (80.00)	4 (66.67)
Week 24	9 (90.00)	5 (83.33)
Absolute Change at Week 24	8 (80.00)	4 (66.67)
Week 52	9 (90.00)	5 (83.33)
Absolute Change at Week 52	8 (80.00)	4 (66.67)
Through Week 52	9 (90.00)	5 (83.33)
Absolute Change through Week 52	8 (80.00)	4 (66.67)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.2.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers
Domain: Body

	ELX/TEZ/IVA N = 10 n (%)	VNZ/TEZ/D-IVA N = 6 n (%)
Baseline	8 (80.00)	5 (83.33)
Week 8	8 (80.00)	5 (83.33)
Absolute Change at Week 8	7 (70.00)	5 (83.33)
Week 16	9 (90.00)	5 (83.33)
Absolute Change at Week 16	8 (80.00)	4 (66.67)
Week 24	9 (90.00)	5 (83.33)
Absolute Change at Week 24	8 (80.00)	4 (66.67)
Week 52	9 (90.00)	5 (83.33)
Absolute Change at Week 52	8 (80.00)	4 (66.67)
Through Week 52	9 (90.00)	5 (83.33)
Absolute Change through Week 52	8 (80.00)	4 (66.67)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.2.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers
Domain: Digestion

	ELX/TEZ/IVA N = 10 n (%)	VNZ/TEZ/D-IVA N = 6 n (%)
Baseline	8 (80.00)	5 (83.33)
Week 8	8 (80.00)	5 (83.33)
Absolute Change at Week 8	7 (70.00)	5 (83.33)
Week 16	9 (90.00)	5 (83.33)
Absolute Change at Week 16	8 (80.00)	4 (66.67)
Week 24	9 (90.00)	5 (83.33)
Absolute Change at Week 24	8 (80.00)	4 (66.67)
Week 52	9 (90.00)	5 (83.33)
Absolute Change at Week 52	8 (80.00)	4 (66.67)
Through Week 52	9 (90.00)	5 (83.33)
Absolute Change through Week 52	8 (80.00)	4 (66.67)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.2.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers
Domain: Eat

	ELX/TEZ/IVA N = 10 n (%)	VNZ/TEZ/D-IVA N = 6 n (%)
Baseline	8 (80.00)	5 (83.33)
Week 8	8 (80.00)	5 (83.33)
Absolute Change at Week 8	7 (70.00)	5 (83.33)
Week 16	9 (90.00)	5 (83.33)
Absolute Change at Week 16	8 (80.00)	4 (66.67)
Week 24	9 (90.00)	5 (83.33)
Absolute Change at Week 24	8 (80.00)	4 (66.67)
Week 52	9 (90.00)	5 (83.33)
Absolute Change at Week 52	8 (80.00)	4 (66.67)
Through Week 52	9 (90.00)	5 (83.33)
Absolute Change through Week 52	8 (80.00)	4 (66.67)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.2.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers
Domain: Emotion

	ELX/TEZ/IVA N = 10 n (%)	VNZ/TEZ/D-IVA N = 6 n (%)
Baseline	8 (80.00)	5 (83.33)
Week 8	8 (80.00)	5 (83.33)
Absolute Change at Week 8	7 (70.00)	5 (83.33)
Week 16	9 (90.00)	5 (83.33)
Absolute Change at Week 16	8 (80.00)	4 (66.67)
Week 24	9 (90.00)	5 (83.33)
Absolute Change at Week 24	8 (80.00)	4 (66.67)
Week 52	9 (90.00)	5 (83.33)
Absolute Change at Week 52	8 (80.00)	4 (66.67)
Through Week 52	9 (90.00)	5 (83.33)
Absolute Change through Week 52	8 (80.00)	4 (66.67)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.2.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers
Domain: Health Perceptions

	ELX/TEZ/IVA N = 10 n (%)	VNZ/TEZ/D-IVA N = 6 n (%)
Baseline	8 (80.00)	5 (83.33)
Week 8	8 (80.00)	5 (83.33)
Absolute Change at Week 8	7 (70.00)	5 (83.33)
Week 16	9 (90.00)	5 (83.33)
Absolute Change at Week 16	8 (80.00)	4 (66.67)
Week 24	9 (90.00)	5 (83.33)
Absolute Change at Week 24	8 (80.00)	4 (66.67)
Week 52	9 (90.00)	5 (83.33)
Absolute Change at Week 52	8 (80.00)	4 (66.67)
Through Week 52	9 (90.00)	5 (83.33)
Absolute Change through Week 52	8 (80.00)	4 (66.67)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.2.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers
Domain: Physical

	ELX/TEZ/IVA N = 10 n (%)	VNZ/TEZ/D-IVA N = 6 n (%)
Baseline	8 (80.00)	5 (83.33)
Week 8	8 (80.00)	5 (83.33)
Absolute Change at Week 8	7 (70.00)	5 (83.33)
Week 16	9 (90.00)	5 (83.33)
Absolute Change at Week 16	8 (80.00)	4 (66.67)
Week 24	9 (90.00)	5 (83.33)
Absolute Change at Week 24	8 (80.00)	4 (66.67)
Week 52	9 (90.00)	5 (83.33)
Absolute Change at Week 52	8 (80.00)	4 (66.67)
Through Week 52	9 (90.00)	5 (83.33)
Absolute Change through Week 52	8 (80.00)	4 (66.67)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.2.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers
Domain: School

	ELX/TEZ/IVA N = 10 n (%)	VNZ/TEZ/D-IVA N = 6 n (%)
Baseline	8 (80.00)	5 (83.33)
Week 8	8 (80.00)	5 (83.33)
Absolute Change at Week 8	7 (70.00)	5 (83.33)
Week 16	9 (90.00)	5 (83.33)
Absolute Change at Week 16	8 (80.00)	4 (66.67)
Week 24	9 (90.00)	5 (83.33)
Absolute Change at Week 24	8 (80.00)	4 (66.67)
Week 52	9 (90.00)	5 (83.33)
Absolute Change at Week 52	8 (80.00)	4 (66.67)
Through Week 52	9 (90.00)	5 (83.33)
Absolute Change through Week 52	8 (80.00)	4 (66.67)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.2.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers
Domain: Treatment Burden

	ELX/TEZ/IVA N = 10 n (%)	VNZ/TEZ/D-IVA N = 6 n (%)
Baseline	8 (80.00)	5 (83.33)
Week 8	8 (80.00)	5 (83.33)
Absolute Change at Week 8	7 (70.00)	5 (83.33)
Week 16	9 (90.00)	5 (83.33)
Absolute Change at Week 16	8 (80.00)	4 (66.67)
Week 24	9 (90.00)	5 (83.33)
Absolute Change at Week 24	8 (80.00)	4 (66.67)
Week 52	9 (90.00)	5 (83.33)
Absolute Change at Week 52	8 (80.00)	4 (66.67)
Through Week 52	9 (90.00)	5 (83.33)
Absolute Change through Week 52	8 (80.00)	4 (66.67)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.2.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers
Domain: Vitality

	ELX/TEZ/IVA N = 10 n (%)	VNZ/TEZ/D-IVA N = 6 n (%)
Baseline	8 (80.00)	5 (83.33)
Week 8	8 (80.00)	5 (83.33)
Absolute Change at Week 8	7 (70.00)	5 (83.33)
Week 16	9 (90.00)	5 (83.33)
Absolute Change at Week 16	8 (80.00)	4 (66.67)
Week 24	9 (90.00)	5 (83.33)
Absolute Change at Week 24	8 (80.00)	4 (66.67)
Week 52	9 (90.00)	5 (83.33)
Absolute Change at Week 52	8 (80.00)	4 (66.67)
Through Week 52	9 (90.00)	5 (83.33)
Absolute Change through Week 52	8 (80.00)	4 (66.67)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.2.1
Study VX21-121-102: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers
Domain: Weight

	ELX/TEZ/IVA N = 10 n (%)	VNZ/TEZ/D-IVA N = 6 n (%)
Baseline	8 (80.00)	5 (83.33)
Week 8	8 (80.00)	4 (66.67)
Absolute Change at Week 8	7 (70.00)	4 (66.67)
Week 16	9 (90.00)	5 (83.33)
Absolute Change at Week 16	8 (80.00)	4 (66.67)
Week 24	9 (90.00)	5 (83.33)
Absolute Change at Week 24	8 (80.00)	4 (66.67)
Week 52	9 (90.00)	5 (83.33)
Absolute Change at Week 52	8 (80.00)	4 (66.67)
Through Week 52	9 (90.00)	5 (83.33)
Absolute Change through Week 52	8 (80.00)	4 (66.67)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	197	192
Mean (SD)	76.59 (21.86)	77.84 (23.01)
Week 8 (MMRM)		
n	197	188
LS mean (SE)	78.44 (1.54)	78.95 (1.57)
95% CI of LS mean	(75.41, 81.48)	(75.86, 82.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.51 (-3.83, 4.84)
Absolute Change at Week 8 (MMRM)		
n	193	186
LS mean (SE)	1.61 (0.93)	1.31 (0.95)
95% CI of LS mean	(-0.23, 3.45)	(-0.56, 3.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-2.92, 2.32)
Week 16 (MMRM)		
n	196	189
LS mean (SE)	77.94 (1.52)	80.05 (1.55)
95% CI of LS mean	(74.96, 80.93)	(77.00, 83.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.11 (-2.16, 6.37)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 16 (MMRM)		
n	192	186
LS mean (SE)	0.96 (1.00)	2.63 (1.02)
95% CI of LS mean	(-1.00, 2.93)	(0.63, 4.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.67 (-1.13, 4.47)
Week 24 (MMRM)		
n	196	188
LS mean (SE)	76.64 (1.59)	79.29 (1.63)
95% CI of LS mean	(73.51, 79.77)	(76.09, 82.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.65 (-1.83, 7.13)
Absolute Change at Week 24 (MMRM)		
n	192	185
LS mean (SE)	-0.37 (1.12)	1.96 (1.14)
95% CI of LS mean	(-2.58, 1.84)	(-0.29, 4.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.33 (-0.82, 5.49)
Week 52		
n	193	184
Mean (SD)	78.81 (20.70)	80.25 (20.65)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52		
n	189	180
Mean (SD)	1.82 (14.58)	2.22 (14.16)
Week 52 (MMRM)		
n	191	180
LS mean (SE)	78.74 (1.48)	79.78 (1.51)
95% CI of LS mean	(75.84, 81.64)	(76.81, 82.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-3.11, 5.20)
Absolute Change at Week 52 (MMRM)		
n	187	177
LS mean (SE)	1.69 (1.05)	2.26 (1.08)
95% CI of LS mean	(-0.39, 3.76)	(0.14, 4.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-2.39, 3.54)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change through Week 52 (MMRM)		
n	192	186
LS mean (SE)	0.76 (0.86)	2.29 (0.88)
95% CI of LS mean	(-0.94, 2.46)	(0.56, 4.02)
P-value within Treatment	0.3799	0.0098
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-0.90, 3.95)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2166
Hedges' G (SE)		0.13 (0.10)
Hedges' 95% CI		(-0.07, 0.33)
Hedges' P-value		0.2169

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	197	191
Mean (SD)	82.66 (18.31)	85.05 (15.70)
Week 8 (MMRM)		
n	196	188
LS mean (SE)	81.74 (1.27)	86.32 (1.29)
95% CI of LS mean	(79.24, 84.23)	(83.78, 88.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.58 (1.02, 8.15)
Absolute Change at Week 8 (MMRM)		
n	192	185
LS mean (SE)	-1.16 (1.08)	1.82 (1.11)
95% CI of LS mean	(-3.30, 0.97)	(-0.35, 4.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.99 (-0.06, 6.03)
Week 16 (MMRM)		
n	196	189
LS mean (SE)	81.42 (1.36)	83.65 (1.38)
95% CI of LS mean	(78.75, 84.09)	(80.93, 86.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.23 (-1.58, 6.04)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 16 (MMRM)		
n	192	185
LS mean (SE)	-1.49 (1.11)	-1.09 (1.13)
95% CI of LS mean	(-3.66, 0.69)	(-3.31, 1.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.40 (-2.71, 3.51)
Week 24 (MMRM)		
n	196	186
LS mean (SE)	82.26 (1.20)	85.91 (1.23)
95% CI of LS mean	(79.90, 84.62)	(83.50, 88.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.65 (0.28, 7.03)
Absolute Change at Week 24 (MMRM)		
n	192	183
LS mean (SE)	-0.56 (1.02)	1.24 (1.04)
95% CI of LS mean	(-2.56, 1.44)	(-0.81, 3.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.80 (-1.06, 4.66)
Week 52		
n	192	184
Mean (SD)	82.64 (18.25)	82.37 (17.67)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52		
n	188	179
Mean (SD)	-0.03 (16.42)	-2.17 (12.63)
Week 52 (MMRM)		
n	190	180
LS mean (SE)	82.83 (1.27)	82.36 (1.30)
95% CI of LS mean	(80.33, 85.34)	(79.80, 84.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-4.05, 3.11)
Absolute Change at Week 52 (MMRM)		
n	186	176
LS mean (SE)	0.04 (1.07)	-2.12 (1.10)
95% CI of LS mean	(-2.07, 2.15)	(-4.28, 0.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.16 (-5.18, 0.86)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change through Week 52 (MMRM)		
n	192	185
LS mean (SE)	-0.67 (0.89)	-0.66 (0.91)
95% CI of LS mean	(-2.43, 1.09)	(-2.45, 1.14)
P-value within Treatment	0.4539	0.4717
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-2.50, 2.52)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9923
Hedges' G (SE)		0.00 (0.10)
Hedges' 95% CI		(-0.20, 0.20)
Hedges' P-value		0.9923

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	197	192
Mean (SD)	92.84 (14.40)	91.09 (16.49)
Week 8 (MMRM)		
n	197	188
LS mean (SE)	92.29 (1.15)	90.63 (1.17)
95% CI of LS mean	(90.03, 94.54)	(88.32, 92.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.66 (-4.88, 1.57)
Absolute Change at Week 8 (MMRM)		
n	193	186
LS mean (SE)	-0.93 (0.81)	0.01 (0.82)
95% CI of LS mean	(-2.52, 0.66)	(-1.61, 1.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.94 (-1.33, 3.22)
Week 16 (MMRM)		
n	196	189
LS mean (SE)	91.75 (1.09)	90.56 (1.12)
95% CI of LS mean	(89.60, 93.90)	(88.36, 92.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.19 (-4.27, 1.88)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 16 (MMRM)		
n	192	186
LS mean (SE)	-1.56 (0.85)	-0.12 (0.86)
95% CI of LS mean	(-3.22, 0.11)	(-1.81, 1.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.43 (-0.94, 3.81)
Week 24 (MMRM)		
n	196	188
LS mean (SE)	92.93 (1.16)	90.26 (1.18)
95% CI of LS mean	(90.65, 95.21)	(87.93, 92.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.67 (-5.93, 0.59)
Absolute Change at Week 24 (MMRM)		
n	192	185
LS mean (SE)	-0.33 (0.82)	-0.43 (0.83)
95% CI of LS mean	(-1.94, 1.27)	(-2.07, 1.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-2.39, 2.20)
Week 52		
n	193	184
Mean (SD)	93.72 (12.46)	91.18 (18.30)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52		
n	189	180
Mean (SD)	0.47 (10.30)	0.25 (12.09)
Week 52 (MMRM)		
n	191	180
LS mean (SE)	93.41 (1.11)	90.85 (1.13)
95% CI of LS mean	(91.24, 95.59)	(88.62, 93.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.56 (-5.68, 0.55)
Absolute Change at Week 52 (MMRM)		
n	187	177
LS mean (SE)	0.15 (0.81)	0.30 (0.83)
95% CI of LS mean	(-1.45, 1.75)	(-1.34, 1.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-2.14, 2.44)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change through Week 52 (MMRM)		
n	192	186
LS mean (SE)	-0.58 (0.65)	-0.08 (0.66)
95% CI of LS mean	(-1.86, 0.70)	(-1.39, 1.22)
P-value within Treatment	0.3746	0.9010
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-1.34, 2.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5938
Hedges' G (SE)		0.05 (0.10)
Hedges' 95% CI		(-0.15, 0.26)
Hedges' P-value		0.5937

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	197	192
Mean (SD)	80.79 (18.29)	82.24 (17.46)
Week 8 (MMRM)		
n	197	188
LS mean (SE)	81.46 (1.20)	82.97 (1.23)
95% CI of LS mean	(79.10, 83.82)	(80.55, 85.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-1.87, 4.89)
Absolute Change at Week 8 (MMRM)		
n	193	186
LS mean (SE)	0.22 (0.80)	1.24 (0.82)
95% CI of LS mean	(-1.36, 1.79)	(-0.37, 2.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.02 (-1.22, 3.27)
Week 16 (MMRM)		
n	196	189
LS mean (SE)	81.95 (1.25)	82.44 (1.28)
95% CI of LS mean	(79.49, 84.41)	(79.93, 84.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-3.03, 4.00)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 16 (MMRM)		
n	192	186
LS mean (SE)	0.61 (0.89)	0.77 (0.91)
95% CI of LS mean	(-1.15, 2.37)	(-1.01, 2.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-2.34, 2.67)
Week 24 (MMRM)		
n	196	188
LS mean (SE)	81.63 (1.22)	82.49 (1.25)
95% CI of LS mean	(79.22, 84.03)	(80.04, 84.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-2.57, 4.30)
Absolute Change at Week 24 (MMRM)		
n	192	185
LS mean (SE)	0.49 (0.96)	0.69 (0.98)
95% CI of LS mean	(-1.40, 2.38)	(-1.23, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-2.50, 2.90)
Week 52		
n	193	184
Mean (SD)	81.24 (18.60)	82.90 (16.03)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52		
n	189	180
Mean (SD)	0.34 (12.79)	1.22 (13.31)
Week 52 (MMRM)		
n	191	180
LS mean (SE)	81.27 (1.24)	83.08 (1.27)
95% CI of LS mean	(78.83, 83.71)	(80.58, 85.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.81 (-1.69, 5.31)
Absolute Change at Week 52 (MMRM)		
n	187	177
LS mean (SE)	0.07 (0.95)	1.23 (0.98)
95% CI of LS mean	(-1.80, 1.94)	(-0.68, 3.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-1.52, 3.84)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change through Week 52 (MMRM)		
n	192	186
LS mean (SE)	0.39 (0.80)	0.90 (0.82)
95% CI of LS mean	(-1.19, 1.97)	(-0.71, 2.51)
P-value within Treatment	0.6279	0.2728
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.51 (-1.75, 2.77)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6576
Hedges' G (SE)		0.05 (0.10)
Hedges' 95% CI		(-0.16, 0.25)
Hedges' P-value		0.6575

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	197	192
Mean (SD)	82.46 (18.57)	83.16 (19.78)
Week 8 (MMRM)		
n	197	188
LS mean (SE)	80.60 (1.44)	82.79 (1.48)
95% CI of LS mean	(77.77, 83.44)	(79.89, 85.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-1.87, 6.25)
Absolute Change at Week 8 (MMRM)		
n	193	186
LS mean (SE)	-2.09 (1.08)	0.04 (1.10)
95% CI of LS mean	(-4.21, 0.04)	(-2.12, 2.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.13 (-0.90, 5.16)
Week 16 (MMRM)		
n	196	189
LS mean (SE)	80.68 (1.41)	83.34 (1.44)
95% CI of LS mean	(77.92, 83.45)	(80.51, 86.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.65 (-1.30, 6.61)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 16 (MMRM)		
n	192	186
LS mean (SE)	-1.95 (1.08)	0.44 (1.09)
95% CI of LS mean	(-4.07, 0.16)	(-1.71, 2.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.39 (-0.62, 5.41)
Week 24 (MMRM)		
n	196	188
LS mean (SE)	82.54 (1.40)	83.53 (1.43)
95% CI of LS mean	(79.78, 85.29)	(80.72, 86.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.99 (-2.94, 4.93)
Absolute Change at Week 24 (MMRM)		
n	192	185
LS mean (SE)	-0.15 (0.98)	0.68 (0.99)
95% CI of LS mean	(-2.07, 1.77)	(-1.27, 2.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.83 (-1.91, 3.57)
Week 52		
n	193	184
Mean (SD)	83.78 (18.56)	84.67 (18.95)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52		
n	189	180
Mean (SD)	1.08 (12.59)	2.00 (12.11)
Week 52 (MMRM)		
n	191	180
LS mean (SE)	83.67 (1.30)	84.88 (1.33)
95% CI of LS mean	(81.11, 86.22)	(82.26, 87.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-2.45, 4.87)
Absolute Change at Week 52 (MMRM)		
n	187	177
LS mean (SE)	1.08 (0.90)	2.07 (0.92)
95% CI of LS mean	(-0.69, 2.85)	(0.25, 3.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.99 (-1.54, 3.53)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change through Week 52 (MMRM)		
n	192	186
LS mean (SE)	-0.34 (0.77)	1.06 (0.79)
95% CI of LS mean	(-1.86, 1.18)	(-0.49, 2.61)
P-value within Treatment	0.6584	0.1785
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-0.77, 3.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2044
Hedges' G (SE)		0.13 (0.10)
Hedges' 95% CI		(-0.07, 0.33)
Hedges' P-value		0.2047

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	197	192
Mean (SD)	74.28 (17.18)	75.10 (18.37)
Week 8 (MMRM)		
n	197	188
LS mean (SE)	75.52 (1.21)	75.72 (1.24)
95% CI of LS mean	(73.14, 77.91)	(73.28, 78.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-3.21, 3.61)
Absolute Change at Week 8 (MMRM)		
n	193	186
LS mean (SE)	1.14 (0.99)	1.10 (1.00)
95% CI of LS mean	(-0.80, 3.07)	(-0.88, 3.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-2.80, 2.73)
Week 16 (MMRM)		
n	196	189
LS mean (SE)	74.80 (1.31)	74.40 (1.33)
95% CI of LS mean	(72.23, 77.37)	(71.78, 77.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-4.07, 3.28)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 16 (MMRM)		
n	192	186
LS mean (SE)	0.25 (1.06)	-0.18 (1.07)
95% CI of LS mean	(-1.83, 2.32)	(-2.29, 1.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-3.39, 2.54)
Week 24 (MMRM)		
n	196	188
LS mean (SE)	76.49 (1.23)	76.68 (1.25)
95% CI of LS mean	(74.08, 78.90)	(74.22, 79.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-3.26, 3.63)
Absolute Change at Week 24 (MMRM)		
n	192	185
LS mean (SE)	1.98 (0.95)	2.08 (0.97)
95% CI of LS mean	(0.11, 3.85)	(0.18, 3.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-2.57, 2.77)
Week 52		
n	193	184
Mean (SD)	77.71 (16.15)	77.40 (17.49)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52		
n	189	180
Mean (SD)	3.15 (13.44)	2.71 (14.18)
Week 52 (MMRM)		
n	191	180
LS mean (SE)	77.74 (1.19)	77.50 (1.22)
95% CI of LS mean	(75.40, 80.08)	(75.11, 79.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-3.59, 3.12)
Absolute Change at Week 52 (MMRM)		
n	187	177
LS mean (SE)	3.21 (1.00)	2.82 (1.03)
95% CI of LS mean	(1.24, 5.18)	(0.80, 4.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-3.21, 2.43)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change through Week 52 (MMRM)		
n	192	186
LS mean (SE)	1.81 (0.85)	1.57 (0.87)
95% CI of LS mean	(0.13, 3.49)	(-0.13, 3.28)
P-value within Treatment	0.0343	0.0708
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-2.63, 2.16)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8454
Hedges' G (SE)		-0.02 (0.10)
Hedges' 95% CI		(-0.22, 0.18)
Hedges' P-value		0.8453

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline		
n	197	192
Mean (SD)	70.39 (20.08)	72.28 (19.76)
Week 8 (MMRM)		
n	196	188
LS mean (SE)	70.90 (1.38)	73.08 (1.41)
95% CI of LS mean	(68.18, 73.61)	(70.31, 75.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-1.70, 6.07)
Absolute Change at Week 8 (MMRM)		
n	192	186
LS mean (SE)	0.58 (0.99)	1.19 (1.01)
95% CI of LS mean	(-1.38, 2.53)	(-0.80, 3.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.61 (-2.18, 3.40)
Week 16 (MMRM)		
n	196	189
LS mean (SE)	70.56 (1.46)	72.92 (1.49)
95% CI of LS mean	(67.70, 73.43)	(69.99, 75.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.36 (-1.74, 6.45)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 16 (MMRM)		
n	192	186
LS mean (SE)	0.07 (1.07)	1.33 (1.09)
95% CI of LS mean	(-2.04, 2.17)	(-0.81, 3.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.27 (-1.73, 4.27)
Week 24 (MMRM)		
n	196	188
LS mean (SE)	72.38 (1.44)	73.01 (1.46)
95% CI of LS mean	(69.56, 75.21)	(70.13, 75.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-3.41, 4.66)
Absolute Change at Week 24 (MMRM)		
n	192	185
LS mean (SE)	1.93 (1.04)	1.11 (1.05)
95% CI of LS mean	(-0.11, 3.96)	(-0.96, 3.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-3.72, 2.09)
Week 52		
n	193	184
Mean (SD)	73.69 (19.92)	76.33 (18.96)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52		
n	189	180
Mean (SD)	3.17 (16.02)	4.44 (15.43)
Week 52 (MMRM)		
n	191	180
LS mean (SE)	73.45 (1.39)	76.17 (1.42)
95% CI of LS mean	(70.73, 76.18)	(73.38, 78.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.72 (-1.18, 6.62)
Absolute Change at Week 52 (MMRM)		
n	187	177
LS mean (SE)	2.95 (1.15)	4.22 (1.18)
95% CI of LS mean	(0.69, 5.22)	(1.91, 6.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.27 (-1.97, 4.51)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Absolute Change through Week 52 (MMRM)		
n	192	186
LS mean (SE)	1.65 (0.93)	2.22 (0.94)
95% CI of LS mean	(-0.17, 3.47)	(0.37, 4.08)
P-value within Treatment	0.0760	0.0189
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-2.02, 3.18)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6636
Hedges' G (SE)		0.04 (0.10)
Hedges' 95% CI		(-0.16, 0.25)
Hedges' P-value		0.6635

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Baseline		
n	189	187
Mean (SD)	71.13 (19.24)	73.92 (19.53)
Week 8 (MMRM)		
n	189	183
LS mean (SE)	70.41 (1.38)	72.98 (1.40)
95% CI of LS mean	(67.69, 73.13)	(70.21, 75.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.56 (-1.31, 6.44)
Absolute Change at Week 8 (MMRM)		
n	186	181
LS mean (SE)	-1.03 (1.03)	-0.71 (1.04)
95% CI of LS mean	(-3.06, 1.00)	(-2.76, 1.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-2.57, 3.20)
Week 16 (MMRM)		
n	187	184
LS mean (SE)	71.40 (1.46)	72.82 (1.47)
95% CI of LS mean	(68.54, 74.26)	(69.93, 75.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-2.65, 5.49)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Absolute Change at Week 16 (MMRM)		
n	184	182
LS mean (SE)	-0.31 (1.06)	-0.81 (1.06)
95% CI of LS mean	(-2.38, 1.77)	(-2.90, 1.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-3.45, 2.45)
Week 24 (MMRM)		
n	187	183
LS mean (SE)	70.33 (1.49)	74.04 (1.51)
95% CI of LS mean	(67.39, 73.27)	(71.07, 77.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.72 (-0.46, 7.89)
Absolute Change at Week 24 (MMRM)		
n	184	181
LS mean (SE)	-1.28 (1.04)	0.20 (1.05)
95% CI of LS mean	(-3.32, 0.76)	(-1.86, 2.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.48 (-1.42, 4.38)
Week 52		
n	184	179
Mean (SD)	72.68 (19.98)	74.98 (20.05)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Absolute Change at Week 52		
n	181	176
Mean (SD)	1.20 (12.89)	1.07 (15.01)
Week 52 (MMRM)		
n	182	175
LS mean (SE)	73.06 (1.44)	75.21 (1.46)
95% CI of LS mean	(70.23, 75.88)	(72.34, 78.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.15 (-1.88, 6.18)
Absolute Change at Week 52 (MMRM)		
n	179	173
LS mean (SE)	1.43 (1.04)	1.28 (1.06)
95% CI of LS mean	(-0.62, 3.48)	(-0.80, 3.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-3.06, 2.78)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Absolute Change through Week 52 (MMRM)		
n	184	182
LS mean (SE)	-0.05 (0.83)	0.22 (0.84)
95% CI of LS mean	(-1.69, 1.58)	(-1.42, 1.87)
P-value within Treatment	0.9481	0.7894
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.28 (-2.04, 2.60)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8139
Hedges' G (SE)		0.02 (0.10)
Hedges' 95% CI		(-0.18, 0.23)
Hedges' P-value		0.8138

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Baseline		
n	189	186
Mean (SD)	87.65 (16.92)	87.37 (15.77)
Week 8 (MMRM)		
n	188	183
LS mean (SE)	87.07 (1.09)	87.74 (1.10)
95% CI of LS mean	(84.93, 89.21)	(85.57, 89.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.67 (-2.38, 3.72)
Absolute Change at Week 8 (MMRM)		
n	185	180
LS mean (SE)	-0.62 (0.94)	0.51 (0.96)
95% CI of LS mean	(-2.48, 1.23)	(-1.37, 2.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-1.51, 3.78)
Week 16 (MMRM)		
n	187	184
LS mean (SE)	85.91 (1.15)	88.82 (1.17)
95% CI of LS mean	(83.64, 88.18)	(86.52, 91.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.90 (-0.32, 6.13)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Absolute Change at Week 16 (MMRM)		
n	184	181
LS mean (SE)	-1.62 (1.06)	2.01 (1.07)
95% CI of LS mean	(-3.72, 0.47)	(-0.11, 4.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.63 (0.66, 6.60)
Week 24 (MMRM)		
n	187	182
LS mean (SE)	86.89 (1.11)	88.19 (1.12)
95% CI of LS mean	(84.71, 89.07)	(85.98, 90.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.30 (-1.81, 4.41)
Absolute Change at Week 24 (MMRM)		
n	184	179
LS mean (SE)	-0.85 (1.01)	1.16 (1.03)
95% CI of LS mean	(-2.84, 1.14)	(-0.86, 3.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.01 (-0.83, 4.84)
Week 52		
n	183	179
Mean (SD)	88.80 (14.76)	88.73 (14.77)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Absolute Change at Week 52		
n	180	175
Mean (SD)	1.06 (12.30)	1.81 (14.65)
Week 52 (MMRM)		
n	181	175
LS mean (SE)	88.69 (1.08)	88.71 (1.10)
95% CI of LS mean	(86.57, 90.82)	(86.56, 90.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-3.01, 3.05)
Absolute Change at Week 52 (MMRM)		
n	178	172
LS mean (SE)	1.05 (1.01)	1.59 (1.02)
95% CI of LS mean	(-0.94, 3.03)	(-0.43, 3.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.54 (-2.29, 3.37)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Absolute Change through Week 52 (MMRM)		
n	184	181
LS mean (SE)	-0.47 (0.87)	1.58 (0.88)
95% CI of LS mean	(-2.18, 1.23)	(-0.14, 3.31)
P-value within Treatment	0.5841	0.0717
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.06 (-0.37, 4.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0959
Hedges' G (SE)		0.17 (0.10)
Hedges' 95% CI		(-0.03, 0.38)
Hedges' P-value		0.0964

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Baseline		
n	189	187
Mean (SD)	66.78 (17.71)	69.65 (20.07)
Week 8 (MMRM)		
n	189	183
LS mean (SE)	65.05 (1.41)	67.84 (1.43)
95% CI of LS mean	(62.28, 67.81)	(65.03, 70.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.79 (-1.15, 6.74)
Absolute Change at Week 8 (MMRM)		
n	186	181
LS mean (SE)	-2.04 (1.28)	-1.62 (1.30)
95% CI of LS mean	(-4.56, 0.48)	(-4.17, 0.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-3.17, 4.02)
Week 16 (MMRM)		
n	187	184
LS mean (SE)	64.62 (1.49)	67.76 (1.50)
95% CI of LS mean	(61.70, 67.54)	(64.81, 70.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.14 (-1.01, 7.30)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Absolute Change at Week 16 (MMRM)		
n	184	182
LS mean (SE)	-2.25 (1.20)	-1.44 (1.21)
95% CI of LS mean	(-4.61, 0.11)	(-3.82, 0.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-2.54, 4.16)
Week 24 (MMRM)		
n	187	183
LS mean (SE)	64.31 (1.51)	67.55 (1.53)
95% CI of LS mean	(61.34, 67.28)	(64.55, 70.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.24 (-0.98, 7.47)
Absolute Change at Week 24 (MMRM)		
n	184	181
LS mean (SE)	-2.70 (1.23)	-2.00 (1.24)
95% CI of LS mean	(-5.13, -0.28)	(-4.45, 0.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.70 (-2.75, 4.15)
Week 52		
n	184	179
Mean (SD)	66.89 (18.61)	68.95 (20.02)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Absolute Change at Week 52		
n	181	176
Mean (SD)	-0.26 (14.86)	-0.62 (18.13)
Week 52 (MMRM)		
n	182	175
LS mean (SE)	66.76 (1.41)	69.02 (1.44)
95% CI of LS mean	(63.98, 69.54)	(66.20, 71.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.26 (-1.71, 6.22)
Absolute Change at Week 52 (MMRM)		
n	179	173
LS mean (SE)	-0.33 (1.24)	-0.59 (1.26)
95% CI of LS mean	(-2.77, 2.10)	(-3.06, 1.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-3.72, 3.22)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Absolute Change through Week 52 (MMRM)		
n	184	182
LS mean (SE)	-1.76 (1.00)	-1.34 (1.01)
95% CI of LS mean	(-3.73, 0.20)	(-3.33, 0.64)
P-value within Treatment	0.0786	0.1833
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.42 (-2.37, 3.21)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7681
Hedges' G (SE)		0.03 (0.10)
Hedges' 95% CI		(-0.17, 0.24)
Hedges' P-value		0.7680

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Baseline		
n	189	187
Mean (SD)	84.83 (26.95)	82.35 (28.98)
Week 8 (MMRM)		
n	188	183
LS mean (SE)	85.44 (1.94)	83.20 (1.97)
95% CI of LS mean	(81.62, 89.26)	(79.33, 87.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.24 (-7.68, 3.20)
Absolute Change at Week 8 (MMRM)		
n	185	181
LS mean (SE)	0.51 (1.55)	1.13 (1.57)
95% CI of LS mean	(-2.54, 3.56)	(-1.95, 4.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-3.72, 4.97)
Week 16 (MMRM)		
n	187	184
LS mean (SE)	82.31 (2.10)	82.85 (2.13)
95% CI of LS mean	(78.17, 86.44)	(78.67, 87.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.54 (-5.34, 6.42)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Absolute Change at Week 16 (MMRM)		
n	184	182
LS mean (SE)	-2.69 (1.78)	0.76 (1.79)
95% CI of LS mean	(-6.18, 0.81)	(-2.76, 4.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.45 (-1.52, 8.41)
Week 24 (MMRM)		
n	187	182
LS mean (SE)	84.81 (2.09)	82.72 (2.12)
95% CI of LS mean	(80.69, 88.92)	(78.55, 86.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.09 (-7.94, 3.77)
Absolute Change at Week 24 (MMRM)		
n	184	180
LS mean (SE)	0.03 (1.80)	0.62 (1.82)
95% CI of LS mean	(-3.52, 3.58)	(-2.96, 4.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-4.45, 5.64)
Week 52		
n	183	179
Mean (SD)	86.16 (24.76)	82.50 (27.21)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Absolute Change at Week 52		
n	180	176
Mean (SD)	1.11 (24.89)	-0.19 (21.82)
Week 52 (MMRM)		
n	181	175
LS mean (SE)	85.54 (1.95)	81.59 (1.98)
95% CI of LS mean	(81.70, 89.37)	(77.70, 85.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.94 (-9.41, 1.52)
Absolute Change at Week 52 (MMRM)		
n	178	173
LS mean (SE)	0.62 (1.75)	-0.56 (1.77)
95% CI of LS mean	(-2.82, 4.06)	(-4.04, 2.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.17 (-6.07, 3.72)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.3.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 192	VNZ/TEZ/D-IVA N = 190
Absolute Change through Week 52 (MMRM)		
n	184	182
LS mean (SE)	-0.68 (1.51)	0.28 (1.53)
95% CI of LS mean	(-3.65, 2.30)	(-2.73, 3.28)
P-value within Treatment	0.6535	0.8566
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.96 (-3.27, 5.18)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6569
Hedges' G (SE)		0.05 (0.10)
Hedges' 95% CI		(-0.16, 0.25)
Hedges' P-value		0.6569

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Baseline		
n	8	5
Mean (SD)	73.61 (13.20)	73.33 (20.18)
Week 8 (MMRM)		
n	8	5
LS mean (SE)	74.21 (8.28)	80.76 (10.58)
95% CI of LS mean	(55.94, 92.48)	(57.51, 104.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.54 (-24.54, 37.63)
Absolute Change at Week 8 (MMRM)		
n	7	5
LS mean (SE)	7.28 (6.39)	8.67 (8.06)
95% CI of LS mean	(-7.59, 22.16)	(-10.20, 27.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-23.38, 26.15)
Week 16 (MMRM)		
n	9	5
LS mean (SE)	68.91 (8.42)	70.41 (11.53)
95% CI of LS mean	(50.30, 87.52)	(45.39, 95.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.50 (-31.24, 34.24)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	8	4
LS mean (SE)	-6.81 (7.51)	6.12 (9.94)
95% CI of LS mean	(-24.41, 10.79)	(-16.64, 28.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.93 (-16.34, 42.21)
Week 24 (MMRM)		
n	9	5
LS mean (SE)	66.44 (8.17)	86.07 (11.02)
95% CI of LS mean	(48.59, 84.30)	(62.35, 109.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	19.62 (-11.71, 50.95)
Absolute Change at Week 24 (MMRM)		
n	8	4
LS mean (SE)	-6.81 (6.93)	9.40 (10.04)
95% CI of LS mean	(-22.58, 8.96)	(-12.97, 31.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	16.21 (-11.87, 44.29)
Week 52		
n	9	5
Mean (SD)	80.25 (19.86)	82.22 (28.97)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52		
n	8	4
Mean (SD)	9.72 (13.85)	0.00 (32.71)
Week 52 (MMRM)		
n	9	5
LS mean (SE)	81.26 (8.41)	81.71 (11.23)
95% CI of LS mean	(62.93, 99.59)	(57.58, 105.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-31.42, 32.32)
Absolute Change at Week 52 (MMRM)		
n	8	4
LS mean (SE)	9.86 (8.42)	5.14 (11.78)
95% CI of LS mean	(-9.40, 29.12)	(-21.19, 31.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.71 (-37.80, 28.37)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	8	4
LS mean (SE)	-1.25 (6.91)	6.89 (9.56)
95% CI of LS mean	(-17.44, 14.94)	(-14.84, 28.61)
P-value within Treatment	0.8609	0.4900
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.14 (-19.56, 35.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5209
Hedges' G (SE)		0.39 (0.57)
Hedges' 95% CI		(-0.88, 1.66)
Hedges' P-value		0.5130

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Baseline		
n	8	5
Mean (SD)	75.00 (16.53)	97.78 (4.97)
Week 8 (MMRM)		
n	8	5
LS mean (SE)	89.06 (4.17)	91.64 (5.33)
95% CI of LS mean	(79.71, 98.40)	(79.73, 103.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.59 (-13.42, 18.59)
Absolute Change at Week 8 (MMRM)		
n	7	5
LS mean (SE)	18.27 (4.46)	-9.31 (5.37)
95% CI of LS mean	(8.42, 28.13)	(-21.26, 2.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-27.58 (-43.39, -11.78)
Week 16 (MMRM)		
n	9	5
LS mean (SE)	80.52 (5.37)	87.86 (7.04)
95% CI of LS mean	(68.67, 92.37)	(72.59, 103.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.34 (-12.51, 27.20)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	8	4
LS mean (SE)	7.21 (3.39)	-9.78 (4.98)
95% CI of LS mean	(-0.69, 15.10)	(-21.10, 1.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-16.98 (-31.27, -2.70)
Week 24 (MMRM)		
n	9	5
LS mean (SE)	81.75 (5.30)	94.11 (7.36)
95% CI of LS mean	(70.16, 93.35)	(78.19, 110.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.35 (-7.99, 32.70)
Absolute Change at Week 24 (MMRM)		
n	8	4
LS mean (SE)	8.60 (4.93)	-3.39 (7.28)
95% CI of LS mean	(-2.43, 19.62)	(-19.57, 12.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-11.99 (-31.90, 7.93)
Week 52		
n	9	5
Mean (SD)	82.72 (13.73)	91.11 (9.30)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52		
n	8	4
Mean (SD)	5.56 (11.88)	-2.78 (5.56)
Week 52 (MMRM)		
n	9	5
LS mean (SE)	81.75 (4.40)	91.15 (5.99)
95% CI of LS mean	(72.00, 91.50)	(78.13, 104.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.39 (-7.64, 26.42)
Absolute Change at Week 52 (MMRM)		
n	8	4
LS mean (SE)	7.21 (3.04)	-7.23 (4.42)
95% CI of LS mean	(0.01, 14.41)	(-17.35, 2.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-14.44 (-27.38, -1.50)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	8	4
LS mean (SE)	7.67 (2.72)	-6.80 (4.08)
95% CI of LS mean	(1.39, 13.95)	(-16.01, 2.41)
P-value within Treatment	0.0226	0.1294
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-14.47 (-26.30, -2.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0219
Hedges' G (SE)		-1.71 (0.66)
Hedges' 95% CI		(-3.18, -0.23)
Hedges' P-value		0.0279

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Baseline		
n	8	5
Mean (SD)	89.58 (19.80)	90.00 (14.91)
Week 8 (MMRM)		
n	8	5
LS mean (SE)	87.43 (6.75)	89.07 (8.59)
95% CI of LS mean	(72.25, 102.61)	(69.88, 108.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-23.57, 26.86)
Absolute Change at Week 8 (MMRM)		
n	7	5
LS mean (SE)	-1.08 (4.76)	4.33 (5.66)
95% CI of LS mean	(-11.96, 9.81)	(-8.71, 17.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.40 (-11.72, 22.53)
Week 16 (MMRM)		
n	9	5
LS mean (SE)	87.87 (5.91)	80.60 (7.91)
95% CI of LS mean	(74.92, 100.82)	(63.55, 97.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.27 (-29.65, 15.12)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	8	4
LS mean (SE)	-2.70 (4.16)	-2.17 (5.97)
95% CI of LS mean	(-12.21, 6.80)	(-15.60, 11.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.54 (-16.07, 17.14)
Week 24 (MMRM)		
n	9	5
LS mean (SE)	86.01 (8.42)	77.32 (11.13)
95% CI of LS mean	(67.49, 104.54)	(53.20, 101.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.69 (-39.67, 22.28)
Absolute Change at Week 24 (MMRM)		
n	8	4
LS mean (SE)	-4.79 (3.13)	0.17 (4.58)
95% CI of LS mean	(-12.41, 2.84)	(-10.78, 11.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.95 (-8.68, 18.58)
Week 52		
n	9	5
Mean (SD)	90.74 (16.90)	80.00 (29.81)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52		
n	8	4
Mean (SD)	0.00 (8.91)	-4.17 (20.97)
Week 52 (MMRM)		
n	9	5
LS mean (SE)	87.87 (5.71)	87.24 (7.77)
95% CI of LS mean	(75.22, 100.52)	(70.34, 104.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-22.75, 21.50)
Absolute Change at Week 52 (MMRM)		
n	8	4
LS mean (SE)	-2.70 (2.95)	3.11 (4.44)
95% CI of LS mean	(-9.46, 4.05)	(-6.97, 13.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.82 (-6.59, 18.22)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	8	4
LS mean (SE)	-3.40 (2.45)	0.37 (3.75)
95% CI of LS mean	(-8.98, 2.18)	(-8.10, 8.84)
P-value within Treatment	0.2006	0.9236
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.77 (-6.73, 14.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4395
Hedges' G (SE)		0.49 (0.57)
Hedges' 95% CI		(-0.79, 1.77)
Hedges' P-value		0.4142

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Baseline		
n	8	5
Mean (SD)	79.17 (14.00)	78.67 (10.95)
Week 8 (MMRM)		
n	8	5
LS mean (SE)	87.47 (4.65)	77.20 (5.90)
95% CI of LS mean	(77.25, 97.69)	(64.25, 90.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.27 (-27.97, 7.43)
Absolute Change at Week 8 (MMRM)		
n	7	5
LS mean (SE)	5.27 (3.07)	0.18 (3.91)
95% CI of LS mean	(-2.01, 12.56)	(-9.10, 9.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.10 (-17.26, 7.06)
Week 16 (MMRM)		
n	9	5
LS mean (SE)	89.41 (5.49)	68.93 (7.07)
95% CI of LS mean	(77.35, 101.46)	(53.62, 84.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-20.48 (-40.86, -0.10)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	8	4
LS mean (SE)	7.39 (3.37)	-9.10 (4.83)
95% CI of LS mean	(-0.17, 14.94)	(-19.70, 1.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-16.49 (-29.87, -3.11)
Week 24 (MMRM)		
n	9	5
LS mean (SE)	85.70 (4.99)	72.95 (6.36)
95% CI of LS mean	(74.74, 96.67)	(59.08, 86.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-12.76 (-31.49, 5.97)
Absolute Change at Week 24 (MMRM)		
n	8	4
LS mean (SE)	3.22 (4.28)	-3.72 (5.56)
95% CI of LS mean	(-6.54, 12.99)	(-16.25, 8.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.94 (-23.03, 9.14)
Week 52		
n	9	5
Mean (SD)	87.41 (14.70)	61.33 (17.26)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52		
n	8	4
Mean (SD)	6.67 (5.04)	-11.67 (13.74)
Week 52 (MMRM)		
n	9	5
LS mean (SE)	88.67 (5.80)	58.31 (7.57)
95% CI of LS mean	(75.98, 101.36)	(42.01, 74.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-30.36 (-51.85, -8.86)
Absolute Change at Week 52 (MMRM)		
n	8	4
LS mean (SE)	6.56 (3.23)	-12.30 (4.69)
95% CI of LS mean	(-1.01, 14.12)	(-23.01, -1.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-18.86 (-32.33, -5.38)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	8	4
LS mean (SE)	5.72 (2.98)	-8.37 (4.06)
95% CI of LS mean	(-0.99, 12.43)	(-17.33, 0.58)
P-value within Treatment	0.0860	0.0640
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-14.09 (-25.70, -2.49)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0218
Hedges' G (SE)		-1.56 (0.65)
Hedges' 95% CI		(-3.01, -0.11)
Hedges' P-value		0.0370

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Baseline		
n	8	5
Mean (SD)	69.44 (12.94)	82.22 (21.66)
Week 8 (MMRM)		
n	8	5
LS mean (SE)	84.00 (4.01)	82.23 (5.13)
95% CI of LS mean	(74.89, 93.11)	(70.62, 93.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.77 (-17.51, 13.96)
Absolute Change at Week 8 (MMRM)		
n	7	5
LS mean (SE)	18.92 (4.50)	-1.97 (5.58)
95% CI of LS mean	(8.94, 28.89)	(-14.38, 10.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-20.89 (-37.14, -4.64)
Week 16 (MMRM)		
n	9	5
LS mean (SE)	75.79 (5.10)	80.40 (6.73)
95% CI of LS mean	(64.63, 86.94)	(65.91, 94.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.61 (-14.29, 23.52)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	8	4
LS mean (SE)	9.57 (6.67)	-1.04 (8.82)
95% CI of LS mean	(-5.22, 24.36)	(-20.33, 18.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.61 (-35.07, 13.86)
Week 24 (MMRM)		
n	9	5
LS mean (SE)	80.72 (5.63)	80.61 (7.30)
95% CI of LS mean	(68.43, 93.02)	(64.88, 96.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.12 (-20.59, 20.36)
Absolute Change at Week 24 (MMRM)		
n	8	4
LS mean (SE)	12.34 (4.85)	-2.63 (6.69)
95% CI of LS mean	(1.45, 23.24)	(-17.35, 12.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-14.97 (-33.57, 3.63)
Week 52		
n	9	5
Mean (SD)	85.19 (14.70)	80.00 (18.26)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52		
n	8	4
Mean (SD)	13.89 (11.50)	2.78 (5.56)
Week 52 (MMRM)		
n	9	5
LS mean (SE)	83.19 (5.28)	86.99 (7.06)
95% CI of LS mean	(71.49, 94.90)	(71.64, 102.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.80 (-16.08, 23.68)
Absolute Change at Week 52 (MMRM)		
n	8	4
LS mean (SE)	15.12 (4.35)	1.91 (6.28)
95% CI of LS mean	(5.08, 25.17)	(-12.29, 16.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-13.21 (-30.94, 4.52)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	8	4
LS mean (SE)	12.34 (4.57)	-0.58 (6.16)
95% CI of LS mean	(2.16, 22.52)	(-14.09, 12.92)
P-value within Treatment	0.0223	0.9261
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-12.93 (-30.15, 4.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1270
Hedges' G (SE)		-0.94 (0.60)
Hedges' 95% CI		(-2.27, 0.39)
Hedges' P-value		0.1477

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Baseline		
n	8	5
Mean (SD)	90.10 (10.67)	87.50 (13.18)
Week 8 (MMRM)		
n	8	5
LS mean (SE)	93.17 (9.67)	77.71 (12.03)
95% CI of LS mean	(71.22, 115.11)	(50.53, 104.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-15.46 (-51.08, 20.16)
Absolute Change at Week 8 (MMRM)		
n	7	5
LS mean (SE)	2.23 (3.38)	5.13 (4.15)
95% CI of LS mean	(-5.30, 9.76)	(-4.15, 14.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.90 (-9.26, 15.07)
Week 16 (MMRM)		
n	9	5
LS mean (SE)	89.11 (6.33)	80.17 (8.71)
95% CI of LS mean	(75.05, 103.17)	(61.19, 99.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.94 (-34.07, 16.19)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	8	4
LS mean (SE)	-2.17 (4.50)	-0.94 (6.62)
95% CI of LS mean	(-12.29, 7.96)	(-15.77, 13.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.22 (-16.95, 19.40)
Week 24 (MMRM)		
n	9	5
LS mean (SE)	94.67 (8.47)	79.33 (10.69)
95% CI of LS mean	(76.32, 113.02)	(56.26, 102.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-15.34 (-45.88, 15.19)
Absolute Change at Week 24 (MMRM)		
n	8	4
LS mean (SE)	4.08 (2.52)	5.19 (3.53)
95% CI of LS mean	(-1.52, 9.68)	(-2.50, 12.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.11 (-8.76, 10.98)
Week 52		
n	9	5
Mean (SD)	90.28 (15.02)	83.33 (30.33)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52		
n	8	4
Mean (SD)	-1.04 (14.22)	11.46 (12.90)
Week 52 (MMRM)		
n	9	5
LS mean (SE)	91.89 (7.34)	82.83 (9.54)
95% CI of LS mean	(75.89, 107.90)	(62.23, 103.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.07 (-36.45, 18.32)
Absolute Change at Week 52 (MMRM)		
n	8	4
LS mean (SE)	0.96 (3.69)	6.26 (5.37)
95% CI of LS mean	(-7.42, 9.34)	(-5.79, 18.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.31 (-9.58, 20.19)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	8	4
LS mean (SE)	0.96 (2.01)	3.50 (3.07)
95% CI of LS mean	(-3.63, 5.55)	(-3.44, 10.44)
P-value within Treatment	0.6452	0.2832
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.55 (-6.29, 11.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5309
Hedges' G (SE)		0.40 (0.57)
Hedges' 95% CI		(-0.87, 1.68)
Hedges' P-value		0.4958

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Baseline		
n	8	5
Mean (SD)	84.38 (14.39)	85.00 (14.91)
Week 8 (MMRM)		
n	8	5
LS mean (SE)	75.41 (6.99)	90.51 (8.85)
95% CI of LS mean	(59.83, 90.99)	(70.89, 110.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.10 (-11.21, 41.40)
Absolute Change at Week 8 (MMRM)		
n	7	5
LS mean (SE)	-9.57 (6.78)	3.29 (8.40)
95% CI of LS mean	(-25.00, 5.86)	(-15.95, 22.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.86 (-12.18, 37.90)
Week 16 (MMRM)		
n	9	5
LS mean (SE)	72.76 (8.33)	84.30 (10.78)
95% CI of LS mean	(53.53, 91.98)	(60.03, 108.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.54 (-20.30, 43.38)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	8	4
LS mean (SE)	-11.43 (9.05)	-4.03 (12.20)
95% CI of LS mean	(-33.88, 11.02)	(-33.19, 25.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.40 (-29.53, 44.33)
Week 24 (MMRM)		
n	9	5
LS mean (SE)	78.31 (6.00)	89.06 (7.95)
95% CI of LS mean	(64.94, 91.69)	(71.58, 106.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.75 (-13.02, 34.52)
Absolute Change at Week 24 (MMRM)		
n	8	4
LS mean (SE)	-6.22 (5.38)	2.38 (7.39)
95% CI of LS mean	(-19.25, 6.80)	(-14.89, 19.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.61 (-13.55, 30.76)
Week 52		
n	9	5
Mean (SD)	81.48 (18.99)	85.00 (10.87)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52		
n	8	4
Mean (SD)	-5.21 (8.84)	6.25 (7.98)
Week 52 (MMRM)		
n	9	5
LS mean (SE)	78.31 (6.04)	87.35 (7.98)
95% CI of LS mean	(64.88, 91.75)	(69.81, 104.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.03 (-14.80, 32.87)
Absolute Change at Week 52 (MMRM)		
n	8	4
LS mean (SE)	-6.22 (3.97)	4.24 (5.69)
95% CI of LS mean	(-16.22, 3.77)	(-9.39, 17.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.46 (-7.31, 28.23)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	8	4
LS mean (SE)	-7.96 (5.71)	0.87 (7.71)
95% CI of LS mean	(-22.15, 6.24)	(-17.63, 19.36)
P-value within Treatment	0.2160	0.9140
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.82 (-14.91, 32.56)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4036
Hedges' G (SE)		0.51 (0.57)
Hedges' 95% CI		(-0.77, 1.79)
Hedges' P-value		0.3948

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Baseline		
n	8	5
Mean (SD)	61.11 (16.80)	57.78 (18.26)
Week 8 (MMRM)		
n	8	5
LS mean (SE)	67.23 (6.85)	57.69 (8.74)
95% CI of LS mean	(51.47, 82.99)	(37.70, 77.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.55 (-36.42, 17.33)
Absolute Change at Week 8 (MMRM)		
n	7	5
LS mean (SE)	4.66 (3.06)	2.83 (3.69)
95% CI of LS mean	(-2.44, 11.77)	(-5.74, 11.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.84 (-13.51, 9.84)
Week 16 (MMRM)		
n	9	5
LS mean (SE)	64.78 (7.29)	70.99 (9.94)
95% CI of LS mean	(48.80, 80.75)	(49.55, 92.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.21 (-21.88, 34.30)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	8	4
LS mean (SE)	1.01 (6.14)	16.22 (9.11)
95% CI of LS mean	(-12.84, 14.87)	(-4.21, 36.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.21 (-9.78, 40.20)
Week 24 (MMRM)		
n	9	5
LS mean (SE)	67.25 (8.03)	74.55 (10.60)
95% CI of LS mean	(49.68, 84.81)	(51.71, 97.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.31 (-22.64, 37.25)
Absolute Change at Week 24 (MMRM)		
n	8	4
LS mean (SE)	1.01 (4.60)	20.94 (6.81)
95% CI of LS mean	(-9.47, 11.49)	(5.64, 36.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	19.93 (1.04, 38.82)
Week 52		
n	9	5
Mean (SD)	66.67 (20.79)	84.44 (12.67)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52		
n	8	4
Mean (SD)	4.17 (10.18)	25.00 (26.25)
Week 52 (MMRM)		
n	9	5
LS mean (SE)	66.01 (6.50)	83.76 (8.64)
95% CI of LS mean	(51.69, 80.33)	(65.04, 102.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	17.75 (-7.38, 42.87)
Absolute Change at Week 52 (MMRM)		
n	8	4
LS mean (SE)	2.40 (4.21)	28.70 (6.21)
95% CI of LS mean	(-7.89, 12.69)	(14.13, 43.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	26.30 (8.19, 44.41)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	8	4
LS mean (SE)	1.47 (4.19)	21.95 (6.28)
95% CI of LS mean	(-8.46, 11.41)	(7.41, 36.50)
P-value within Treatment	0.7354	0.0085
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	20.48 (2.50, 38.46)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0303
Hedges' G (SE)		1.57 (0.65)
Hedges' 95% CI		(0.12, 3.01)
Hedges' P-value		0.0366

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Baseline		
n	8	5
Mean (SD)	66.67 (16.71)	69.33 (18.01)
Week 8 (MMRM)		
n	8	5
LS mean (SE)	73.55 (6.21)	72.10 (7.74)
95% CI of LS mean	(60.03, 87.08)	(55.27, 88.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.46 (-23.78, 20.87)
Absolute Change at Week 8 (MMRM)		
n	7	5
LS mean (SE)	5.83 (5.77)	1.48 (7.32)
95% CI of LS mean	(-7.20, 18.85)	(-15.04, 18.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.34 (-25.84, 17.15)
Week 16 (MMRM)		
n	9	5
LS mean (SE)	76.62 (5.74)	58.84 (7.70)
95% CI of LS mean	(63.97, 89.27)	(42.17, 75.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-17.78 (-39.55, 4.00)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	8	4
LS mean (SE)	8.24 (4.29)	-4.90 (6.74)
95% CI of LS mean	(-1.78, 18.26)	(-20.30, 10.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-13.14 (-32.39, 6.12)
Week 24 (MMRM)		
n	9	5
LS mean (SE)	72.92 (7.25)	64.24 (9.00)
95% CI of LS mean	(57.18, 88.65)	(44.78, 83.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.67 (-34.26, 16.91)
Absolute Change at Week 24 (MMRM)		
n	8	4
LS mean (SE)	4.07 (6.79)	-6.50 (8.72)
95% CI of LS mean	(-11.35, 19.49)	(-26.19, 13.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.57 (-35.89, 14.75)
Week 52		
n	9	5
Mean (SD)	74.07 (18.69)	61.33 (14.45)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52		
n	8	4
Mean (SD)	4.17 (7.92)	0.00 (9.43)
Week 52 (MMRM)		
n	9	5
LS mean (SE)	73.66 (6.50)	57.29 (8.28)
95% CI of LS mean	(59.49, 87.83)	(39.42, 75.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-16.37 (-39.85, 7.10)
Absolute Change at Week 52 (MMRM)		
n	8	4
LS mean (SE)	4.91 (4.25)	-8.28 (6.03)
95% CI of LS mean	(-6.90, 16.71)	(-23.92, 7.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-13.19 (-33.53, 7.16)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	8	4
LS mean (SE)	5.74 (4.32)	-6.56 (5.98)
95% CI of LS mean	(-5.57, 17.04)	(-21.52, 8.40)
P-value within Treatment	0.2445	0.3185
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-12.30 (-31.82, 7.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1688
Hedges' G (SE)		-0.94 (0.60)
Hedges' 95% CI		(-2.26, 0.39)
Hedges' P-value		0.1481

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Baseline		
n	8	5
Mean (SD)	66.67 (25.20)	73.33 (43.46)
Week 8 (MMRM)		
n	8	4
LS mean (SE)	69.30 (5.47)	80.55 (8.04)
95% CI of LS mean	(56.94, 81.67)	(62.51, 98.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.25 (-12.02, 34.53)
Absolute Change at Week 8 (MMRM)		
n	7	4
LS mean (SE)	11.13 (5.49)	3.99 (7.94)
95% CI of LS mean	(-1.53, 23.79)	(-14.43, 22.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.14 (-30.97, 16.69)
Week 16 (MMRM)		
n	9	5
LS mean (SE)	63.65 (8.27)	78.77 (11.30)
95% CI of LS mean	(45.47, 81.82)	(54.00, 103.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.13 (-16.37, 46.62)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	8	4
LS mean (SE)	6.34 (8.20)	12.32 (11.87)
95% CI of LS mean	(-12.60, 25.28)	(-14.94, 39.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.98 (-27.99, 39.95)
Week 24 (MMRM)		
n	9	5
LS mean (SE)	63.65 (8.92)	98.77 (12.15)
95% CI of LS mean	(44.17, 83.12)	(72.29, 125.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	35.13 (1.55, 68.70)
Absolute Change at Week 24 (MMRM)		
n	8	4
LS mean (SE)	2.17 (11.51)	20.65 (16.48)
95% CI of LS mean	(-23.79, 28.14)	(-16.40, 57.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.48 (-27.31, 64.27)
Week 52		
n	9	5
Mean (SD)	88.89 (16.67)	80.00 (29.81)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52		
n	8	4
Mean (SD)	20.83 (24.80)	25.00 (56.93)
Week 52 (MMRM)		
n	9	5
LS mean (SE)	85.87 (8.32)	85.44 (11.37)
95% CI of LS mean	(67.59, 104.14)	(60.54, 110.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-32.08, 31.22)
Absolute Change at Week 52 (MMRM)		
n	8	4
LS mean (SE)	23.01 (12.51)	20.65 (17.88)
95% CI of LS mean	(-5.23, 51.24)	(-19.57, 60.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.35 (-51.99, 47.29)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.9.4
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	8	4
LS mean (SE)	10.51 (9.99)	17.88 (14.36)
95% CI of LS mean	(-12.29, 33.30)	(-14.74, 50.49)
P-value within Treatment	0.3218	0.2454
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.37 (-33.05, 47.79)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6896
Hedges' G (SE)		0.24 (0.57)
Hedges' 95% CI		(-1.02, 1.50)
Hedges' P-value		0.6818

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.12.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	31	25
Mean (SD)	80.65 (14.62)	79.56 (27.72)
Week 52		
n	28	24
Mean (SD)	82.94 (16.63)	84.95 (15.50)
Absolute Change at Week 52		
n	28	23
Mean (SD)	2.18 (19.85)	7.00 (29.17)
Absolute Change at Week 52 (MMRM)		
n	28	22
LS mean (SE)	2.13 (4.78)	7.39 (5.40)
95% CI of LS mean	(-7.49, 11.75)	(-3.47, 18.25)
P-value within Treatment	0.6575	0.1776
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.25 (-9.29, 19.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4709

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.12.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Hedges' G (SE)		0.20 (0.28)
Hedges' 95% CI		(-0.36, 0.77)
Hedges' P-value		0.4708

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.12.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	31	24
Mean (SD)	96.17 (13.28)	98.70 (4.11)
Week 52		
n	28	24
Mean (SD)	96.88 (8.59)	95.31 (13.19)
Absolute Change at Week 52		
n	28	22
Mean (SD)	-0.67 (9.82)	-2.56 (10.50)
Absolute Change at Week 52 (MMRM)		
n	28	21
LS mean (SE)	-0.83 (1.92)	-2.47 (2.22)
95% CI of LS mean	(-4.70, 3.04)	(-6.93, 2.00)
P-value within Treatment	0.6676	0.2725
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.64 (-7.56, 4.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5813

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.12.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Hedges' G (SE)		-0.16 (0.28)
Hedges' 95% CI		(-0.73, 0.41)
Hedges' P-value		0.5804

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.12.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	31	25
Mean (SD)	78.67 (14.78)	83.11 (15.51)
Week 52		
n	28	24
Mean (SD)	82.34 (21.91)	86.11 (12.90)
Absolute Change at Week 52		
n	28	23
Mean (SD)	3.57 (18.16)	3.38 (15.14)
Absolute Change at Week 52 (MMRM)		
n	28	22
LS mean (SE)	3.39 (3.23)	3.77 (3.65)
95% CI of LS mean	(-3.12, 9.90)	(-3.58, 11.11)
P-value within Treatment	0.2998	0.3077
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.37 (-9.47, 10.21)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9393

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.12.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Hedges' G (SE)		0.02 (0.28)
Hedges' 95% CI		(-0.54, 0.59)
Hedges' P-value		0.9391

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.12.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	31	25
Mean (SD)	81.80 (15.95)	86.57 (14.91)
Week 52		
n	28	24
Mean (SD)	87.24 (15.84)	86.90 (14.69)
Absolute Change at Week 52		
n	28	23
Mean (SD)	5.36 (13.56)	1.24 (17.58)
Absolute Change at Week 52 (MMRM)		
n	28	22
LS mean (SE)	5.58 (2.90)	1.02 (3.27)
95% CI of LS mean	(-0.26, 11.41)	(-5.57, 7.61)
P-value within Treatment	0.0607	0.7564
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.55 (-13.38, 4.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3044
Hedges' G (SE)		-0.29 (0.28)

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.12.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Hedges' 95% CI		(-0.86, 0.27)
Hedges' P-value		0.3055

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.1.12.1.1
Study VX21-121-102: Compliance Rate for TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Baseline	31 (100.00)	25 (96.15)
Week 52	28 (90.32)	24 (92.31)
Absolute Change at Week 52	28 (90.32)	23 (88.46)

- n (%): For "Change at Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and Week 52 are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.12.1.1
Study VX21-121-102: Compliance Rate for TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Baseline	31 (100.00)	24 (92.31)
Week 52	28 (90.32)	24 (92.31)
Absolute Change at Week 52	28 (90.32)	22 (84.62)

- n (%): For "Change at Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and Week 52 are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.12.1.1
Study VX21-121-102: Compliance Rate for TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Baseline	31 (100.00)	25 (96.15)
Week 52	28 (90.32)	24 (92.31)
Absolute Change at Week 52	28 (90.32)	23 (88.46)

- n (%): For "Change at Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and Week 52 are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.12.1.1
Study VX21-121-102: Compliance Rate for TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Baseline	31 (100.00)	25 (96.15)
Week 52	28 (90.32)	24 (92.31)
Absolute Change at Week 52	28 (90.32)	23 (88.46)

- n (%): For "Change at Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and Week 52 are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3541
Age at screening (<18 years vs. ≥18 years) [2]	0.9881
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0190
Sex (Male vs. Female) [1]	0.2633
Region (North America vs. Rest of the World) [1]	0.3374

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.7716

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	114	101
mean (SD)	56.46 (8.96)	54.80 (9.18)
Week 52		
n	107	93
mean (SD)	57.09 (9.89)	55.52 (10.91)
Absolute Change at Week 52		
n	107	93
mean (SD)	0.77 (5.42)	0.86 (4.91)
Absolute Change through Week 52 (MMRM)		
n	113	98
LS mean (SE)	0.81 (0.42)	1.04 (0.45)
95% CI of LS mean	(-0.01, 1.64)	(0.15, 1.93)
P-value within Treatment	0.0542	0.0226

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-0.99, 1.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7152
Hedges' G (SE)		0.05 (0.14)
Hedges' 95% CI		(-0.22, 0.32)
Hedges' P-value		0.7145

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	87	92
mean (SD)	81.31 (6.20)	80.47 (7.44)
Week 52		
n	77	82
mean (SD)	80.86 (8.01)	79.92 (9.54)
Absolute Change at Week 52		
n	77	82
mean (SD)	-0.42 (5.10)	-0.45 (6.08)
Absolute Change through Week 52 (MMRM)		
n	83	91
LS mean (SE)	-0.17 (0.48)	-0.22 (0.46)
95% CI of LS mean	(-1.11, 0.77)	(-1.12, 0.69)
P-value within Treatment	0.7220	0.6346

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-1.36, 1.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9422
Hedges' G (SE)		-0.01 (0.15)
Hedges' 95% CI		(-0.31, 0.29)
Hedges' P-value		0.9422

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	31	25
mean (SD)	78.12 (14.20)	79.27 (11.07)
Week 52		
n	25	24
mean (SD)	79.74 (14.47)	79.33 (11.35)
Absolute Change at Week 52		
n	25	23
mean (SD)	1.61 (5.89)	0.23 (6.42)
Absolute Change through Week 52 (MMRM)		
n	29	24
LS mean (SE)	0.95 (0.90)	0.27 (0.98)
95% CI of LS mean	(-0.85, 2.75)	(-1.70, 2.24)
P-value within Treatment	0.2943	0.7850

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.68 (-3.37, 2.00)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6123
Hedges' G (SE)		-0.14 (0.27)
Hedges' 95% CI		(-0.69, 0.41)
Hedges' P-value		0.6114

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	170	168
mean (SD)	65.23 (13.85)	65.21 (15.08)
Week 52		
n	159	153
mean (SD)	65.04 (13.97)	65.13 (15.66)
Absolute Change at Week 52		
n	159	152
mean (SD)	0.07 (5.20)	0.25 (5.38)
Absolute Change through Week 52 (MMRM)		
n	167	165
LS mean (SE)	0.27 (0.33)	0.52 (0.34)
95% CI of LS mean	(-0.38, 0.93)	(-0.15, 1.18)
P-value within Treatment	0.4163	0.1268

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-0.69, 1.18)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6060
Hedges' G (SE)		0.06 (0.11)
Hedges' 95% CI		(-0.16, 0.27)
Hedges' P-value		0.6059

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
mean (SD)	66.75 (11.18)	63.90 (14.79)
Week 52		
n	18	14
mean (SD)	66.37 (12.66)	67.37 (15.56)
Absolute Change at Week 52		
n	18	13
mean (SD)	-0.31 (3.51)	2.45 (4.42)
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	-1.68 (0.89)	3.19 (0.99)
95% CI of LS mean	(-3.50, 0.15)	(1.16, 5.22)
P-value within Treatment	0.0710	0.0031

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.87 (2.08, 7.66)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0013
Hedges' G (SE)		1.21 (0.36)
Hedges' 95% CI		(0.47, 1.95)
Hedges' P-value		0.0021

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	181	175
mean (SD)	67.19 (14.98)	67.47 (15.41)
Week 52		
n	165	162
mean (SD)	67.08 (15.18)	67.17 (15.91)
Absolute Change at Week 52		
n	165	161
mean (SD)	0.40 (5.43)	0.09 (5.57)
Absolute Change through Week 52 (MMRM)		
n	177	173
LS mean (SE)	0.54 (0.33)	0.26 (0.33)
95% CI of LS mean	(-0.11, 1.19)	(-0.40, 0.91)
P-value within Treatment	0.1020	0.4418

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-1.21, 0.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5478
Hedges' G (SE)		-0.06 (0.11)
Hedges' 95% CI		(-0.27, 0.15)
Hedges' P-value		0.5476

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	118	116
mean (SD)	66.72 (14.86)	65.51 (15.58)
Week 52		
n	106	107
mean (SD)	67.25 (14.88)	64.99 (15.87)
Absolute Change at Week 52		
n	106	107
mean (SD)	1.03 (5.03)	0.01 (6.17)
Absolute Change through Week 52 (MMRM)		
n	115	115
LS mean (SE)	0.77 (0.44)	0.38 (0.44)
95% CI of LS mean	(-0.10, 1.63)	(-0.49, 1.24)
P-value within Treatment	0.0815	0.3919

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-1.62, 0.84)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5327
Hedges' G (SE)		-0.08 (0.13)
Hedges' 95% CI		(-0.34, 0.18)
Hedges' P-value		0.5314

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
mean (SD)	67.94 (14.37)	69.33 (14.78)
Week 52		
n	78	70
mean (SD)	66.75 (14.98)	70.21 (15.49)
Absolute Change at Week 52		
n	78	68
mean (SD)	-0.75 (5.54)	0.61 (4.29)
Absolute Change through Week 52 (MMRM)		
n	81	74
LS mean (SE)	-0.13 (0.44)	0.53 (0.46)
95% CI of LS mean	(-1.00, 0.74)	(-0.38, 1.45)
P-value within Treatment	0.7670	0.2489

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.66 (-0.60, 1.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2993
Hedges' G (SE)		0.17 (0.16)
Hedges' 95% CI		(-0.15, 0.48)
Hedges' P-value		0.2989

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	91	87
mean (SD)	68.31 (14.15)	66.88 (15.20)
Week 52		
n	88	75
mean (SD)	67.65 (14.45)	67.18 (15.92)
Absolute Change at Week 52		
n	88	75
mean (SD)	0.03 (5.18)	0.09 (4.09)
Absolute Change through Week 52 (MMRM)		
n	89	85
LS mean (SE)	0.05 (0.39)	0.62 (0.41)
95% CI of LS mean	(-0.73, 0.82)	(-0.18, 1.43)
P-value within Treatment	0.9077	0.1283

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-0.54, 1.70)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3102
Hedges' G (SE)		0.15 (0.15)
Hedges' 95% CI		(-0.14, 0.45)
Hedges' P-value		0.3102

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	110	106
mean (SD)	66.32 (15.03)	67.16 (15.53)
Week 52		
n	96	102
mean (SD)	66.48 (15.32)	66.96 (15.94)
Absolute Change at Week 52		
n	96	100
mean (SD)	0.51 (5.44)	0.36 (6.39)
Absolute Change through Week 52 (MMRM)		
n	107	104
LS mean (SE)	0.59 (0.47)	0.38 (0.48)
95% CI of LS mean	(-0.34, 1.51)	(-0.56, 1.33)
P-value within Treatment	0.2152	0.4237

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-1.53, 1.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7631
Hedges' G (SE)		-0.04 (0.14)
Hedges' 95% CI		(-0.31, 0.23)
Hedges' P-value		0.7631

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Baseline		
n	176	167
mean (SD)	66.29 (14.41)	65.94 (14.98)
Week 52		
n	160	152
mean (SD)	65.94 (14.87)	65.66 (15.49)
Absolute Change at Week 52		
n	160	150
mean (SD)	0.16 (5.04)	0.04 (5.45)
Absolute Change through Week 52 (MMRM)		
n	171	163
LS mean (SE)	0.17 (0.33)	0.37 (0.34)
95% CI of LS mean	(-0.47, 0.82)	(-0.30, 1.03)
P-value within Treatment	0.5967	0.2772

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.19 (-0.73, 1.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6807
Hedges' G (SE)		0.05 (0.11)
Hedges' 95% CI		(-0.17, 0.26)
Hedges' P-value		0.6806

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Baseline		
n	25	26
mean (SD)	73.74 (14.87)	74.04 (16.09)
Week 52		
n	24	25
mean (SD)	74.39 (12.97)	75.53 (15.92)
Absolute Change at Week 52		
n	24	25
mean (SD)	1.08 (6.94)	1.48 (5.84)
Absolute Change through Week 52 (MMRM)		
n	25	26
LS mean (SE)	1.60 (0.95)	1.22 (0.94)
95% CI of LS mean	(-0.32, 3.52)	(-0.67, 3.10)
P-value within Treatment	0.1009	0.1998

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-3.08, 2.32)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7787
Hedges' G (SE)		-0.08 (0.28)
Hedges' 95% CI		(-0.63, 0.48)
Hedges' P-value		0.7779

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9662
Age at screening (<18 years vs. ≥18 years) [2]	0.5181
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5200
Sex (Male vs. Female) [1]	0.8992
Region (North America vs. Rest of the World) [1]	0.4571

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.2722

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	114	100
mean (SD)	22.98 (3.46)	23.15 (3.67)
Week 52		
n	111	93
mean (SD)	23.06 (3.61)	23.35 (3.61)
Absolute Change at Week 52		
n	111	93
mean (SD)	0.05 (1.28)	0.16 (1.02)
Absolute Change at Week 52 (MMRM)		
n	111	92
LS mean (SE)	0.04 (0.11)	0.12 (0.12)
95% CI of LS mean	(-0.17, 0.26)	(-0.12, 0.35)
P-value within Treatment	0.7069	0.3287

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-0.24, 0.39)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6415
Hedges' G (SE)		0.07 (0.14)
Hedges' 95% CI		(-0.21, 0.34)
Hedges' P-value		0.6417

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	87	92
mean (SD)	23.14 (4.33)	22.24 (3.07)
Week 52		
n	77	87
mean (SD)	23.42 (4.14)	22.75 (2.92)
Absolute Change at Week 52		
n	77	87
mean (SD)	0.11 (1.55)	0.47 (1.43)
Absolute Change at Week 52 (MMRM)		
n	76	87
LS mean (SE)	0.13 (0.17)	0.51 (0.16)
95% CI of LS mean	(-0.19, 0.46)	(0.20, 0.82)
P-value within Treatment	0.4201	0.0015

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.37 (-0.08, 0.82)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1035
Hedges' G (SE)		0.26 (0.16)
Hedges' 95% CI		(-0.05, 0.57)
Hedges' P-value		0.1054

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	31	26
mean (SD)	20.11 (3.50)	19.77 (2.85)
Week 52		
n	27	25
mean (SD)	20.58 (3.27)	21.00 (2.36)
Absolute Change at Week 52		
n	27	25
mean (SD)	0.44 (1.70)	1.26 (1.52)
Absolute Change at Week 52 (MMRM)		
n	27	24
LS mean (SE)	0.30 (0.31)	1.21 (0.34)
95% CI of LS mean	(-0.32, 0.92)	(0.53, 1.89)
P-value within Treatment	0.3361	0.0008

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-0.01, 1.83)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0522
Hedges' G (SE)		0.55 (0.28)
Hedges' 95% CI		(-0.02, 1.12)
Hedges' P-value		0.0564

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	171	169
mean (SD)	23.56 (3.67)	23.16 (3.25)
Week 52		
n	162	158
mean (SD)	23.63 (3.74)	23.38 (3.29)
Absolute Change at Week 52		
n	162	158
mean (SD)	0.02 (1.33)	0.16 (1.12)
Absolute Change at Week 52 (MMRM)		
n	160	155
LS mean (SE)	0.04 (0.10)	0.16 (0.10)
95% CI of LS mean	(-0.15, 0.22)	(-0.03, 0.35)
P-value within Treatment	0.7145	0.1049

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-0.15, 0.39)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3674
Hedges' G (SE)		0.10 (0.11)
Hedges' 95% CI		(-0.12, 0.32)
Hedges' P-value		0.3677

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	17
mean (SD)	22.04 (3.10)	22.98 (2.66)
Week 52		
n	17	14
mean (SD)	22.32 (3.78)	23.91 (3.22)
Absolute Change at Week 52		
n	17	14
mean (SD)	0.24 (1.53)	0.80 (1.45)
Absolute Change at Week 52 (MMRM)		
n	17	13
LS mean (SE)	0.22 (0.33)	0.89 (0.37)
95% CI of LS mean	(-0.47, 0.90)	(0.13, 1.65)
P-value within Treatment	0.5246	0.0234

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.67 (-0.35, 1.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1899
Hedges' G (SE)		0.48 (0.36)
Hedges' 95% CI		(-0.27, 1.22)
Hedges' P-value		0.1982

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	182	176
mean (SD)	23.02 (3.57)	22.70 (3.47)
Week 52		
n	171	168
mean (SD)	23.17 (3.57)	22.98 (3.29)
Absolute Change at Week 52		
n	171	168
mean (SD)	0.08 (1.37)	0.27 (1.22)
Absolute Change at Week 52 (MMRM)		
n	170	166
LS mean (SE)	0.06 (0.10)	0.25 (0.10)
95% CI of LS mean	(-0.13, 0.26)	(0.05, 0.45)
P-value within Treatment	0.5188	0.0128

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.19 (-0.09, 0.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1839
Hedges' G (SE)		0.14 (0.11)
Hedges' 95% CI		(-0.07, 0.36)
Hedges' P-value		0.1844

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	119	115
mean (SD)	23.37 (3.57)	23.12 (3.67)
Week 52		
n	111	110
mean (SD)	23.45 (3.55)	23.44 (3.43)
Absolute Change at Week 52		
n	111	110
mean (SD)	0.00 (1.30)	0.17 (1.20)
Absolute Change at Week 52 (MMRM)		
n	110	110
LS mean (SE)	0.00 (0.12)	0.16 (0.12)
95% CI of LS mean	(-0.23, 0.23)	(-0.07, 0.39)
P-value within Treatment	0.9675	0.1702

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.17, 0.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3451
Hedges' G (SE)		0.13 (0.13)
Hedges' 95% CI		(-0.14, 0.39)
Hedges' P-value		0.3454

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	80
mean (SD)	22.56 (4.18)	22.11 (2.87)
Week 52		
n	78	73
mean (SD)	22.83 (4.19)	22.47 (2.97)
Absolute Change at Week 52		
n	78	73
mean (SD)	0.19 (1.52)	0.51 (1.28)
Absolute Change at Week 52 (MMRM)		
n	77	69
LS mean (SE)	0.16 (0.16)	0.51 (0.17)
95% CI of LS mean	(-0.16, 0.48)	(0.18, 0.85)
P-value within Treatment	0.3105	0.0031

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.35 (-0.12, 0.81)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1404
Hedges' G (SE)		0.24 (0.17)
Hedges' 95% CI		(-0.08, 0.57)
Hedges' P-value		0.1418

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	91	87
mean (SD)	23.86 (4.50)	23.30 (3.58)
Week 52		
n	89	78
mean (SD)	23.71 (4.35)	23.43 (3.44)
Absolute Change at Week 52		
n	89	78
mean (SD)	-0.17 (1.47)	-0.03 (1.11)
Absolute Change at Week 52 (MMRM)		
n	88	77
LS mean (SE)	-0.13 (0.14)	-0.07 (0.14)
95% CI of LS mean	(-0.40, 0.14)	(-0.35, 0.22)
P-value within Treatment	0.3552	0.6526

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-0.33, 0.46)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7540
Hedges' G (SE)		0.05 (0.16)
Hedges' 95% CI		(-0.26, 0.36)
Hedges' P-value		0.7544

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	111	108
mean (SD)	22.36 (3.07)	22.23 (3.17)
Week 52		
n	100	105
mean (SD)	22.73 (3.25)	22.77 (3.14)
Absolute Change at Week 52		
n	100	105
mean (SD)	0.30 (1.28)	0.56 (1.27)
Absolute Change at Week 52 (MMRM)		
n	99	102
LS mean (SE)	0.27 (0.13)	0.58 (0.13)
95% CI of LS mean	(0.01, 0.52)	(0.33, 0.83)
P-value within Treatment	0.0380	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-0.04, 0.67)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0812
Hedges' G (SE)		0.25 (0.14)
Hedges' 95% CI		(-0.03, 0.52)
Hedges' P-value		0.0824

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Baseline		
n	177	169
mean (SD)	23.15 (3.85)	22.92 (3.44)
Week 52		
n	165	157
mean (SD)	23.24 (3.76)	23.16 (3.35)
Absolute Change at Week 52		
n	165	157
mean (SD)	0.00 (1.43)	0.18 (1.16)
Absolute Change at Week 52 (MMRM)		
n	163	153
LS mean (SE)	0.01 (0.10)	0.17 (0.10)
95% CI of LS mean	(-0.19, 0.20)	(-0.04, 0.37)
P-value within Treatment	0.9595	0.1080

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.12, 0.45)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2623
Hedges' G (SE)		0.13 (0.11)
Hedges' 95% CI		(-0.10, 0.35)
Hedges' P-value		0.2627

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Baseline		
n	25	26
mean (SD)	22.24 (3.80)	21.30 (2.73)
Week 52		
n	24	26
mean (SD)	22.89 (4.35)	22.39 (2.76)
Absolute Change at Week 52		
n	24	26
mean (SD)	0.58 (0.96)	1.09 (1.44)
Absolute Change at Week 52 (MMRM)		
n	24	26
LS mean (SE)	0.57 (0.25)	1.10 (0.24)
95% CI of LS mean	(0.08, 1.07)	(0.61, 1.59)
P-value within Treatment	0.0248	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.2.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-0.17, 1.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1358
Hedges' G (SE)		0.42 (0.28)
Hedges' 95% CI		(-0.14, 0.99)
Hedges' P-value		0.1403

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52
for Subjects ≤20 Years at Baseline
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.8166
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.0603
Region (North America vs. Rest of the World) [1]	0.0050

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 for Subgroup Prior CFTR Modulator Use
for Subjects ≤20 Years at Baseline
Full Analysis Set

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.5174

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 7
Baseline		
n	13	7
mean (SD)	-0.66 (0.86)	-0.75 (0.99)
Week 52		
n	10	6
mean (SD)	-0.54 (0.95)	-0.59 (0.91)
Absolute Change at Week 52		
n	10	6
mean (SD)	0.13 (0.35)	0.21 (0.49)
Absolute Change at Week 52 (MMRM)		
n	10	6
LS mean (SE)	0.08 (0.16)	0.24 (0.22)
95% CI of LS mean	(-0.28, 0.43)	(-0.25, 0.72)
P-value within Treatment	0.6395	0.3053

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 7
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.45, 0.76)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5723
Hedges' G (SE)		0.29 (0.49)
Hedges' 95% CI		(-0.76, 1.34)
Hedges' P-value		0.5648

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 27	VNZ/TEZ/D-IVA N = 24
Baseline		
n	27	24
mean (SD)	0.10 (0.78)	-0.29 (1.12)
Week 52		
n	22	21
mean (SD)	0.04 (0.71)	-0.02 (0.95)
Absolute Change at Week 52		
n	22	21
mean (SD)	-0.10 (0.59)	0.30 (0.49)
Absolute Change at Week 52 (MMRM)		
n	22	21
LS mean (SE)	-0.14 (0.11)	0.25 (0.12)
95% CI of LS mean	(-0.36, 0.09)	(0.01, 0.48)
P-value within Treatment	0.2225	0.0388

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 27	VNZ/TEZ/D-IVA N = 24
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.38 (0.06, 0.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0209
Hedges' G (SE)		0.72 (0.31)
Hedges' 95% CI		(0.09, 1.34)
Hedges' P-value		0.0254

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 36	VNZ/TEZ/D-IVA N = 31

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 13
Baseline		
n	24	13
mean (SD)	-0.12 (0.86)	-0.73 (1.52)
Week 52		
n	20	11
mean (SD)	-0.19 (0.77)	-0.51 (1.20)
Absolute Change at Week 52		
n	20	11
mean (SD)	-0.20 (0.53)	0.43 (0.54)
Absolute Change at Week 52 (MMRM)		
n	20	11
LS mean (SE)	-0.22 (0.12)	0.35 (0.17)
95% CI of LS mean	(-0.48, 0.03)	(0.00, 0.70)
P-value within Treatment	0.0827	0.0471

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 13
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (0.15, 1.01)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0107
Hedges' G (SE)		1.00 (0.39)
Hedges' 95% CI		(0.21, 1.80)
Hedges' P-value		0.0147

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 19
Baseline		
n	16	19
mean (SD)	-0.18 (0.94)	-0.11 (0.57)
Week 52		
n	12	17
mean (SD)	-0.05 (0.94)	0.13 (0.68)
Absolute Change at Week 52		
n	12	17
mean (SD)	0.27 (0.39)	0.19 (0.42)
Absolute Change at Week 52 (MMRM)		
n	12	16
LS mean (SE)	0.18 (0.11)	0.17 (0.10)
95% CI of LS mean	(-0.04, 0.40)	(-0.03, 0.38)
P-value within Treatment	0.0995	0.0886

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 19
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-0.31, 0.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9515
Hedges' G (SE)		-0.02 (0.37)
Hedges' 95% CI		(-0.78, 0.74)
Hedges' P-value		0.9519

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 11
Baseline		
n	20	11
mean (SD)	0.11 (0.97)	0.09 (0.93)
Week 52		
n	16	10
mean (SD)	0.10 (0.97)	0.21 (0.75)
Absolute Change at Week 52		
n	16	10
mean (SD)	-0.13 (0.60)	0.04 (0.45)
Absolute Change at Week 52 (MMRM)		
n	16	10
LS mean (SE)	-0.22 (0.16)	0.02 (0.20)
95% CI of LS mean	(-0.55, 0.11)	(-0.40, 0.45)
P-value within Treatment	0.1753	0.9087

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 11
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-0.29, 0.78)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3516
Hedges' G (SE)		0.37 (0.39)
Hedges' 95% CI		(-0.44, 1.19)
Hedges' P-value		0.3529

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 21
Baseline		
n	20	21
mean (SD)	-0.39 (0.71)	-0.60 (1.11)
Week 52		
n	16	18
mean (SD)	-0.38 (0.58)	-0.30 (1.02)
Absolute Change at Week 52		
n	16	18
mean (SD)	0.08 (0.44)	0.42 (0.45)
Absolute Change at Week 52 (MMRM)		
n	16	17
LS mean (SE)	0.01 (0.11)	0.39 (0.11)
95% CI of LS mean	(-0.21, 0.24)	(0.16, 0.61)
P-value within Treatment	0.9040	0.0014

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 21
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.37 (0.06, 0.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0224
Hedges' G (SE)		0.81 (0.35)
Hedges' 95% CI		(0.09, 1.54)
Hedges' P-value		0.0284

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52
for Subjects ≤20 Years at Baseline for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 33	VNZ/TEZ/D-IVA N = 24
Baseline		
n	33	24
mean (SD)	-0.12 (0.94)	-0.43 (1.21)
Week 52		
n	25	22
mean (SD)	-0.05 (0.89)	-0.22 (1.03)
Absolute Change at Week 52		
n	25	22
mean (SD)	0.02 (0.57)	0.23 (0.46)
Absolute Change at Week 52 (MMRM)		
n	25	21
LS mean (SE)	-0.08 (0.11)	0.20 (0.12)
95% CI of LS mean	(-0.30, 0.13)	(-0.05, 0.44)
P-value within Treatment	0.4368	0.1188

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52
for Subjects ≤20 Years at Baseline for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 33	VNZ/TEZ/D-IVA N = 24
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.28 (-0.05, 0.61)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0934
Hedges' G (SE)		0.50 (0.30)
Hedges' 95% CI		(-0.09, 1.10)
Hedges' P-value		0.0969

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52
for Subjects ≤20 Years at Baseline for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 8
Baseline		
n	7	8
mean (SD)	-0.27 (0.49)	-0.17 (0.59)
Week 52		
n	7	6
mean (SD)	-0.46 (0.43)	0.26 (0.50)
Absolute Change at Week 52		
n	7	6
mean (SD)	-0.20 (0.36)	0.49 (0.52)
Absolute Change at Week 52 (MMRM)		
n	7	6
LS mean (SE)	-0.21 (0.17)	0.39 (0.17)
95% CI of LS mean	(-0.59, 0.17)	(0.01, 0.77)
P-value within Treatment	0.2448	0.0453

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52
for Subjects ≤20 Years at Baseline for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 8
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (0.06, 1.14)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0317
Hedges' G (SE)		1.27 (0.57)
Hedges' 95% CI		(0.00, 2.53)
Hedges' P-value		0.0494

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4819
Age at screening (<18 years vs. ≥18 years) [2]	0.9853
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.7441
Sex (Male vs. Female) [1]	0.7924
Region (North America vs. Rest of the World) [1]	0.5840

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.4.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.5553

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	114	99
mean (SD)	54.09 (18.79)	52.37 (17.15)
Week 52		
n	107	86
mean (SD)	53.81 (18.80)	44.25 (18.94)
Absolute Change at Week 52		
n	107	85
mean (SD)	-0.76 (10.16)	-9.58 (10.82)
Absolute Change through Week 52 (MMRM)		
n	112	98
LS mean (SE)	0.85 (0.93)	-7.87 (1.01)
95% CI of LS mean	(-0.99, 2.69)	(-9.85, -5.88)
P-value within Treatment	0.3623	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.72 (-11.43, -6.01)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.88 (0.14)
Hedges' 95% CI		(-1.16, -0.59)
Hedges' P-value		<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	86	92
mean (SD)	54.49 (17.65)	54.66 (16.55)
Week 52		
n	78	82
mean (SD)	52.79 (19.08)	48.73 (22.70)
Absolute Change at Week 52		
n	77	82
mean (SD)	-1.37 (14.27)	-6.91 (14.11)
Absolute Change through Week 52 (MMRM)		
n	83	90
LS mean (SE)	0.28 (0.96)	-7.26 (0.93)
95% CI of LS mean	(-1.62, 2.18)	(-9.10, -5.43)
P-value within Treatment	0.7696	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.55 (-10.19, -4.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.85 (0.16)
Hedges' 95% CI		(-1.17, -0.54)
Hedges' P-value		<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	31	26
mean (SD)	50.43 (13.77)	54.83 (16.58)
Week 52		
n	26	22
mean (SD)	53.69 (19.56)	51.14 (24.87)
Absolute Change at Week 52		
n	26	22
mean (SD)	2.79 (16.77)	-5.90 (15.76)
Absolute Change through Week 52 (MMRM)		
n	29	24
LS mean (SE)	2.03 (2.06)	-5.79 (2.27)
95% CI of LS mean	(-2.10, 6.16)	(-10.34, -1.24)
P-value within Treatment	0.3275	0.0137

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.82 (-13.99, -1.65)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0140
Hedges' G (SE)		-0.70 (0.28)
Hedges' 95% CI		(-1.26, -0.13)
Hedges' P-value		0.0164

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	170	168
mean (SD)	54.98 (18.86)	53.35 (17.16)
Week 52		
n	160	149
mean (SD)	53.39 (18.78)	45.86 (20.14)
Absolute Change at Week 52		
n	159	148
mean (SD)	-1.59 (10.98)	-8.58 (12.10)
Absolute Change through Week 52 (MMRM)		
n	166	164
LS mean (SE)	0.22 (0.70)	-7.74 (0.71)
95% CI of LS mean	(-1.16, 1.60)	(-9.15, -6.34)
P-value within Treatment	0.7568	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.96 (-9.93, -5.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.87 (0.11)
Hedges' 95% CI		(-1.10, -0.65)
Hedges' P-value		<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	17
mean (SD)	23.78 (6.24)	24.96 (2.17)
Week 52		
n	16	12
mean (SD)	24.53 (7.90)	23.21 (7.27)
Absolute Change at Week 52		
n	16	12
mean (SD)	0.23 (5.81)	-1.67 (6.87)
Absolute Change through Week 52 (MMRM)		
n	18	16
LS mean (SE)	7.82 (2.09)	-1.71 (2.25)
95% CI of LS mean	(3.54, 12.11)	(-6.31, 2.89)
P-value within Treatment	0.0008	0.4526

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.53 (-15.88, -3.19)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0046
Hedges' G (SE)		-1.04 (0.36)
Hedges' 95% CI		(-1.77, -0.31)
Hedges' P-value		0.0066

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	182	177
mean (SD)	57.46 (15.97)	56.30 (15.22)
Week 52		
n	169	158
mean (SD)	56.28 (17.17)	48.29 (20.50)
Absolute Change at Week 52		
n	169	158
mean (SD)	-1.09 (12.43)	-8.74 (12.82)
Absolute Change through Week 52 (MMRM)		
n	177	172
LS mean (SE)	-0.17 (0.70)	-8.07 (0.72)
95% CI of LS mean	(-1.55, 1.21)	(-9.48, -6.66)
P-value within Treatment	0.8087	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.90 (-9.88, -5.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.84 (0.11)
Hedges' 95% CI		(-1.06, -0.62)
Hedges' P-value		<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	119	116
mean (SD)	57.27 (17.13)	54.20 (16.36)
Week 52		
n	112	105
mean (SD)	56.98 (17.51)	47.49 (20.16)
Absolute Change at Week 52		
n	112	105
mean (SD)	-0.13 (12.79)	-8.03 (12.79)
Absolute Change through Week 52 (MMRM)		
n	115	115
LS mean (SE)	0.63 (0.90)	-6.75 (0.91)
95% CI of LS mean	(-1.15, 2.41)	(-8.54, -4.96)
P-value within Treatment	0.4848	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.38 (-9.91, -4.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.76 (0.14)
Hedges' 95% CI		(-1.03, -0.49)
Hedges' P-value		<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	82	78
mean (SD)	49.92 (18.96)	52.59 (18.08)
Week 52		
n	74	66
mean (SD)	48.05 (19.60)	45.02 (21.86)
Absolute Change at Week 52		
n	73	65
mean (SD)	-2.27 (10.63)	-8.58 (12.42)
Absolute Change through Week 52 (MMRM)		
n	80	73
LS mean (SE)	0.49 (0.99)	-8.83 (1.05)
95% CI of LS mean	(-1.47, 2.44)	(-10.92, -6.75)
P-value within Treatment	0.6243	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.32 (-12.18, -6.45)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-1.04 (0.17)
Hedges' 95% CI		(-1.38, -0.70)
Hedges' P-value		<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	90	85
mean (SD)	57.05 (16.97)	55.27 (17.04)
Week 52		
n	86	73
mean (SD)	57.67 (18.13)	49.05 (20.49)
Absolute Change at Week 52		
n	85	72
mean (SD)	1.01 (12.42)	-8.68 (10.96)
Absolute Change through Week 52 (MMRM)		
n	89	85
LS mean (SE)	0.76 (0.88)	-9.03 (0.92)
95% CI of LS mean	(-0.98, 2.50)	(-10.84, -7.21)
P-value within Treatment	0.3889	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.79 (-12.30, -7.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-1.16 (0.16)
Hedges' 95% CI		(-1.48, -0.84)
Hedges' P-value		<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	111	109
mean (SD)	52.02 (18.94)	52.21 (17.01)
Week 52		
n	100	98
mean (SD)	49.79 (18.75)	44.66 (20.94)
Absolute Change at Week 52		
n	100	98
mean (SD)	-2.66 (11.43)	-7.91 (13.75)
Absolute Change through Week 52 (MMRM)		
n	106	103
LS mean (SE)	0.32 (0.98)	-6.26 (1.00)
95% CI of LS mean	(-1.62, 2.26)	(-8.23, -4.29)
P-value within Treatment	0.7468	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.58 (-9.34, -3.81)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.65 (0.14)
Hedges' 95% CI		(-0.93, -0.37)
Hedges' P-value		<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Baseline		
n	176	168
mean (SD)	53.02 (17.81)	52.93 (16.27)
Week 52		
n	163	147
mean (SD)	53.36 (18.97)	46.43 (20.19)
Absolute Change at Week 52		
n	162	146
mean (SD)	0.10 (11.69)	-7.65 (12.60)
Absolute Change through Week 52 (MMRM)		
n	170	162
LS mean (SE)	0.89 (0.69)	-6.91 (0.71)
95% CI of LS mean	(-0.46, 2.25)	(-8.32, -5.51)
P-value within Treatment	0.1961	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.81 (-9.76, -5.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.86 (0.11)
Hedges' 95% CI		(-1.09, -0.64)
Hedges' P-value		<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Baseline		
n	25	26
mean (SD)	63.14 (18.95)	57.54 (21.38)
Week 52		
n	23	24
mean (SD)	53.93 (18.20)	47.19 (24.73)
Absolute Change at Week 52		
n	23	24
mean (SD)	-8.58 (11.65)	-11.79 (12.37)
Absolute Change through Week 52 (MMRM)		
n	25	26
LS mean (SE)	-1.98 (2.26)	-11.15 (2.22)
95% CI of LS mean	(-6.53, 2.57)	(-15.61, -6.69)
P-value within Treatment	0.3862	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.17 (-15.57, -2.78)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0059
Hedges' G (SE)		-0.80 (0.29)
Hedges' 95% CI		(-1.38, -0.22)
Hedges' P-value		0.0076

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.4.2.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1930*
Age at screening (<18 years vs. ≥18 years) [2]	0.8045*
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5013
Sex (Male vs. Female) [1]	0.4966*
Region (North America vs. Rest of the World) [1]	0.6613*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.4.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Subgroup	P-value for Interaction based on Relative Risk
Prior CFTR modulator use (yes vs. no)	0.0956*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline <70%

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Non-missing value at Week 52, N1	107	86
Number of subjects with missing value at Week 52	7	15
SwCl <30 mmol/L at Week 52, n (%)	60 (52.63)	68 (67.33)
Relative Risk (RR) (95% CI)		1.2685 (1.0363, 1.5528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0211*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline ≥70%

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Non-missing value at Week 52, N1	78	82
Number of subjects with missing value at Week 52	9	10
SwCl <30 mmol/L at Week 52, n (%)	57 (65.52)	62 (67.39)
Relative Risk (RR) (95% CI)		1.0335 (0.8492, 1.2577)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7426*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening < 18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Non-missing value at Week 52, N1	26	22
Number of subjects with missing value at Week 52	5	4
SwCl <30 mmol/L at Week 52, n (%)	18 (58.06)	16 (61.54)
Relative Risk (RR) (95% CI)		1.0968 (0.7092, 1.6963)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6778

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening ≥ 18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Non-missing value at Week 52, N1	160	149
Number of subjects with missing value at Week 52	11	21
SwCl <30 mmol/L at Week 52, n (%)	99 (57.89)	116 (68.24)
Relative Risk (RR) (95% CI)		1.1629 (1.0012, 1.3506)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0482*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Non-missing value at Week 52, N1	16	12
Number of subjects with missing value at Week 52	3	5
SwCl <30 mmol/L at Week 52, n (%)	16 (84.21)	12 (70.59)
Relative Risk (RR) (95% CI)		0.7455 (0.5239, 1.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1026*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Non-missing value at Week 52, N1	169	158
Number of subjects with missing value at Week 52	13	19
SwCl <30 mmol/L at Week 52, n (%)	100 (54.95)	119 (67.23)
Relative Risk (RR) (95% CI)		1.1157 (0.9825, 1.2668)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0913

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Non-missing value at Week 52, N1	112	105
Number of subjects with missing value at Week 52	7	11
SwCl <30 mmol/L at Week 52, n (%)	64 (53.78)	80 (68.97)
Relative Risk (RR) (95% CI)		1.1129 (0.9112, 1.3593)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2943

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Non-missing value at Week 52, N1	74	66
Number of subjects with missing value at Week 52	9	14
SwCl <30 mmol/L at Week 52, n (%)	53 (63.86)	52 (65.00)
Relative Risk (RR) (95% CI)		1.0880 (0.8813, 1.3433)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4328*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Non-missing value at Week 52, N1	86	73
Number of subjects with missing value at Week 52	5	14
SwCl <30 mmol/L at Week 52, n (%)	48 (52.75)	52 (59.77)
Relative Risk (RR) (95% CI)		1.1035 (0.8662, 1.4058)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4254*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.2.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Non-missing value at Week 52, N1	100	98
Number of subjects with missing value at Week 52	11	11
SwCl <30 mmol/L at Week 52, n (%)	69 (62.16)	80 (73.39)
Relative Risk (RR) (95% CI)		1.1809 (0.9954, 1.4010)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0565*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.4.2.2.1
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Non-missing value at Week 52, N1	163	147
Number of subjects with missing value at Week 52	14	23
SwCl <60 mmol/L at Week 52, n (%)	99 (55.93)	113 (66.47)
Relative Risk (RR) (95% CI)		1.2006 (1.0263, 1.4046)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0224*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- N/C: model does not converge.

Table 1.2.2.4.2.2.1
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Non-missing value at Week 52, N1	23	24
Number of subjects with missing value at Week 52	2	2
SwCl <60 mmol/L at Week 52, n (%)	18 (72.00)	19 (73.08)
Relative Risk (RR) (95% CI)		0.9088 (0.6583, 1.2546)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5611*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- Generalized Linear Model: treatment group and age at screening (<18 vs ≥18 years) as factors, baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.4.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.8520*
Age at screening (<18 years vs. ≥18 years) [2]	0.3259*
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0562*
Sex (Male vs. Female) [1]	0.5638*
Region (North America vs. Rest of the World) [1]	0.2015*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.4.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 for Subgroup
Prior CFTR Modulator Use
Full Analysis Set

Subgroup	P-value for Interaction based on Relative Risk
Prior CFTR modulator use (yes vs. no)	0.8040*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline ppFEV$_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline <70%

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Non-missing value at Week 52, N1	107	86
Number of subjects with missing value at Week 52	7	15
SwCl <30 mmol/L at Week 52, n (%)	15 (13.16)	24 (23.76)
Relative Risk (RR) (95% CI)		2.1099 (1.2915, 3.4470)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0029*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline ≥70%

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Non-missing value at Week 52, N1	78	82
Number of subjects with missing value at Week 52	9	10
SwCl <30 mmol/L at Week 52, n (%)	10 (11.49)	17 (18.48)
Relative Risk (RR) (95% CI)		1.8813 (0.9901, 3.5746)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0536*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening < 18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Non-missing value at Week 52, N1	26	22
Number of subjects with missing value at Week 52	5	4
SwCl <30 mmol/L at Week 52, n (%)	5 (16.13)	4 (15.38)
Relative Risk (RR) (95% CI)		1.3516 (0.4579, 3.9897)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5854*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening ≥ 18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Non-missing value at Week 52, N1	160	149
Number of subjects with missing value at Week 52	11	21
SwCl <30 mmol/L at Week 52, n (%)	20 (11.70)	37 (21.76)
Relative Risk (RR) (95% CI)		2.1451 (1.4042, 3.2769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0004*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Non-missing value at Week 52, N1	16	12
Number of subjects with missing value at Week 52	3	5
SwCl <30 mmol/L at Week 52, n (%)	13 (68.42)	10 (58.82)
Relative Risk (RR) (95% CI)		0.9255 (0.5760, 1.4869)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7488

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Non-missing value at Week 52, N1	169	158
Number of subjects with missing value at Week 52	13	19
SwCl <30 mmol/L at Week 52, n (%)	12 (6.59)	31 (17.51)
Relative Risk (RR) (95% CI)		2.7920 (1.5863, 4.9142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0004*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Non-missing value at Week 52, N1	112	105
Number of subjects with missing value at Week 52	7	11
SwCl <30 mmol/L at Week 52, n (%)	9 (7.56)	22 (18.97)
Relative Risk (RR) (95% CI)		2.3565 (1.2977, 4.2792)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0049*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Non-missing value at Week 52, N1	74	66
Number of subjects with missing value at Week 52	9	14
SwCl <30 mmol/L at Week 52, n (%)	16 (19.28)	19 (23.75)
Relative Risk (RR) (95% CI)		1.6772 (1.0117, 2.7803)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0449*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Non-missing value at Week 52, N1	86	73
Number of subjects with missing value at Week 52	5	14
SwCl <30 mmol/L at Week 52, n (%)	5 (5.49)	15 (17.24)
Relative Risk (RR) (95% CI)		2.9524 (1.4412, 6.0483)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0031*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Non-missing value at Week 52, N1	100	98
Number of subjects with missing value at Week 52	11	11
SwCl <30 mmol/L at Week 52, n (%)	20 (18.02)	26 (23.85)
Relative Risk (RR) (95% CI)		1.6460 (1.0479, 2.5854)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0305*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 1.2.2.4.3.2.1
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Non-missing value at Week 52, N1	163	147
Number of subjects with missing value at Week 52	14	23
SwCl <30 mmol/L at Week 52, n (%)	24 (13.56)	36 (21.18)
Relative Risk (RR) (95% CI)		2.0349 (1.3485, 3.0707)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0007*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- N/C: model does not converge.

Table 1.2.2.4.3.2.1
Study VX20-121-102: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Non-missing value at Week 52, N1	23	24
Number of subjects with missing value at Week 52	2	2
SwCl <30 mmol/L at Week 52, n (%)	1 (4.00)	5 (19.23)
Relative Risk (RR) (95% CI)		3.6849 (0.5796, 23.4279)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1670*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- Generalized Linear Model: treatment group, baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- N/C: model does not converge.

Table 1.2.2.5.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9737
Age at screening (<18 years vs. ≥18 years) [2]	0.5553
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.8257
Sex (Male vs. Female) [1]	0.8473
Region (North America vs. Rest of the World) [1]	0.4315

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.5.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.2798

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	114	100
mean (SD)	64.31 (12.83)	66.55 (13.57)
Week 52		
n	111	93
mean (SD)	64.86 (12.99)	67.76 (13.21)
Absolute Change at Week 52		
n	111	93
mean (SD)	0.35 (3.64)	0.55 (3.10)
Absolute Change at Week 52 (MMRM)		
n	111	92
LS mean (SE)	0.31 (0.32)	0.44 (0.35)
95% CI of LS mean	(-0.31, 0.94)	(-0.24, 1.12)
P-value within Treatment	0.3252	0.2026

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.80, 1.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7842
Hedges' G (SE)		0.04 (0.14)
Hedges' 95% CI		(-0.24, 0.32)
Hedges' P-value		0.7844

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	87	92
mean (SD)	64.90 (15.00)	63.68 (13.08)
Week 52		
n	77	87
mean (SD)	66.22 (14.12)	65.42 (12.33)
Absolute Change at Week 52		
n	77	87
mean (SD)	0.74 (4.74)	1.56 (4.25)
Absolute Change at Week 52 (MMRM)		
n	76	87
LS mean (SE)	0.77 (0.49)	1.65 (0.47)
95% CI of LS mean	(-0.20, 1.75)	(0.72, 2.58)
P-value within Treatment	0.1195	0.0006

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-0.47, 2.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2022
Hedges' G (SE)		0.20 (0.16)
Hedges' 95% CI		(-0.11, 0.51)
Hedges' P-value		0.2039

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	31	26
mean (SD)	52.79 (13.27)	52.30 (10.26)
Week 52		
n	27	25
mean (SD)	55.90 (11.49)	56.60 (8.21)
Absolute Change at Week 52		
n	27	25
mean (SD)	2.82 (5.45)	4.64 (4.01)
Absolute Change at Week 52 (MMRM)		
n	27	24
LS mean (SE)	2.47 (0.93)	4.61 (1.01)
95% CI of LS mean	(0.60, 4.34)	(2.57, 6.65)
P-value within Treatment	0.0106	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.14 (-0.62, 4.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1260
Hedges' G (SE)		0.43 (0.28)
Hedges' 95% CI		(-0.13, 0.99)
Hedges' P-value		0.1298

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	171	169
mean (SD)	66.67 (12.75)	67.05 (12.65)
Week 52		
n	162	158
mean (SD)	66.98 (13.08)	68.09 (12.66)
Absolute Change at Week 52		
n	162	158
mean (SD)	0.13 (3.72)	0.46 (3.34)
Absolute Change at Week 52 (MMRM)		
n	160	155
LS mean (SE)	0.16 (0.28)	0.46 (0.28)
95% CI of LS mean	(-0.38, 0.71)	(-0.10, 1.01)
P-value within Treatment	0.5542	0.1047

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-0.48, 1.07)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4569
Hedges' G (SE)		0.08 (0.11)
Hedges' 95% CI		(-0.14, 0.31)
Hedges' P-value		0.4571

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	17
mean (SD)	58.59 (12.74)	65.53 (8.06)
Week 52		
n	17	14
mean (SD)	60.35 (14.93)	69.02 (10.01)
Absolute Change at Week 52		
n	17	14
mean (SD)	1.05 (4.76)	2.45 (4.28)
Absolute Change at Week 52 (MMRM)		
n	17	13
LS mean (SE)	0.95 (1.02)	2.62 (1.13)
95% CI of LS mean	(-1.12, 3.02)	(0.32, 4.92)
P-value within Treatment	0.3556	0.0271

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.66 (-1.44, 4.76)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2824
Hedges' G (SE)		0.39 (0.36)
Hedges' 95% CI		(-0.35, 1.13)
Hedges' P-value		0.2894

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	182	176
mean (SD)	64.91 (13.36)	65.17 (13.73)
Week 52		
n	171	168
mean (SD)	65.68 (12.93)	66.34 (13.00)
Absolute Change at Week 52		
n	171	168
mean (SD)	0.50 (4.02)	0.91 (3.67)
Absolute Change at Week 52 (MMRM)		
n	170	166
LS mean (SE)	0.45 (0.29)	0.88 (0.30)
95% CI of LS mean	(-0.12, 1.03)	(0.29, 1.46)
P-value within Treatment	0.1209	0.0033

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.42 (-0.40, 1.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3093
Hedges' G (SE)		0.11 (0.11)
Hedges' 95% CI		(-0.10, 0.33)
Hedges' P-value		0.3096

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	119	115
mean (SD)	69.01 (13.62)	69.99 (14.06)
Week 52		
n	111	110
mean (SD)	69.83 (13.13)	71.26 (12.81)
Absolute Change at Week 52		
n	111	110
mean (SD)	0.34 (4.13)	0.72 (3.78)
Absolute Change at Week 52 (MMRM)		
n	110	110
LS mean (SE)	0.34 (0.37)	0.69 (0.37)
95% CI of LS mean	(-0.38, 1.07)	(-0.04, 1.42)
P-value within Treatment	0.3489	0.0635

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (-0.68, 1.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5104
Hedges' G (SE)		0.09 (0.13)
Hedges' 95% CI		(-0.18, 0.35)
Hedges' P-value		0.5104

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	80
mean (SD)	58.14 (11.22)	58.03 (8.05)
Week 52		
n	78	73
mean (SD)	59.09 (11.16)	59.37 (8.78)
Absolute Change at Week 52		
n	78	73
mean (SD)	0.75 (4.10)	1.51 (3.60)
Absolute Change at Week 52 (MMRM)		
n	77	69
LS mean (SE)	0.68 (0.44)	1.52 (0.47)
95% CI of LS mean	(-0.20, 1.55)	(0.59, 2.44)
P-value within Treatment	0.1296	0.0015

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.84 (-0.44, 2.11)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1956
Hedges' G (SE)		0.21 (0.17)
Hedges' 95% CI		(-0.11, 0.54)
Hedges' P-value		0.1968

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	91	87
mean (SD)	65.11 (15.37)	66.99 (13.97)
Week 52		
n	89	78
mean (SD)	64.99 (14.46)	68.05 (13.51)
Absolute Change at Week 52		
n	89	78
mean (SD)	-0.19 (4.21)	0.04 (3.12)
Absolute Change at Week 52 (MMRM)		
n	88	77
LS mean (SE)	-0.08 (0.39)	-0.07 (0.41)
95% CI of LS mean	(-0.85, 0.69)	(-0.88, 0.73)
P-value within Treatment	0.8439	0.8620

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-1.11, 1.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9918
Hedges' G (SE)		0.00 (0.16)
Hedges' 95% CI		(-0.31, 0.31)
Hedges' P-value		0.9918

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	111	108
mean (SD)	64.08 (12.31)	63.55 (12.62)
Week 52		
n	100	105
mean (SD)	65.76 (12.47)	65.38 (12.12)
Absolute Change at Week 52		
n	100	105
mean (SD)	1.13 (3.94)	1.77 (3.96)
Absolute Change at Week 52 (MMRM)		
n	99	102
LS mean (SE)	1.02 (0.39)	1.85 (0.39)
95% CI of LS mean	(0.26, 1.79)	(1.08, 2.62)
P-value within Treatment	0.0091	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.83 (-0.26, 1.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1334
Hedges' G (SE)		0.21 (0.14)
Hedges' 95% CI		(-0.07, 0.49)
Hedges' P-value		0.1346

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Baseline		
n	177	169
mean (SD)	64.79 (13.99)	65.59 (13.44)
Week 52		
n	165	157
mean (SD)	65.44 (13.58)	66.76 (12.95)
Absolute Change at Week 52		
n	165	157
mean (SD)	0.26 (4.20)	0.66 (3.50)
Absolute Change at Week 52 (MMRM)		
n	163	153
LS mean (SE)	0.26 (0.30)	0.63 (0.31)
95% CI of LS mean	(-0.33, 0.84)	(0.03, 1.24)
P-value within Treatment	0.3894	0.0398

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.38 (-0.46, 1.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3775
Hedges' G (SE)		0.10 (0.11)
Hedges' 95% CI		(-0.12, 0.32)
Hedges' P-value		0.3777

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Baseline		
n	25	26
mean (SD)	62.80 (12.03)	61.81 (12.22)
Week 52		
n	24	26
mean (SD)	65.11 (12.45)	65.08 (11.71)
Absolute Change at Week 52		
n	24	26
mean (SD)	2.24 (2.90)	3.27 (4.27)
Absolute Change at Week 52 (MMRM)		
n	24	26
LS mean (SE)	2.20 (0.74)	3.29 (0.72)
95% CI of LS mean	(0.70, 3.69)	(1.83, 4.74)
P-value within Treatment	0.0048	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.5.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-0.99, 3.18)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2978
Hedges' G (SE)		0.29 (0.28)
Hedges' 95% CI		(-0.27, 0.86)
Hedges' P-value		0.3004

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.6.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9963
Age at screening (<18 years vs. ≥18 years) [2]	0.3480
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0951
Sex (Male vs. Female) [1]	0.4719
Region (North America vs. Rest of the World) [1]	0.8818

-Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride, and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride.

Table 1.2.2.6.1.1.1

Study VX20-121-102: Treatment by Subgroup Factor Interaction for Time-to-First Pulmonary Exacerbation through Week 52 for Subgroup Prior CFTR Modulator Use

Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
Prior CFTR modulator use (yes vs. no)	0.5446

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline ppFEV$_1$ and baseline sweat chloride, and age at screening (<18 vs ≥18 years).

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	41 (35.96)	32 (31.68)
Subjects Censored	73 (64.04)	69 (68.32)
Event-free time (weeks)		
75 percent subjects	24.4286	27.7143
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9737 (0.9206, 0.9914)	0.9901 (0.9318, 0.9986)
4 Weeks	0.9474 (0.8866, 0.9760)	0.9802 (0.9231, 0.9950)
8 Weeks	0.9120 (0.8425, 0.9516)	0.9304 (0.8595, 0.9662)
12 Weeks	0.8677 (0.7901, 0.9180)	0.9004 (0.8227, 0.9451)
16 Weeks	0.8323 (0.7497, 0.8896)	0.8604 (0.7756, 0.9148)
24 Weeks	0.7614 (0.6717, 0.8297)	0.7703 (0.6749, 0.8410)
36 Weeks	0.6905 (0.5964, 0.7669)	0.7095 (0.6096, 0.7882)
52 Weeks	0.6367 (0.5407, 0.7179)	0.6777 (0.5759, 0.7601)
Hazard Ratio (95% CI)*	-	0.8410 (0.5274, 1.3412)
Two-sided P-value, superiority*	-	0.4672

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	19 (21.84)	18 (19.57)
Subjects Censored	68 (78.16)	74 (80.43)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9885 (0.9212, 0.9984)	0.9891 (0.9253, 0.9985)
4 Weeks	0.9885 (0.9212, 0.9984)	0.9783 (0.9159, 0.9945)
8 Weeks	0.9652 (0.8961, 0.9887)	0.9457 (0.8744, 0.9770)
12 Weeks	0.9420 (0.8662, 0.9754)	0.9239 (0.8470, 0.9630)
16 Weeks	0.9181 (0.8359, 0.9601)	0.9022 (0.8204, 0.9479)
24 Weeks	0.8943 (0.8067, 0.9436)	0.8689 (0.7807, 0.9233)
36 Weeks	0.8105 (0.7093, 0.8794)	0.8466 (0.7547, 0.9062)
52 Weeks	0.7705 (0.6635, 0.8473)	0.8021 (0.7043, 0.8704)
Hazard Ratio (95% CI)*	-	0.8557 (0.4483, 1.6331)
Two-sided P-value, superiority*	-	0.6365

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	6 (19.35)	2 (7.69)
Subjects Censored	25 (80.65)	24 (92.31)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	0.9615 (0.7569, 0.9945)
12 Weeks	1.0000 (-, -)	0.9615 (0.7569, 0.9945)
16 Weeks	1.0000 (-, -)	0.9615 (0.7569, 0.9945)
24 Weeks	0.9310 (0.7514, 0.9823)	0.9215 (0.7208, 0.9798)
36 Weeks	0.8607 (0.6701, 0.9453)	0.9215 (0.7208, 0.9798)
52 Weeks	0.7873 (0.5861, 0.8985)	0.9215 (0.7208, 0.9798)
Hazard Ratio (95% CI)*	-	0.3827 (0.0752, 1.9486)
Two-sided P-value, superiority*	-	0.2474

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	54 (31.58)	48 (28.24)
Subjects Censored	117 (68.42)	122 (71.76)
Event-free time (weeks)		
75 percent subjects	27.1429	37.7143
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9766 (0.9389, 0.9912)	0.9882 (0.9538, 0.9970)
4 Weeks	0.9591 (0.9161, 0.9803)	0.9765 (0.9385, 0.9911)
8 Weeks	0.9238 (0.8723, 0.9550)	0.9351 (0.8860, 0.9636)
12 Weeks	0.8825 (0.8238, 0.9225)	0.9056 (0.8505, 0.9410)
16 Weeks	0.8469 (0.7834, 0.8931)	0.8700 (0.8094, 0.9124)
24 Weeks	0.7995 (0.7310, 0.8524)	0.8045 (0.7363, 0.8568)
36 Weeks	0.7224 (0.6483, 0.7835)	0.7563 (0.6841, 0.8143)
52 Weeks	0.6803 (0.6041, 0.7449)	0.7133 (0.6383, 0.7756)
Hazard Ratio (95% CI)*	-	0.8842 (0.5989, 1.3054)
Two-sided P-value, superiority*	-	0.5358

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	7 (36.84)	2 (11.76)
Subjects Censored	12 (63.16)	15 (88.24)
Event-free time (weeks)		
75 percent subjects	18.2857	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
4 Weeks	0.8947 (0.6408, 0.9726)	1.0000 (-, -)
8 Weeks	0.8947 (0.6408, 0.9726)	1.0000 (-, -)
12 Weeks	0.7895 (0.5319, 0.9153)	1.0000 (-, -)
16 Weeks	0.7895 (0.5319, 0.9153)	1.0000 (-, -)
24 Weeks	0.6842 (0.4279, 0.8439)	0.9412 (0.6502, 0.9915)
36 Weeks	0.6842 (0.4279, 0.8439)	0.8824 (0.6060, 0.9692)
52 Weeks	0.6272 (0.3725, 0.8022)	0.8824 (0.6060, 0.9692)
Hazard Ratio (95% CI)*	-	0.1796 (0.0272, 1.1873)
Two-sided P-value, superiority*	-	0.0748

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	53 (29.12)	48 (27.12)
Subjects Censored	129 (70.88)	129 (72.88)
Event-free time (weeks)		
75 percent subjects	36.1429	38.7143
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9835 (0.9498, 0.9947)	0.9887 (0.9556, 0.9972)
4 Weeks	0.9725 (0.9351, 0.9884)	0.9774 (0.9409, 0.9915)
8 Weeks	0.9391 (0.8928, 0.9658)	0.9320 (0.8834, 0.9608)
12 Weeks	0.9113 (0.8592, 0.9447)	0.9036 (0.8495, 0.9390)
16 Weeks	0.8775 (0.8199, 0.9176)	0.8694 (0.8101, 0.9113)
24 Weeks	0.8325 (0.7693, 0.8798)	0.8061 (0.7395, 0.8574)
36 Weeks	0.7480 (0.6775, 0.8053)	0.7656 (0.6955, 0.8216)
52 Weeks	0.7011 (0.6276, 0.7628)	0.7250 (0.6522, 0.7851)
Hazard Ratio (95% CI)*	-	0.9320 (0.6304, 1.3778)
Two-sided P-value, superiority*	-	0.7239

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	29 (24.37)	29 (25.00)
Subjects Censored	90 (75.63)	87 (75.00)
Event-free time (weeks)		
75 percent subjects	51.7143	40.1429
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9916 (0.9419, 0.9988)	0.9914 (0.9404, 0.9988)
4 Weeks	0.9831 (0.9342, 0.9958)	0.9741 (0.9220, 0.9916)
8 Weeks	0.9404 (0.8790, 0.9711)	0.9483 (0.8885, 0.9764)
12 Weeks	0.9146 (0.8470, 0.9531)	0.9138 (0.8457, 0.9527)
16 Weeks	0.8887 (0.8160, 0.9338)	0.8791 (0.8045, 0.9266)
24 Weeks	0.8542 (0.7759, 0.9067)	0.8008 (0.7156, 0.8629)
36 Weeks	0.8022 (0.7175, 0.8639)	0.7745 (0.6868, 0.8405)
52 Weeks	0.7477 (0.6574, 0.8175)	0.7481 (0.6582, 0.8176)
Hazard Ratio (95% CI)*	-	0.9911 (0.5896, 1.6659)
Two-sided P-value, superiority*	-	0.9730

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	31 (37.35)	21 (26.25)
Subjects Censored	52 (62.65)	59 (73.75)
Event-free time (weeks)		
75 percent subjects	24.7143	42.8571
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9639 (0.8921, 0.9882)	0.9875 (0.9146, 0.9982)
4 Weeks	0.9398 (0.8613, 0.9745)	0.9875 (0.9146, 0.9982)
8 Weeks	0.9277 (0.8462, 0.9669)	0.9245 (0.8396, 0.9654)
12 Weeks	0.8794 (0.7874, 0.9332)	0.9118 (0.8239, 0.9570)
16 Weeks	0.8427 (0.7446, 0.9055)	0.8865 (0.7932, 0.9393)
24 Weeks	0.7694 (0.6626, 0.8463)	0.8480 (0.7478, 0.9107)
36 Weeks	0.6591 (0.5457, 0.7505)	0.7827 (0.6738, 0.8590)
52 Weeks	0.6213 (0.5069, 0.7165)	0.7287 (0.6146, 0.8141)
Hazard Ratio (95% CI)*	-	0.7426 (0.4263, 1.2935)
Two-sided P-value, superiority*	-	0.2932

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	25 (27.47)	21 (24.14)
Subjects Censored	66 (72.53)	66 (75.86)
Event-free time (weeks)		
75 percent subjects	48.1429	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9670 (0.9013, 0.9892)	0.9770 (0.9112, 0.9942)
4 Weeks	0.9670 (0.9013, 0.9892)	0.9770 (0.9112, 0.9942)
8 Weeks	0.9226 (0.8444, 0.9623)	0.9310 (0.8529, 0.9684)
12 Weeks	0.9003 (0.8172, 0.9469)	0.9080 (0.8245, 0.9529)
16 Weeks	0.8781 (0.7907, 0.9306)	0.8966 (0.8106, 0.9448)
24 Weeks	0.8559 (0.7648, 0.9137)	0.8150 (0.7159, 0.8824)
36 Weeks	0.7892 (0.6896, 0.8600)	0.7909 (0.6887, 0.8628)
52 Weeks	0.7190 (0.6127, 0.8008)	0.7538 (0.6476, 0.8321)
Hazard Ratio (95% CI)*	-	0.8874 (0.4955, 1.5895)
Two-sided P-value, superiority*	-	0.6880

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	35 (31.53)	29 (26.61)
Subjects Censored	76 (68.47)	80 (73.39)
Event-free time (weeks)		
75 percent subjects	26.1429	38.7143
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9910 (0.9378, 0.9987)	1.0000 (-, -)
4 Weeks	0.9640 (0.9068, 0.9863)	0.9817 (0.9286, 0.9954)
8 Weeks	0.9458 (0.8833, 0.9753)	0.9449 (0.8814, 0.9748)
12 Weeks	0.8998 (0.8263, 0.9432)	0.9171 (0.8467, 0.9560)
16 Weeks	0.8627 (0.7825, 0.9148)	0.8706 (0.7912, 0.9212)
24 Weeks	0.7884 (0.6990, 0.8541)	0.8238 (0.7377, 0.8838)
36 Weeks	0.7046 (0.6089, 0.7811)	0.7676 (0.6757, 0.8365)
52 Weeks	0.6758 (0.5785, 0.7553)	0.7301 (0.6355, 0.8040)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Hazard Ratio (95% CI)*	-	0.8166 (0.4991, 1.3362)
Two-sided P-value, superiority*	-	0.4200

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.6.1.2.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	54 (30.51)	43 (25.29)
Subjects Censored	123 (69.49)	127 (74.71)
Event-free time (weeks)		
75 percent subjects	34.1429	40.7143
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9774 (0.9409, 0.9915)	0.9882 (0.9538, 0.9970)
4 Weeks	0.9604 (0.9186, 0.9809)	0.9765 (0.9385, 0.9911)
8 Weeks	0.9261 (0.8761, 0.9564)	0.9292 (0.8787, 0.9592)
12 Weeks	0.8858 (0.8286, 0.9248)	0.9056 (0.8505, 0.9410)
16 Weeks	0.8511 (0.7890, 0.8961)	0.8759 (0.8161, 0.9173)
24 Weeks	0.8048 (0.7377, 0.8564)	0.8040 (0.7355, 0.8564)
36 Weeks	0.7350 (0.6625, 0.7943)	0.7736 (0.7024, 0.8298)
52 Weeks	0.6860 (0.6106, 0.7498)	0.7426 (0.6691, 0.8022)
Hazard Ratio (95% CI)*	-	0.8083 (0.5412, 1.2073)
Two-sided P-value, superiority*	-	0.2985

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- '-' indicates that point estimate, CI or p-value is not estimable.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).

Table 1.2.2.6.1.2.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	6 (24.00)	7 (26.92)
Subjects Censored	19 (76.00)	19 (73.08)
Event-free time (weeks)		
75 percent subjects	-	42.8571
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	0.9615 (0.7569, 0.9945)
16 Weeks	1.0000 (-, -)	0.9231 (0.7260, 0.9802)
24 Weeks	0.9200 (0.7164, 0.9794)	0.9231 (0.7260, 0.9802)
36 Weeks	0.8000 (0.5844, 0.9115)	0.8077 (0.5981, 0.9151)
52 Weeks	0.7600 (0.5420, 0.8843)	0.7308 (0.5169, 0.8615)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- '-' indicates that point estimate, CI or p-value is not estimable.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).

Table 1.2.2.6.1.2.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Hazard Ratio (95% CI)*	-	1.1873 (0.3980, 3.5419)
Two-sided P-value, superiority*	-	0.7581

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- '-' indicates that point estimate, CI or p-value is not estimable.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.7.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation Requiring Hospitalizatio through Week 52
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3324
Age at screening (<18 years vs. ≥18 years) [2]	0.9400
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.9903
Sex (Male vs. Female) [1]	0.4584
Region (North America vs. Rest of the World) [1]	0.9452

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride, and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.7.1.1.1

Study VX20-121-102: Treatment by Subgroup Factor Interaction for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Subgroup Prior CFTR Modulator Use

Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
Prior CFTR modulator use (yes vs. no)	0.9997

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline ppFEV$_1$ and baseline sweat chloride, and age at screening (<18 vs ≥18 years).

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

$ppFEV_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	11 (9.65)	3 (2.97)
Subjects Censored	103 (90.35)	98 (97.03)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9825 (0.9317, 0.9956)	0.9901 (0.9318, 0.9986)
4 Weeks	0.9825 (0.9317, 0.9956)	0.9901 (0.9318, 0.9986)
8 Weeks	0.9825 (0.9317, 0.9956)	0.9901 (0.9318, 0.9986)
12 Weeks	0.9648 (0.9088, 0.9866)	0.9901 (0.9318, 0.9986)
16 Weeks	0.9648 (0.9088, 0.9866)	0.9901 (0.9318, 0.9986)
24 Weeks	0.9559 (0.8973, 0.9814)	0.9801 (0.9228, 0.9950)
36 Weeks	0.9293 (0.8635, 0.9640)	0.9697 (0.9089, 0.9901)
52 Weeks	0.9024 (0.8306, 0.9447)	0.9697 (0.9089, 0.9901)
Hazard Ratio (95% CI)*	-	0.3184 (0.0884, 1.1469)
Two-sided P-value, superiority*	-	0.0801

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

$ppFEV_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	6 (6.90)	5 (5.43)
Subjects Censored	81 (93.10)	87 (94.57)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	0.9884 (0.9203, 0.9984)	0.9891 (0.9253, 0.9985)
12 Weeks	0.9884 (0.9203, 0.9984)	0.9783 (0.9159, 0.9945)
16 Weeks	0.9646 (0.8941, 0.9884)	0.9783 (0.9159, 0.9945)
24 Weeks	0.9646 (0.8941, 0.9884)	0.9673 (0.9020, 0.9893)
36 Weeks	0.9287 (0.8481, 0.9673)	0.9562 (0.8874, 0.9833)
52 Weeks	0.9287 (0.8481, 0.9673)	0.9450 (0.8730, 0.9767)
Hazard Ratio (95% CI)*	-	0.6994 (0.2099, 2.3302)
Two-sided P-value, superiority*	-	0.5603

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	2 (6.45)	1 (3.85)
Subjects Censored	29 (93.55)	25 (96.15)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	1.0000 (-, -)
16 Weeks	1.0000 (-, -)	1.0000 (-, -)
24 Weeks	1.0000 (-, -)	1.0000 (-, -)
36 Weeks	0.9643 (0.7724, 0.9949)	1.0000 (-, -)
52 Weeks	0.9286 (0.7435, 0.9816)	0.9600 (0.7484, 0.9943)
Hazard Ratio (95% CI)*	-	0.3035 (0.0187, 4.9211)
Two-sided P-value, superiority*	-	0.4015

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	15 (8.77)	7 (4.12)
Subjects Censored	156 (91.23)	163 (95.88)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9883 (0.9540, 0.9971)	0.9941 (0.9590, 0.9992)
4 Weeks	0.9883 (0.9540, 0.9971)	0.9941 (0.9590, 0.9992)
8 Weeks	0.9824 (0.9465, 0.9943)	0.9882 (0.9538, 0.9970)
12 Weeks	0.9706 (0.9309, 0.9877)	0.9823 (0.9462, 0.9943)
16 Weeks	0.9588 (0.9155, 0.9801)	0.9823 (0.9462, 0.9943)
24 Weeks	0.9529 (0.9080, 0.9761)	0.9704 (0.9305, 0.9876)
36 Weeks	0.9232 (0.8714, 0.9547)	0.9583 (0.9145, 0.9799)
52 Weeks	0.9111 (0.8569, 0.9455)	0.9583 (0.9145, 0.9799)
Hazard Ratio (95% CI)*	-	0.4783 (0.1948, 1.1744)
Two-sided P-value, superiority*	-	0.1076

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	2 (10.53)	0
Subjects Censored	17 (89.47)	17 (100.00)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
4 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
8 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
12 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
16 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
24 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
36 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
52 Weeks	0.8916 (0.6315, 0.9718)	1.0000 (-, -)
Hazard Ratio (95% CI)*	-	N/C
Two-sided P-value, superiority*	-	0.9976

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	15 (8.24)	8 (4.52)
Subjects Censored	167 (91.76)	169 (95.48)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9945 (0.9616, 0.9992)	0.9944 (0.9606, 0.9992)
4 Weeks	0.9945 (0.9616, 0.9992)	0.9944 (0.9606, 0.9992)
8 Weeks	0.9889 (0.9565, 0.9972)	0.9887 (0.9556, 0.9972)
12 Weeks	0.9778 (0.9419, 0.9916)	0.9830 (0.9483, 0.9945)
16 Weeks	0.9665 (0.9270, 0.9848)	0.9830 (0.9483, 0.9945)
24 Weeks	0.9609 (0.9198, 0.9812)	0.9716 (0.9330, 0.9881)
36 Weeks	0.9271 (0.8777, 0.9570)	0.9599 (0.9178, 0.9807)
52 Weeks	0.9157 (0.8641, 0.9483)	0.9541 (0.9103, 0.9768)
Hazard Ratio (95% CI)*	-	0.5516 (0.2338, 1.3015)
Two-sided P-value, superiority*	-	0.1744

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	6 (5.04)	4 (3.45)
Subjects Censored	113 (94.96)	112 (96.55)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9914 (0.9404, 0.9988)
4 Weeks	1.0000 (-, -)	0.9914 (0.9404, 0.9988)
8 Weeks	1.0000 (-, -)	0.9914 (0.9404, 0.9988)
12 Weeks	0.9914 (0.9404, 0.9988)	0.9828 (0.9328, 0.9957)
16 Weeks	0.9828 (0.9328, 0.9957)	0.9828 (0.9328, 0.9957)
24 Weeks	0.9741 (0.9220, 0.9916)	0.9741 (0.9217, 0.9916)
36 Weeks	0.9567 (0.8992, 0.9818)	0.9652 (0.9099, 0.9868)
52 Weeks	0.9480 (0.8878, 0.9763)	0.9652 (0.9099, 0.9868)
Hazard Ratio (95% CI)*	-	0.7180 (0.2004, 2.5725)
Two-sided P-value, superiority*	-	0.6109

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	11 (13.25)	4 (5.00)
Subjects Censored	72 (86.75)	76 (95.00)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9759 (0.9071, 0.9939)	1.0000 (-, -)
4 Weeks	0.9759 (0.9071, 0.9939)	1.0000 (-, -)
8 Weeks	0.9639 (0.8921, 0.9882)	0.9875 (0.9146, 0.9982)
12 Weeks	0.9518 (0.8767, 0.9816)	0.9875 (0.9146, 0.9982)
16 Weeks	0.9396 (0.8610, 0.9744)	0.9875 (0.9146, 0.9982)
24 Weeks	0.9396 (0.8610, 0.9744)	0.9747 (0.9025, 0.9936)
36 Weeks	0.8906 (0.8003, 0.9415)	0.9615 (0.8853, 0.9874)
52 Weeks	0.8655 (0.7703, 0.9232)	0.9481 (0.8676, 0.9802)
Hazard Ratio (95% CI)*	-	0.3688 (0.1162, 1.1707)
Two-sided P-value, superiority*	-	0.0905

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	11 (12.09)	5 (5.75)
Subjects Censored	80 (87.91)	82 (94.25)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9890 (0.9246, 0.9984)	0.9885 (0.9212, 0.9984)
4 Weeks	0.9890 (0.9246, 0.9984)	0.9885 (0.9212, 0.9984)
8 Weeks	0.9779 (0.9145, 0.9944)	0.9885 (0.9212, 0.9984)
12 Weeks	0.9668 (0.9006, 0.9892)	0.9770 (0.9112, 0.9942)
16 Weeks	0.9557 (0.8862, 0.9831)	0.9770 (0.9112, 0.9942)
24 Weeks	0.9446 (0.8719, 0.9765)	0.9654 (0.8965, 0.9887)
36 Weeks	0.9001 (0.8168, 0.9467)	0.9533 (0.8803, 0.9822)
52 Weeks	0.8777 (0.7901, 0.9304)	0.9409 (0.8638, 0.9750)
Hazard Ratio (95% CI)*	-	0.4779 (0.1658, 1.3774)
Two-sided P-value, superiority*	-	0.1716

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	6 (5.41)	3 (2.75)
Subjects Censored	105 (94.59)	106 (97.25)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9910 (0.9378, 0.9987)	1.0000 (-, -)
4 Weeks	0.9910 (0.9378, 0.9987)	1.0000 (-, -)
8 Weeks	0.9910 (0.9378, 0.9987)	0.9908 (0.9367, 0.9987)
12 Weeks	0.9817 (0.9289, 0.9954)	0.9908 (0.9367, 0.9987)
16 Weeks	0.9725 (0.9171, 0.9910)	0.9908 (0.9367, 0.9987)
24 Weeks	0.9725 (0.9171, 0.9910)	0.9815 (0.9280, 0.9953)
36 Weeks	0.9539 (0.8929, 0.9806)	0.9721 (0.9161, 0.9909)
52 Weeks	0.9444 (0.8804, 0.9746)	0.9721 (0.9161, 0.9909)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.7.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Hazard Ratio (95% CI)*	-	0.5036 (0.1258, 2.0161)
Two-sided P-value, superiority*	-	0.3324

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.7.1.2.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	17 (9.60)	8 (4.71)
Subjects Censored	160 (90.40)	162 (95.29)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9887 (0.9556, 0.9972)	0.9941 (0.9590, 0.9992)
4 Weeks	0.9887 (0.9556, 0.9972)	0.9941 (0.9590, 0.9992)
8 Weeks	0.9830 (0.9482, 0.9945)	0.9882 (0.9538, 0.9970)
12 Weeks	0.9715 (0.9329, 0.9880)	0.9823 (0.9462, 0.9943)
16 Weeks	0.9599 (0.9178, 0.9807)	0.9823 (0.9462, 0.9943)
24 Weeks	0.9541 (0.9104, 0.9768)	0.9704 (0.9303, 0.9876)
36 Weeks	0.9193 (0.8676, 0.9514)	0.9581 (0.9142, 0.9798)
52 Weeks	0.9017 (0.8466, 0.9377)	0.9519 (0.9062, 0.9757)
Hazard Ratio (95% CI)*	-	0.4872 (0.2102, 1.1293)
Two-sided P-value, superiority*	-	0.0937

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- '-' indicates that point estimate, CI or p-value is not estimable.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).

Table 1.2.2.7.1.2.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	0	0
Subjects Censored	25 (100.00)	26 (100.00)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	1.0000 (-, -)
16 Weeks	1.0000 (-, -)	1.0000 (-, -)
24 Weeks	1.0000 (-, -)	1.0000 (-, -)
36 Weeks	1.0000 (-, -)	1.0000 (-, -)
52 Weeks	1.0000 (-, -)	1.0000 (-, -)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- '-' indicates that point estimate, CI or p-value is not estimable.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).

Table 1.2.2.7.1.2.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Hazard Ratio (95% CI)*	-	-
Two-sided P-value, superiority*	-	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- '-' indicates that point estimate, CI or p-value is not estimable.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.8.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3101
Age at screening (<18 years vs. ≥18 years) [2]	0.7359
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.9888
Sex (Male vs. Female) [1]	0.6524
Region (North America vs. Rest of the World) [1]	0.9544

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride, and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride.

Table 1.2.2.8.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
Prior CFTR modulator use (yes vs. no)	0.1527

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline ppFEV$_1$ and baseline sweat chloride, and age at screening (<18 vs ≥18 years).

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

$ppFEV_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	19 (16.67)	5 (4.95)
Subjects Censored	95 (83.33)	96 (95.05)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9825 (0.9317, 0.9956)	0.9901 (0.9318, 0.9986)
4 Weeks	0.9825 (0.9317, 0.9956)	0.9901 (0.9318, 0.9986)
8 Weeks	0.9825 (0.9317, 0.9956)	0.9901 (0.9318, 0.9986)
12 Weeks	0.9382 (0.8747, 0.9701)	0.9801 (0.9228, 0.9950)
16 Weeks	0.9382 (0.8747, 0.9701)	0.9801 (0.9228, 0.9950)
24 Weeks	0.9116 (0.8420, 0.9515)	0.9701 (0.9102, 0.9903)
36 Weeks	0.8585 (0.7794, 0.9108)	0.9495 (0.8828, 0.9787)
52 Weeks	0.8314 (0.7485, 0.8890)	0.9495 (0.8828, 0.9787)
Hazard Ratio (95% CI)*	-	0.2867 (0.1065, 0.7721)
Two-sided P-value, superiority*	-	0.0134

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

$ppFEV_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	7 (8.05)	5 (5.43)
Subjects Censored	80 (91.95)	87 (94.57)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	0.9884 (0.9203, 0.9984)	0.9891 (0.9253, 0.9985)
12 Weeks	0.9884 (0.9203, 0.9984)	0.9783 (0.9159, 0.9945)
16 Weeks	0.9646 (0.8941, 0.9884)	0.9783 (0.9159, 0.9945)
24 Weeks	0.9646 (0.8941, 0.9884)	0.9673 (0.9020, 0.9893)
36 Weeks	0.9168 (0.8333, 0.9594)	0.9562 (0.8874, 0.9833)
52 Weeks	0.9168 (0.8333, 0.9594)	0.9450 (0.8730, 0.9767)
Hazard Ratio (95% CI)*	-	0.6112 (0.1913, 1.9522)
Two-sided P-value, superiority*	-	0.4060

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	2 (6.45)	1 (3.85)
Subjects Censored	29 (93.55)	25 (96.15)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	1.0000 (-, -)
16 Weeks	1.0000 (-, -)	1.0000 (-, -)
24 Weeks	1.0000 (-, -)	1.0000 (-, -)
36 Weeks	0.9643 (0.7724, 0.9949)	1.0000 (-, -)
52 Weeks	0.9286 (0.7435, 0.9816)	0.9600 (0.7484, 0.9943)
Hazard Ratio (95% CI)*	-	0.3035 (0.0187, 4.9211)
Two-sided P-value, superiority*	-	0.4015

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	24 (14.04)	9 (5.29)
Subjects Censored	147 (85.96)	161 (94.71)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9883 (0.9540, 0.9971)	0.9941 (0.9590, 0.9992)
4 Weeks	0.9883 (0.9540, 0.9971)	0.9941 (0.9590, 0.9992)
8 Weeks	0.9824 (0.9465, 0.9943)	0.9882 (0.9538, 0.9970)
12 Weeks	0.9529 (0.9080, 0.9762)	0.9764 (0.9383, 0.9911)
16 Weeks	0.9411 (0.8932, 0.9678)	0.9764 (0.9383, 0.9911)
24 Weeks	0.9233 (0.8716, 0.9547)	0.9645 (0.9228, 0.9839)
36 Weeks	0.8700 (0.8092, 0.9124)	0.9463 (0.8994, 0.9717)
52 Weeks	0.8578 (0.7953, 0.9023)	0.9463 (0.8994, 0.9717)
Hazard Ratio (95% CI)*	-	0.3696 (0.1716, 0.7961)
Two-sided P-value, superiority*	-	0.0110

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	5 (26.32)	0
Subjects Censored	14 (73.68)	17 (100.00)
Event-free time (weeks)		
75 percent subjects	45.5714	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
4 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
8 Weeks	0.9474 (0.6812, 0.9924)	1.0000 (-, -)
12 Weeks	0.8421 (0.5865, 0.9462)	1.0000 (-, -)
16 Weeks	0.8421 (0.5865, 0.9462)	1.0000 (-, -)
24 Weeks	0.7895 (0.5319, 0.9153)	1.0000 (-, -)
36 Weeks	0.7895 (0.5319, 0.9153)	1.0000 (-, -)
52 Weeks	0.7331 (0.4723, 0.8794)	1.0000 (-, -)
Hazard Ratio (95% CI)*	-	N/C
Two-sided P-value, superiority*	-	0.9958

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	21 (11.54)	10 (5.65)
Subjects Censored	161 (88.46)	167 (94.35)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9945 (0.9616, 0.9992)	0.9944 (0.9606, 0.9992)
4 Weeks	0.9945 (0.9616, 0.9992)	0.9944 (0.9606, 0.9992)
8 Weeks	0.9889 (0.9565, 0.9972)	0.9887 (0.9556, 0.9972)
12 Weeks	0.9722 (0.9345, 0.9883)	0.9773 (0.9407, 0.9914)
16 Weeks	0.9610 (0.9199, 0.9812)	0.9773 (0.9407, 0.9914)
24 Weeks	0.9497 (0.9056, 0.9735)	0.9659 (0.9256, 0.9845)
36 Weeks	0.8934 (0.8380, 0.9307)	0.9484 (0.9032, 0.9728)
52 Weeks	0.8819 (0.8247, 0.9214)	0.9426 (0.8959, 0.9687)
Hazard Ratio (95% CI)*	-	0.4894 (0.2303, 1.0397)
Two-sided P-value, superiority*	-	0.0631

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	12 (10.08)	4 (3.45)
Subjects Censored	107 (89.92)	112 (96.55)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9914 (0.9404, 0.9988)
4 Weeks	1.0000 (-, -)	0.9914 (0.9404, 0.9988)
8 Weeks	1.0000 (-, -)	0.9914 (0.9404, 0.9988)
12 Weeks	0.9742 (0.9222, 0.9916)	0.9828 (0.9328, 0.9957)
16 Weeks	0.9656 (0.9109, 0.9869)	0.9828 (0.9328, 0.9957)
24 Weeks	0.9483 (0.8886, 0.9765)	0.9741 (0.9217, 0.9916)
36 Weeks	0.9137 (0.8455, 0.9526)	0.9652 (0.9099, 0.9868)
52 Weeks	0.8960 (0.8242, 0.9396)	0.9652 (0.9099, 0.9868)
Hazard Ratio (95% CI)*	-	0.3120 (0.0999, 0.9745)
Two-sided P-value, superiority*	-	0.0450

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	14 (16.87)	6 (7.50)
Subjects Censored	69 (83.13)	74 (92.50)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9759 (0.9071, 0.9939)	1.0000 (-, -)
4 Weeks	0.9759 (0.9071, 0.9939)	1.0000 (-, -)
8 Weeks	0.9639 (0.8921, 0.9882)	0.9875 (0.9146, 0.9982)
12 Weeks	0.9396 (0.8610, 0.9744)	0.9748 (0.9031, 0.9936)
16 Weeks	0.9274 (0.8455, 0.9667)	0.9748 (0.9031, 0.9936)
24 Weeks	0.9152 (0.8303, 0.9586)	0.9620 (0.8868, 0.9876)
36 Weeks	0.8418 (0.7432, 0.9049)	0.9358 (0.8526, 0.9728)
52 Weeks	0.8291 (0.7284, 0.8950)	0.9225 (0.8354, 0.9644)
Hazard Ratio (95% CI)*	-	0.4474 (0.1710, 1.1709)
Two-sided P-value, superiority*	-	0.1013

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	13 (14.29)	5 (5.75)
Subjects Censored	78 (85.71)	82 (94.25)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9890 (0.9246, 0.9984)	0.9885 (0.9212, 0.9984)
4 Weeks	0.9890 (0.9246, 0.9984)	0.9885 (0.9212, 0.9984)
8 Weeks	0.9779 (0.9145, 0.9944)	0.9885 (0.9212, 0.9984)
12 Weeks	0.9668 (0.9006, 0.9892)	0.9770 (0.9112, 0.9942)
16 Weeks	0.9557 (0.8862, 0.9831)	0.9770 (0.9112, 0.9942)
24 Weeks	0.9446 (0.8719, 0.9765)	0.9654 (0.8965, 0.9887)
36 Weeks	0.8890 (0.8035, 0.9387)	0.9533 (0.8803, 0.9822)
52 Weeks	0.8554 (0.7640, 0.9133)	0.9409 (0.8638, 0.9750)
Hazard Ratio (95% CI)*	-	0.4029 (0.1435, 1.1307)
Two-sided P-value, superiority*	-	0.0842

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	13 (11.71)	5 (4.59)
Subjects Censored	98 (88.29)	104 (95.41)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9910 (0.9378, 0.9987)	1.0000 (-, -)
4 Weeks	0.9910 (0.9378, 0.9987)	1.0000 (-, -)
8 Weeks	0.9910 (0.9378, 0.9987)	0.9908 (0.9367, 0.9987)
12 Weeks	0.9541 (0.8932, 0.9806)	0.9816 (0.9283, 0.9954)
16 Weeks	0.9448 (0.8813, 0.9748)	0.9816 (0.9283, 0.9954)
24 Weeks	0.9263 (0.8581, 0.9625)	0.9722 (0.9163, 0.9910)
36 Weeks	0.8800 (0.8023, 0.9285)	0.9535 (0.8919, 0.9804)
52 Weeks	0.8800 (0.8023, 0.9285)	0.9535 (0.8919, 0.9804)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Hazard Ratio (95% CI)*	-	0.3767 (0.1342, 1.0574)
Two-sided P-value, superiority*	-	0.0637

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 1.2.2.8.1.2.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	25 (14.12)	8 (4.71)
Subjects Censored	152 (85.88)	162 (95.29)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9887 (0.9556, 0.9972)	0.9941 (0.9590, 0.9992)
4 Weeks	0.9887 (0.9556, 0.9972)	0.9941 (0.9590, 0.9992)
8 Weeks	0.9830 (0.9482, 0.9945)	0.9882 (0.9538, 0.9970)
12 Weeks	0.9542 (0.9105, 0.9768)	0.9823 (0.9462, 0.9943)
16 Weeks	0.9426 (0.8960, 0.9687)	0.9823 (0.9462, 0.9943)
24 Weeks	0.9311 (0.8818, 0.9603)	0.9704 (0.9303, 0.9876)
36 Weeks	0.8731 (0.8137, 0.9146)	0.9581 (0.9142, 0.9798)
52 Weeks	0.8554 (0.7935, 0.8999)	0.9519 (0.9062, 0.9757)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- '-' indicates that point estimate, CI or p-value is not estimable.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).

Table 1.2.2.8.1.2.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Hazard Ratio (95% CI)*	-	0.3221 (0.1452, 0.7143)
Two-sided P-value, superiority*	-	0.0053

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- '-' indicates that point estimate, CI or p-value is not estimable.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).

Table 1.2.2.8.1.2.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	1 (4.00)	2 (7.69)
Subjects Censored	24 (96.00)	24 (92.31)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	0.9615 (0.7569, 0.9945)
16 Weeks	1.0000 (-, -)	0.9615 (0.7569, 0.9945)
24 Weeks	0.9600 (0.7484, 0.9943)	0.9615 (0.7569, 0.9945)
36 Weeks	0.9600 (0.7484, 0.9943)	0.9231 (0.7260, 0.9802)
52 Weeks	0.9600 (0.7484, 0.9943)	0.9231 (0.7260, 0.9802)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- '-' indicates that point estimate, CI or p-value is not estimable.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).

Table 1.2.2.8.1.2.1
Study VX20-121-102: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Hazard Ratio (95% CI)*	-	1.8763 (0.1675, 21.0165)
Two-sided P-value, superiority*	-	0.6097

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- '-' indicates that point estimate, CI or p-value is not estimable.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).

Table 1.2.2.9.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0800
Age at screening (<18 years vs. ≥18 years) [2]	0.9395
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1486
Sex (Male vs. Female) [1]	0.5110
Region (North America vs. Rest of the World) [1]	0.5904

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.9.1.1.1

Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use

Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.1031

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	81.13 (15.67)	83.67 (15.37)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	78.37 (1.74)	84.07 (1.87)
95% CI of LS mean	(74.95, 81.79)	(80.39, 87.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.70 (0.66, 10.73)
Absolute Change at Week 8 (MMRM)		
n	110	96
LS mean (SE)	-2.90 (1.63)	0.45 (1.75)
95% CI of LS mean	(-6.11, 0.32)	(-3.00, 3.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.35 (-1.37, 8.06)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	76.93 (1.74)	84.89 (1.87)
95% CI of LS mean	(73.50, 80.36)	(81.20, 88.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.96 (2.91, 13.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	-4.05 (1.61)	1.87 (1.72)
95% CI of LS mean	(-7.21, -0.88)	(-1.52, 5.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.92 (1.27, 10.57)
Week 24 (MMRM)		
n	113	97
LS mean (SE)	78.48 (1.78)	82.98 (1.91)
95% CI of LS mean	(74.98, 81.98)	(79.20, 86.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.50 (-0.65, 9.66)
Absolute Change at Week 24 (MMRM)		
n	110	95
LS mean (SE)	-2.77 (1.68)	-0.62 (1.81)
95% CI of LS mean	(-6.09, 0.54)	(-4.19, 2.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.15 (-2.73, 7.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	78.55 (17.83)	85.48 (14.54)
Absolute Change at Week 52		
n	109	92
Mean (SD)	-3.54 (15.79)	2.32 (14.49)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	78.10 (1.55)	85.55 (1.68)
95% CI of LS mean	(75.05, 81.14)	(82.23, 88.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.45 (2.94, 11.96)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	-3.40 (1.48)	1.81 (1.60)
95% CI of LS mean	(-6.32, -0.49)	(-1.35, 4.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.22 (0.91, 9.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	-3.41 (1.27)	1.02 (1.37)
95% CI of LS mean	(-5.92, -0.90)	(-1.68, 3.72)
P-value within Treatment	0.0081	0.4560
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.43 (0.73, 8.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0191
Hedges' G (SE)		0.33 (0.14)
Hedges' 95% CI		(0.05, 0.61)
Hedges' P-value		0.0195

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	85.16 (15.53)	88.13 (13.78)
Week 8 (MMRM)		
n	83	90
LS mean (SE)	84.14 (1.64)	86.14 (1.57)
95% CI of LS mean	(80.90, 87.37)	(83.03, 89.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.00 (-2.48, 6.49)
Absolute Change at Week 8 (MMRM)		
n	82	90
LS mean (SE)	-1.20 (1.82)	-2.09 (1.74)
95% CI of LS mean	(-4.80, 2.39)	(-5.53, 1.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-5.87, 4.09)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	85.40 (1.69)	87.80 (1.62)
95% CI of LS mean	(82.06, 88.74)	(84.60, 91.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.40 (-2.23, 7.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	0.28 (1.80)	-0.35 (1.72)
95% CI of LS mean	(-3.27, 3.83)	(-3.74, 3.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-5.54, 4.29)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	85.94 (1.65)	89.40 (1.58)
95% CI of LS mean	(82.68, 89.19)	(86.28, 92.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.46 (-1.05, 7.98)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	0.79 (1.84)	1.35 (1.77)
95% CI of LS mean	(-2.85, 4.43)	(-2.14, 4.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.56 (-4.49, 5.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	79	87
Mean (SD)	86.36 (13.77)	88.83 (12.05)
Absolute Change at Week 52		
n	78	86
Mean (SD)	1.99 (12.23)	0.61 (15.19)
Week 52 (MMRM)		
n	78	87
LS mean (SE)	86.37 (1.44)	89.05 (1.37)
95% CI of LS mean	(83.54, 89.21)	(86.35, 91.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.68 (-1.24, 6.60)
Absolute Change at Week 52 (MMRM)		
n	77	86
LS mean (SE)	1.39 (1.58)	0.87 (1.50)
95% CI of LS mean	(-1.73, 4.50)	(-2.10, 3.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-4.83, 3.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	0.82 (1.45)	0.62 (1.39)
95% CI of LS mean	(-2.05, 3.68)	(-2.12, 3.37)
P-value within Treatment	0.5730	0.6546
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-4.17, 3.77)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9222
Hedges' G (SE)		-0.01 (0.15)
Hedges' 95% CI		(-0.31, 0.29)
Hedges' P-value		0.9221

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	88.51 (13.36)	89.89 (15.69)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	89.13 (2.08)	89.98 (2.28)
95% CI of LS mean	(84.96, 93.30)	(85.40, 94.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.85 (-5.38, 7.07)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	-0.29 (2.66)	1.52 (2.90)
95% CI of LS mean	(-5.63, 5.05)	(-4.31, 7.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.81 (-6.14, 9.75)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	89.38 (2.25)	89.01 (2.48)
95% CI of LS mean	(84.86, 93.90)	(84.04, 93.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-7.13, 6.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	-0.01 (2.75)	0.84 (3.03)
95% CI of LS mean	(-5.53, 5.52)	(-5.26, 6.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.84 (-7.43, 9.12)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	90.27 (2.90)	88.35 (3.19)
95% CI of LS mean	(84.44, 96.11)	(81.94, 94.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.92 (-10.61, 6.77)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	0.89 (3.65)	0.44 (4.02)
95% CI of LS mean	(-6.44, 8.22)	(-7.63, 8.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-11.38, 10.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	27	25
Mean (SD)	86.52 (15.23)	90.67 (13.75)
Absolute Change at Week 52		
n	26	24
Mean (SD)	-3.53 (14.67)	1.50 (19.91)
Week 52 (MMRM)		
n	27	24
LS mean (SE)	86.09 (2.72)	89.99 (2.92)
95% CI of LS mean	(80.63, 91.56)	(84.11, 95.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.89 (-4.16, 11.95)
Absolute Change at Week 52 (MMRM)		
n	26	23
LS mean (SE)	-3.59 (3.41)	1.78 (3.70)
95% CI of LS mean	(-10.44, 3.26)	(-5.65, 9.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.37 (-4.77, 15.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	-0.90 (2.81)	1.02 (3.08)
95% CI of LS mean	(-6.54, 4.73)	(-5.18, 7.22)
P-value within Treatment	0.7489	0.7423
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.92 (-6.49, 10.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6483
Hedges' G (SE)		0.13 (0.28)
Hedges' 95% CI		(-0.43, 0.69)
Hedges' P-value		0.6472

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	81.98 (15.88)	85.20 (14.55)
Week 8 (MMRM)		
n	167	164
LS mean (SE)	79.65 (1.37)	84.05 (1.38)
95% CI of LS mean	(76.96, 82.35)	(81.34, 86.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.40 (0.57, 8.23)
Absolute Change at Week 8 (MMRM)		
n	164	162
LS mean (SE)	-2.49 (1.35)	-1.13 (1.36)
95% CI of LS mean	(-5.14, 0.16)	(-3.80, 1.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.36 (-2.40, 5.12)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	79.23 (1.38)	85.59 (1.39)
95% CI of LS mean	(76.52, 81.94)	(82.87, 88.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.36 (2.52, 10.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-2.58 (1.32)	0.79 (1.32)
95% CI of LS mean	(-5.17, 0.01)	(-1.81, 3.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.37 (-0.30, 7.04)
Week 24 (MMRM)		
n	167	163
LS mean (SE)	80.41 (1.34)	85.45 (1.35)
95% CI of LS mean	(77.78, 83.05)	(82.79, 88.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.04 (1.29, 8.79)
Absolute Change at Week 24 (MMRM)		
n	164	161
LS mean (SE)	-1.63 (1.32)	0.29 (1.33)
95% CI of LS mean	(-4.22, 0.97)	(-2.32, 2.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.92 (-1.76, 5.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	81.08 (16.81)	86.56 (13.32)
Absolute Change at Week 52		
n	162	156
Mean (SD)	-0.86 (14.59)	1.51 (13.85)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	81.06 (1.17)	86.58 (1.19)
95% CI of LS mean	(78.76, 83.36)	(84.25, 88.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.52 (2.24, 8.80)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	-1.01 (1.13)	1.30 (1.15)
95% CI of LS mean	(-3.24, 1.21)	(-0.96, 3.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.31 (-0.86, 5.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-1.74 (1.02)	0.79 (1.02)
95% CI of LS mean	(-3.74, 0.26)	(-1.22, 2.80)
P-value within Treatment	0.0877	0.4382
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.53 (-0.30, 5.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0798
Hedges' G (SE)		0.19 (0.11)
Hedges' 95% CI		(-0.02, 0.41)
Hedges' P-value		0.0804

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	82.16 (14.65)	78.47 (22.58)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	81.91 (3.76)	86.41 (4.11)
95% CI of LS mean	(74.24, 89.58)	(78.04, 94.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.50 (-7.01, 16.01)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	-0.32 (4.64)	8.02 (5.07)
95% CI of LS mean	(-9.77, 9.13)	(-2.30, 18.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.34 (-5.82, 22.50)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	79.86 (3.84)	85.02 (4.19)
95% CI of LS mean	(72.04, 87.69)	(76.48, 93.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.16 (-6.58, 16.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-2.37 (4.47)	6.63 (4.88)
95% CI of LS mean	(-11.47, 6.73)	(-3.31, 16.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.00 (-4.66, 22.66)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	79.57 (3.87)	87.45 (4.22)
95% CI of LS mean	(71.66, 87.48)	(78.81, 96.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.88 (-3.98, 19.75)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	-2.66 (4.86)	9.06 (5.31)
95% CI of LS mean	(-12.59, 7.27)	(-1.78, 19.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.72 (-3.14, 26.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	81.17 (18.68)	82.54 (17.55)
Absolute Change at Week 52		
n	18	13
Mean (SD)	-3.09 (14.03)	4.27 (17.74)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	79.91 (4.17)	81.53 (4.80)
95% CI of LS mean	(71.39, 88.43)	(71.75, 91.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.62 (-11.47, 14.71)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	-2.83 (3.86)	3.68 (4.42)
95% CI of LS mean	(-10.76, 5.10)	(-5.37, 12.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.51 (-5.69, 18.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	-2.62 (3.66)	6.46 (4.02)
95% CI of LS mean	(-10.10, 4.86)	(-1.76, 14.68)
P-value within Treatment	0.4794	0.1191
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.08 (-2.24, 20.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1119
Hedges' G (SE)		0.55 (0.34)
Hedges' 95% CI		(-0.13, 1.24)
Hedges' P-value		0.1107

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	83.11 (15.82)	86.54 (13.71)
Week 8 (MMRM)		
n	177	172
LS mean (SE)	80.87 (1.28)	84.81 (1.30)
95% CI of LS mean	(78.36, 83.38)	(82.26, 87.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.93 (0.36, 7.51)
Absolute Change at Week 8 (MMRM)		
n	173	170
LS mean (SE)	-2.39 (1.25)	-1.59 (1.26)
95% CI of LS mean	(-4.85, 0.07)	(-4.08, 0.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.80 (-2.70, 4.30)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	80.72 (1.30)	86.27 (1.31)
95% CI of LS mean	(78.17, 83.28)	(83.68, 88.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.54 (1.91, 9.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	-2.20 (1.24)	0.27 (1.25)
95% CI of LS mean	(-4.63, 0.24)	(-2.18, 2.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.47 (-0.99, 5.93)
Week 24 (MMRM)		
n	177	171
LS mean (SE)	82.01 (1.28)	85.80 (1.30)
95% CI of LS mean	(79.49, 84.52)	(83.24, 88.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.79 (0.21, 7.38)
Absolute Change at Week 24 (MMRM)		
n	173	168
LS mean (SE)	-1.12 (1.27)	-0.49 (1.28)
95% CI of LS mean	(-3.61, 1.37)	(-3.01, 2.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-2.92, 4.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	173	169
Mean (SD)	82.00 (16.51)	87.65 (12.88)
Absolute Change at Week 52		
n	169	166
Mean (SD)	-1.04 (14.72)	1.34 (14.55)
Week 52 (MMRM)		
n	172	167
LS mean (SE)	81.92 (1.10)	87.53 (1.12)
95% CI of LS mean	(79.75, 84.09)	(85.33, 89.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.61 (2.52, 8.71)
Absolute Change at Week 52 (MMRM)		
n	168	164
LS mean (SE)	-1.28 (1.13)	1.09 (1.14)
95% CI of LS mean	(-3.50, 0.95)	(-1.16, 3.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.36 (-0.80, 5.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	-1.53 (0.98)	0.29 (0.99)
95% CI of LS mean	(-3.46, 0.41)	(-1.66, 2.25)
P-value within Treatment	0.1210	0.7694
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.82 (-0.93, 4.57)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1940
Hedges' G (SE)		0.14 (0.11)
Hedges' 95% CI		(-0.07, 0.35)
Hedges' P-value		0.1944

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	85.26 (16.00)	85.89 (15.26)
Week 8 (MMRM)		
n	115	116
LS mean (SE)	81.58 (1.60)	85.15 (1.60)
95% CI of LS mean	(78.42, 84.73)	(82.00, 88.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.58 (-0.89, 8.05)
Absolute Change at Week 8 (MMRM)		
n	111	115
LS mean (SE)	-3.79 (1.66)	-0.84 (1.63)
95% CI of LS mean	(-7.05, -0.53)	(-4.05, 2.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.95 (-1.64, 7.54)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	81.98 (1.67)	86.29 (1.67)
95% CI of LS mean	(78.69, 85.27)	(82.99, 89.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.31 (-0.36, 8.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	-2.87 (1.70)	0.30 (1.68)
95% CI of LS mean	(-6.22, 0.49)	(-3.02, 3.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.16 (-1.56, 7.89)
Week 24 (MMRM)		
n	115	114
LS mean (SE)	83.12 (1.54)	87.72 (1.55)
95% CI of LS mean	(80.08, 86.16)	(84.67, 90.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.60 (0.28, 8.92)
Absolute Change at Week 24 (MMRM)		
n	111	113
LS mean (SE)	-2.06 (1.65)	2.06 (1.63)
95% CI of LS mean	(-5.31, 1.19)	(-1.15, 5.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.12 (-0.46, 8.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	84.29 (16.26)	86.56 (13.46)
Absolute Change at Week 52		
n	109	110
Mean (SD)	-1.27 (13.38)	0.93 (14.04)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	83.67 (1.38)	87.00 (1.38)
95% CI of LS mean	(80.95, 86.39)	(84.27, 89.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.33 (-0.54, 7.19)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	-1.63 (1.31)	1.11 (1.30)
95% CI of LS mean	(-4.21, 0.96)	(-1.45, 3.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.73 (-0.92, 6.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	-2.19 (1.31)	1.15 (1.30)
95% CI of LS mean	(-4.77, 0.40)	(-1.40, 3.71)
P-value within Treatment	0.0968	0.3737
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.34 (-0.30, 6.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0723
Hedges' G (SE)		0.24 (0.13)
Hedges' 95% CI		(-0.02, 0.50)
Hedges' P-value		0.0723

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	79.75 (14.73)	85.68 (14.04)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	79.98 (1.86)	84.75 (1.97)
95% CI of LS mean	(76.30, 83.65)	(80.86, 88.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.77 (-0.59, 10.12)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	-0.21 (1.77)	-0.37 (1.89)
95% CI of LS mean	(-3.71, 3.30)	(-4.11, 3.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.16 (-5.29, 4.97)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	78.57 (1.78)	86.11 (1.86)
95% CI of LS mean	(75.06, 82.09)	(82.43, 89.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.54 (2.44, 12.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	-1.55 (1.59)	1.92 (1.69)
95% CI of LS mean	(-4.70, 1.59)	(-1.42, 5.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.48 (-1.12, 8.07)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	79.70 (1.97)	83.32 (2.07)
95% CI of LS mean	(75.81, 83.60)	(79.22, 87.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.61 (-2.05, 9.28)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	-0.42 (1.86)	-2.16 (1.99)
95% CI of LS mean	(-4.11, 3.26)	(-6.09, 1.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.73 (-7.13, 3.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	79	73
Mean (SD)	78.34 (16.72)	87.98 (13.38)
Absolute Change at Week 52		
n	79	70
Mean (SD)	-1.16 (16.21)	2.42 (15.83)
Week 52 (MMRM)		
n	78	69
LS mean (SE)	78.83 (1.70)	87.57 (1.80)
95% CI of LS mean	(75.48, 82.19)	(84.02, 91.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.74 (3.84, 13.64)
Absolute Change at Week 52 (MMRM)		
n	78	67
LS mean (SE)	-1.35 (1.86)	1.96 (2.00)
95% CI of LS mean	(-5.03, 2.32)	(-1.99, 5.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.31 (-2.08, 8.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	-1.11 (1.38)	0.57 (1.47)
95% CI of LS mean	(-3.84, 1.62)	(-2.33, 3.48)
P-value within Treatment	0.4224	0.6967
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-2.31, 5.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4059
Hedges' G (SE)		0.13 (0.16)
Hedges' 95% CI		(-0.18, 0.45)
Hedges' P-value		0.4053

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	84.12 (15.14)	85.82 (13.99)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	81.54 (1.87)	85.47 (1.92)
95% CI of LS mean	(77.85, 85.23)	(81.67, 89.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.93 (-1.37, 9.23)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	-2.94 (1.79)	-0.65 (1.83)
95% CI of LS mean	(-6.47, 0.59)	(-4.27, 2.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.29 (-2.77, 7.35)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	83.54 (1.47)	88.32 (1.50)
95% CI of LS mean	(80.65, 86.43)	(85.36, 91.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.78 (0.64, 8.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	-0.79 (1.50)	2.24 (1.54)
95% CI of LS mean	(-3.75, 2.18)	(-0.79, 5.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.03 (-1.22, 7.28)
Week 24 (MMRM)		
n	89	83
LS mean (SE)	82.51 (1.92)	83.92 (1.98)
95% CI of LS mean	(78.71, 86.31)	(80.00, 87.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-4.05, 6.87)
Absolute Change at Week 24 (MMRM)		
n	87	81
LS mean (SE)	-1.90 (1.90)	-1.77 (1.96)
95% CI of LS mean	(-5.65, 1.84)	(-5.64, 2.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-5.25, 5.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	80.81 (16.61)	87.11 (13.20)
Absolute Change at Week 52		
n	86	76
Mean (SD)	-3.46 (13.30)	1.61 (13.27)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	80.97 (1.58)	87.19 (1.65)
95% CI of LS mean	(77.86, 84.09)	(83.93, 90.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.22 (1.70, 10.73)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	-3.42 (1.44)	1.31 (1.51)
95% CI of LS mean	(-6.26, -0.57)	(-1.67, 4.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.73 (0.60, 8.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	-2.04 (1.32)	0.59 (1.36)
95% CI of LS mean	(-4.64, 0.57)	(-2.09, 3.28)
P-value within Treatment	0.1255	0.6636
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-1.12, 6.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1683
Hedges' G (SE)		0.21 (0.15)
Hedges' 95% CI		(-0.09, 0.51)
Hedges' P-value		0.1689

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	81.98 (16.11)	85.80 (15.39)
Week 8 (MMRM)		
n	108	105
LS mean (SE)	80.56 (1.58)	84.56 (1.61)
95% CI of LS mean	(77.44, 83.69)	(81.39, 87.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.00 (-0.45, 8.45)
Absolute Change at Week 8 (MMRM)		
n	106	104
LS mean (SE)	-1.46 (1.64)	-0.94 (1.66)
95% CI of LS mean	(-4.70, 1.78)	(-4.22, 2.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-4.09, 5.13)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	78.19 (1.87)	84.42 (1.90)
95% CI of LS mean	(74.50, 81.89)	(80.67, 88.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.23 (0.96, 11.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	-3.31 (1.78)	-0.42 (1.80)
95% CI of LS mean	(-6.83, 0.20)	(-3.98, 3.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.89 (-2.11, 7.89)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	81.12 (1.57)	87.56 (1.59)
95% CI of LS mean	(78.03, 84.21)	(84.42, 90.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.44 (2.03, 10.85)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	-0.66 (1.62)	1.90 (1.64)
95% CI of LS mean	(-3.85, 2.53)	(-1.32, 5.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.56 (-1.98, 7.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	104	106
Mean (SD)	82.72 (16.75)	87.13 (13.62)
Absolute Change at Week 52		
n	102	104
Mean (SD)	0.65 (15.42)	1.44 (15.78)
Week 52 (MMRM)		
n	103	103
LS mean (SE)	82.41 (1.47)	87.10 (1.48)
95% CI of LS mean	(79.52, 85.31)	(84.19, 90.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.69 (0.58, 8.80)
Absolute Change at Week 52 (MMRM)		
n	101	102
LS mean (SE)	0.38 (1.55)	1.39 (1.56)
95% CI of LS mean	(-2.68, 3.44)	(-1.68, 4.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-3.33, 5.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	-1.20 (1.35)	0.96 (1.36)
95% CI of LS mean	(-3.85, 1.46)	(-1.73, 3.64)
P-value within Treatment	0.3756	0.4823
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.15 (-1.62, 5.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2620
Hedges' G (SE)		0.16 (0.14)
Hedges' 95% CI		(-0.12, 0.43)
Hedges' P-value		0.2627

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Baseline		
n	172	166
Mean (SD)	82.57 (15.87)	85.54 (15.22)
Week 8 (MMRM)		
n	171	162
LS mean (SE)	79.93 (1.34)	85.01 (1.38)
95% CI of LS mean	(77.29, 82.57)	(82.29, 87.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.08 (1.29, 8.86)
Absolute Change at Week 8 (MMRM)		
n	167	160
LS mean (SE)	-2.88 (1.34)	-0.46 (1.37)
95% CI of LS mean	(-5.52, -0.25)	(-3.16, 2.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.42 (-1.35, 6.20)
Week 16 (MMRM)		
n	171	163
LS mean (SE)	79.77 (1.33)	86.08 (1.37)
95% CI of LS mean	(77.14, 82.39)	(83.39, 88.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.31 (2.55, 10.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	167	160
LS mean (SE)	-2.69 (1.30)	1.05 (1.33)
95% CI of LS mean	(-5.25, -0.13)	(-1.56, 3.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.74 (0.08, 7.40)
Week 24 (MMRM)		
n	171	161
LS mean (SE)	80.90 (1.34)	85.17 (1.38)
95% CI of LS mean	(78.25, 83.54)	(82.45, 87.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.27 (0.48, 8.07)
Absolute Change at Week 24 (MMRM)		
n	167	158
LS mean (SE)	-1.77 (1.38)	-0.17 (1.42)
95% CI of LS mean	(-4.49, 0.94)	(-2.96, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.60 (-2.29, 5.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Week 52		
n	168	158
Mean (SD)	80.61 (17.08)	86.90 (13.68)
Absolute Change at Week 52		
n	164	154
Mean (SD)	-2.20 (14.64)	1.60 (15.06)
Week 52 (MMRM)		
n	166	154
LS mean (SE)	80.54 (1.18)	86.92 (1.22)
95% CI of LS mean	(78.22, 82.86)	(84.52, 89.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.38 (3.04, 9.71)
Absolute Change at Week 52 (MMRM)		
n	162	151
LS mean (SE)	-2.28 (1.17)	1.40 (1.21)
95% CI of LS mean	(-4.59, 0.03)	(-0.98, 3.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.68 (0.37, 6.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	167	160
LS mean (SE)	-2.25 (1.05)	0.76 (1.07)
95% CI of LS mean	(-4.31, -0.19)	(-1.35, 2.87)
P-value within Treatment	0.0327	0.4790
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.01 (0.06, 5.96)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0458
Hedges' G (SE)		0.22 (0.11)
Hedges' 95% CI		(0.00, 0.44)
Hedges' P-value		0.0464

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Baseline		
n	25	26
Mean (SD)	85.44 (14.37)	87.50 (11.42)
Week 8 (MMRM)		
n	25	26
LS mean (SE)	88.33 (2.19)	84.41 (2.15)
95% CI of LS mean	(83.93, 92.73)	(80.09, 88.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.92 (-10.11, 2.26)
Absolute Change at Week 8 (MMRM)		
n	25	26
LS mean (SE)	2.66 (2.46)	-2.88 (2.42)
95% CI of LS mean	(-2.29, 7.62)	(-7.74, 1.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.54 (-12.51, 1.42)
Week 16 (MMRM)		
n	25	26
LS mean (SE)	86.77 (2.84)	86.54 (2.78)
95% CI of LS mean	(81.06, 92.48)	(80.94, 92.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-8.24, 7.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	25	26
LS mean (SE)	1.11 (2.91)	-0.74 (2.86)
95% CI of LS mean	(-4.76, 6.97)	(-6.49, 5.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.85 (-10.08, 6.38)
Week 24 (MMRM)		
n	25	26
LS mean (SE)	87.88 (2.61)	90.60 (2.56)
95% CI of LS mean	(82.63, 93.13)	(85.45, 95.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.72 (-4.65, 10.09)
Absolute Change at Week 24 (MMRM)		
n	25	26
LS mean (SE)	2.22 (2.43)	3.32 (2.39)
95% CI of LS mean	(-2.68, 7.12)	(-1.49, 8.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.10 (-5.79, 7.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Week 52		
n	24	26
Mean (SD)	90.51 (10.03)	88.46 (11.83)
Absolute Change at Week 52		
n	24	26
Mean (SD)	5.44 (12.65)	0.96 (12.88)
Week 52 (MMRM)		
n	24	26
LS mean (SE)	90.05 (2.16)	88.36 (2.09)
95% CI of LS mean	(85.70, 94.40)	(84.15, 92.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.69 (-7.76, 4.38)
Absolute Change at Week 52 (MMRM)		
n	24	26
LS mean (SE)	4.61 (2.65)	1.07 (2.57)
95% CI of LS mean	(-0.74, 9.96)	(-4.10, 6.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.54 (-11.00, 3.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	25	26
LS mean (SE)	2.64 (2.14)	1.22 (2.09)
95% CI of LS mean	(-1.67, 6.96)	(-3.00, 5.43)
P-value within Treatment	0.2230	0.5646
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.43 (-7.49, 4.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6370
Hedges' G (SE)		-0.13 (0.28)
Hedges' 95% CI		(-0.69, 0.42)
Hedges' P-value		0.6355

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.2.2.9.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by SubgroupsFull Analysis Set

Version: Parents/Caregivers Version

Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.2.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.8153
Age at screening (<18 years vs. ≥18 years) [2]	0.5609
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.3364
Sex (Male vs. Female) [1]	0.8542
Region (North America vs. Rest of the World) [1]	0.9273

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4566
Age at screening (<18 years vs. ≥18 years) [2]	0.7510
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.9061
Sex (Male vs. Female) [1]	0.9124
Region (North America vs. Rest of the World) [1]	0.2363

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.5781
Age at screening (<18 years vs. ≥18 years) [2]	0.8925
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5484
Sex (Male vs. Female) [1]	0.9382
Region (North America vs. Rest of the World) [1]	0.1820

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1117
Age at screening (<18 years vs. ≥18 years) [2]	0.0116
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5858
Sex (Male vs. Female) [1]	0.1458
Region (North America vs. Rest of the World) [1]	0.7498

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6374
Age at screening (<18 years vs. ≥18 years) [2]	0.1049
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1078
Sex (Male vs. Female) [1]	0.8262
Region (North America vs. Rest of the World) [1]	0.7940

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0697
Age at screening (<18 years vs. ≥18 years) [2]	0.7122
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.3188
Sex (Male vs. Female) [1]	0.5642
Region (North America vs. Rest of the World) [1]	0.6690

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1536
Age at screening (<18 years vs. ≥18 years) [2]	0.9576
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.2094
Sex (Male vs. Female) [1]	0.0355
Region (North America vs. Rest of the World) [1]	0.8422

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1525
Age at screening (<18 years vs. ≥18 years) [2]	0.4447
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.3774
Sex (Male vs. Female) [1]	0.9760
Region (North America vs. Rest of the World) [1]	0.6044

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3420
Age at screening (<18 years vs. ≥18 years) [2]	0.0749
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0457
Sex (Male vs. Female) [1]	0.6674
Region (North America vs. Rest of the World) [1]	0.1078

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0859
Age at screening (<18 years vs. ≥18 years) [2]	0.8917
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.4562
Sex (Male vs. Female) [1]	0.1126
Region (North America vs. Rest of the World) [1]	0.8615

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1735
Age at screening (<18 years vs. ≥18 years) [2]	0.9697
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.9150
Sex (Male vs. Female) [1]	0.1536
Region (North America vs. Rest of the World) [1]	0.6444

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.9149

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.5774

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.0987

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.5227

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.6327

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.6137

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.9636

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.4062

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.1917

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.4454

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.9627

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride, age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	75.38 (22.44)	74.07 (24.02)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	76.36 (2.16)	74.52 (2.32)
95% CI of LS mean	(72.10, 80.62)	(69.95, 79.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.84 (-8.11, 4.42)
Absolute Change at Week 8 (MMRM)		
n	110	96
LS mean (SE)	1.07 (1.29)	0.43 (1.39)
95% CI of LS mean	(-1.49, 3.62)	(-2.30, 3.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-4.39, 3.11)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	76.02 (2.09)	77.04 (2.24)
95% CI of LS mean	(71.90, 80.13)	(72.62, 81.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.02 (-5.04, 7.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	0.22 (1.35)	3.41 (1.44)
95% CI of LS mean	(-2.44, 2.87)	(0.56, 6.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.19 (-0.71, 7.09)
Week 24 (MMRM)		
n	113	98
LS mean (SE)	76.21 (2.22)	76.30 (2.38)
95% CI of LS mean	(71.84, 80.59)	(71.60, 80.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-6.35, 6.52)
Absolute Change at Week 24 (MMRM)		
n	110	96
LS mean (SE)	0.41 (1.51)	2.65 (1.61)
95% CI of LS mean	(-2.56, 3.38)	(-0.53, 5.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.24 (-2.12, 6.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	77.58 (22.02)	77.66 (21.46)
Absolute Change at Week 52		
n	109	92
Mean (SD)	1.94 (14.96)	2.78 (14.79)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	77.46 (2.07)	77.13 (2.24)
95% CI of LS mean	(73.38, 81.54)	(72.72, 81.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-6.36, 5.70)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	1.88 (1.44)	3.21 (1.57)
95% CI of LS mean	(-0.97, 4.72)	(0.12, 6.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.34 (-2.88, 5.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	0.83 (1.18)	3.09 (1.27)
95% CI of LS mean	(-1.50, 3.17)	(0.59, 5.59)
P-value within Treatment	0.4809	0.0158
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.26 (-1.18, 5.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1966
Hedges' G (SE)		0.18 (0.14)
Hedges' 95% CI		(-0.09, 0.46)
Hedges' P-value		0.1959

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	78.95 (19.92)	81.56 (21.42)
Week 8 (MMRM)		
n	84	90
LS mean (SE)	81.26 (2.14)	83.70 (2.06)
95% CI of LS mean	(77.04, 85.48)	(79.64, 87.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.44 (-3.42, 8.30)
Absolute Change at Week 8 (MMRM)		
n	83	90
LS mean (SE)	2.14 (1.35)	2.41 (1.30)
95% CI of LS mean	(-0.53, 4.81)	(-0.15, 4.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-3.44, 3.97)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	80.57 (2.19)	83.27 (2.10)
95% CI of LS mean	(76.25, 84.89)	(79.12, 87.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.70 (-3.30, 8.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	1.77 (1.51)	1.96 (1.44)
95% CI of LS mean	(-1.20, 4.74)	(-0.88, 4.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.19 (-3.93, 4.30)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	77.22 (2.27)	82.49 (2.18)
95% CI of LS mean	(72.75, 81.69)	(78.19, 86.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.26 (-0.94, 11.47)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	-1.61 (1.69)	1.37 (1.62)
95% CI of LS mean	(-4.95, 1.72)	(-1.83, 4.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.98 (-1.64, 7.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	80	87
Mean (SD)	81.11 (18.06)	82.76 (19.60)
Absolute Change at Week 52		
n	79	86
Mean (SD)	1.41 (14.05)	1.55 (13.65)
Week 52 (MMRM)		
n	79	87
LS mean (SE)	80.51 (2.08)	82.65 (1.99)
95% CI of LS mean	(76.40, 84.62)	(78.72, 86.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.14 (-3.55, 7.83)
Absolute Change at Week 52 (MMRM)		
n	78	86
LS mean (SE)	1.25 (1.56)	1.50 (1.48)
95% CI of LS mean	(-1.82, 4.32)	(-1.44, 4.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-4.00, 4.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	0.47 (1.27)	1.61 (1.22)
95% CI of LS mean	(-2.05, 2.98)	(-0.80, 4.02)
P-value within Treatment	0.7129	0.1892
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-2.35, 4.62)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5197
Hedges' G (SE)		0.10 (0.15)
Hedges' 95% CI		(-0.20, 0.40)
Hedges' P-value		0.5196

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	75.86 (24.14)	79.11 (27.84)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	82.38 (4.23)	79.25 (4.64)
95% CI of LS mean	(73.89, 90.87)	(69.93, 88.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.13 (-15.81, 9.54)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	5.89 (2.66)	1.68 (2.89)
95% CI of LS mean	(0.54, 11.24)	(-4.14, 7.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.21 (-12.15, 3.72)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	78.82 (3.90)	82.29 (4.29)
95% CI of LS mean	(70.98, 86.65)	(73.68, 90.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.47 (-8.25, 15.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	2.41 (2.81)	4.79 (3.10)
95% CI of LS mean	(-3.25, 8.06)	(-1.45, 11.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-6.07, 10.83)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	78.82 (4.41)	77.65 (4.85)
95% CI of LS mean	(69.97, 87.68)	(67.92, 87.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.18 (-14.39, 12.04)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	2.41 (3.26)	0.45 (3.59)
95% CI of LS mean	(-4.13, 8.96)	(-6.77, 7.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.96 (-11.74, 7.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	28	25
Mean (SD)	80.95 (21.14)	83.56 (21.06)
Absolute Change at Week 52		
n	27	24
Mean (SD)	4.53 (13.87)	6.02 (14.65)
Week 52 (MMRM)		
n	28	24
LS mean (SE)	81.02 (3.78)	82.78 (4.13)
95% CI of LS mean	(73.44, 88.60)	(74.49, 91.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.76 (-9.55, 13.07)
Absolute Change at Week 52 (MMRM)		
n	27	23
LS mean (SE)	4.74 (2.78)	5.91 (3.04)
95% CI of LS mean	(-0.85, 10.34)	(-0.20, 12.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-7.15, 9.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	3.19 (2.45)	3.71 (2.71)
95% CI of LS mean	(-1.75, 8.12)	(-1.73, 9.15)
P-value within Treatment	0.2002	0.1763
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-6.85, 7.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8866
Hedges' G (SE)		0.04 (0.28)
Hedges' 95% CI		(-0.52, 0.60)
Hedges' P-value		0.8860

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	76.72 (21.52)	77.64 (22.29)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	77.77 (1.65)	78.89 (1.66)
95% CI of LS mean	(74.53, 81.01)	(75.62, 82.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.12 (-3.49, 5.73)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	0.91 (1.00)	1.22 (1.01)
95% CI of LS mean	(-1.06, 2.87)	(-0.77, 3.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-2.49, 3.10)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	77.79 (1.65)	79.72 (1.66)
95% CI of LS mean	(74.54, 81.03)	(76.44, 82.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.93 (-2.68, 6.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	0.74 (1.07)	2.28 (1.08)
95% CI of LS mean	(-1.37, 2.85)	(0.16, 4.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.54 (-1.45, 4.53)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	76.26 (1.70)	79.52 (1.72)
95% CI of LS mean	(72.91, 79.61)	(76.14, 82.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.26 (-1.50, 8.02)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	-0.82 (1.20)	2.14 (1.20)
95% CI of LS mean	(-3.17, 1.54)	(-0.23, 4.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.95 (-0.39, 6.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	78.45 (20.67)	79.73 (20.60)
Absolute Change at Week 52		
n	162	156
Mean (SD)	1.37 (14.69)	1.64 (14.04)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	78.35 (1.61)	79.31 (1.63)
95% CI of LS mean	(75.19, 81.51)	(76.11, 82.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.96 (-3.54, 5.46)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	1.22 (1.14)	1.69 (1.16)
95% CI of LS mean	(-1.03, 3.47)	(-0.59, 3.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.47 (-2.74, 3.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	0.38 (0.93)	2.04 (0.93)
95% CI of LS mean	(-1.44, 2.20)	(0.20, 3.87)
P-value within Treatment	0.6810	0.0298
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.65 (-0.93, 4.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2094
Hedges' G (SE)		0.14 (0.11)
Hedges' 95% CI		(-0.08, 0.36)
Hedges' P-value		0.2097

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	81.29 (15.74)	67.36 (26.75)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	81.12 (4.63)	73.81 (5.07)
95% CI of LS mean	(71.66, 90.58)	(63.46, 84.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.30 (-21.65, 7.05)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	-0.11 (2.68)	6.38 (2.93)
95% CI of LS mean	(-5.60, 5.37)	(0.39, 12.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.50 (-1.80, 14.80)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	82.87 (4.89)	73.12 (5.35)
95% CI of LS mean	(72.89, 92.85)	(62.20, 84.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.75 (-24.85, 5.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	1.64 (3.29)	5.69 (3.60)
95% CI of LS mean	(-5.07, 8.35)	(-1.64, 13.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.05 (-6.03, 14.13)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	79.95 (5.30)	75.20 (5.79)
95% CI of LS mean	(69.12, 90.78)	(63.37, 87.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.75 (-21.06, 11.57)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	-1.28 (3.58)	7.77 (3.91)
95% CI of LS mean	(-8.58, 6.01)	(-0.19, 15.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.06 (-1.87, 19.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	82.10 (21.61)	66.67 (21.35)
Absolute Change at Week 52		
n	18	13
Mean (SD)	0.00 (17.46)	-3.42 (13.13)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	81.08 (5.84)	63.81 (6.56)
95% CI of LS mean	(68.92, 93.24)	(50.22, 77.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-17.26 (-35.75, 1.23)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	-0.09 (3.77)	-3.43 (4.37)
95% CI of LS mean	(-7.86, 7.68)	(-12.40, 5.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.34 (-15.31, 8.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	0.09 (2.91)	3.35 (3.22)
95% CI of LS mean	(-5.88, 6.05)	(-3.24, 9.93)
P-value within Treatment	0.9759	0.3078
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.26 (-5.79, 12.30)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4673
Hedges' G (SE)		0.25 (0.33)
Hedges' 95% CI		(-0.43, 0.93)
Hedges' P-value		0.4600

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	76.21 (22.40)	78.86 (22.59)
Week 8 (MMRM)		
n	178	172
LS mean (SE)	78.19 (1.64)	79.39 (1.66)
95% CI of LS mean	(74.97, 81.41)	(76.13, 82.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-3.38, 5.80)
Absolute Change at Week 8 (MMRM)		
n	174	170
LS mean (SE)	1.77 (0.99)	0.86 (1.00)
95% CI of LS mean	(-0.18, 3.72)	(-1.11, 2.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.91 (-3.69, 1.86)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	77.44 (1.60)	80.66 (1.62)
95% CI of LS mean	(74.29, 80.59)	(77.47, 83.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-1.27, 7.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	0.86 (1.05)	2.37 (1.06)
95% CI of LS mean	(-1.21, 2.92)	(0.29, 4.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-1.42, 4.45)
Week 24 (MMRM)		
n	177	172
LS mean (SE)	76.31 (1.68)	79.64 (1.70)
95% CI of LS mean	(73.01, 79.61)	(76.29, 82.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.33 (-1.37, 8.03)
Absolute Change at Week 24 (MMRM)		
n	173	169
LS mean (SE)	-0.30 (1.19)	1.45 (1.20)
95% CI of LS mean	(-2.63, 2.03)	(-0.91, 3.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.75 (-1.57, 5.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	174	169
Mean (SD)	78.61 (20.62)	81.39 (20.31)
Absolute Change at Week 52		
n	170	166
Mean (SD)	2.03 (14.34)	2.61 (14.21)
Week 52 (MMRM)		
n	173	167
LS mean (SE)	78.48 (1.53)	81.05 (1.55)
95% CI of LS mean	(75.48, 81.49)	(78.00, 84.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.56 (-1.72, 6.84)
Absolute Change at Week 52 (MMRM)		
n	169	164
LS mean (SE)	1.83 (1.11)	2.72 (1.12)
95% CI of LS mean	(-0.34, 4.01)	(0.52, 4.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.89 (-2.20, 3.99)

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- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	0.80 (0.91)	2.18 (0.92)
95% CI of LS mean	(-1.00, 2.59)	(0.37, 3.99)
P-value within Treatment	0.3825	0.0185
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.38 (-1.17, 3.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2867
Hedges' G (SE)		0.12 (0.11)
Hedges' 95% CI		(-0.10, 0.33)
Hedges' P-value		0.2869

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
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- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	74.85 (23.19)	75.07 (25.39)
Week 8 (MMRM)		
n	116	116
LS mean (SE)	76.81 (2.15)	76.92 (2.16)
95% CI of LS mean	(72.57, 81.06)	(72.66, 81.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-5.92, 6.14)
Absolute Change at Week 8 (MMRM)		
n	112	115
LS mean (SE)	1.60 (1.29)	2.11 (1.28)
95% CI of LS mean	(-0.95, 4.14)	(-0.41, 4.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.51 (-3.08, 4.10)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	76.83 (2.14)	77.89 (2.15)
95% CI of LS mean	(72.61, 81.06)	(73.66, 82.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.06 (-4.95, 7.06)

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- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	1.37 (1.39)	3.22 (1.38)
95% CI of LS mean	(-1.38, 4.11)	(0.51, 5.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.85 (-2.02, 5.72)
Week 24 (MMRM)		
n	115	115
LS mean (SE)	74.61 (2.26)	76.20 (2.27)
95% CI of LS mean	(70.16, 79.07)	(71.73, 80.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.59 (-4.74, 7.91)
Absolute Change at Week 24 (MMRM)		
n	111	114
LS mean (SE)	-0.94 (1.56)	1.52 (1.54)
95% CI of LS mean	(-4.02, 2.13)	(-1.52, 4.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.46 (-1.87, 6.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	78.56 (20.88)	77.98 (21.81)
Absolute Change at Week 52		
n	109	110
Mean (SD)	3.26 (14.68)	2.22 (14.42)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	78.48 (1.99)	77.58 (2.00)
95% CI of LS mean	(74.56, 82.41)	(73.64, 81.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.90 (-6.48, 4.68)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	2.94 (1.41)	2.76 (1.40)
95% CI of LS mean	(0.16, 5.72)	(0.01, 5.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-4.10, 3.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	1.12 (1.21)	2.50 (1.20)
95% CI of LS mean	(-1.27, 3.51)	(0.13, 4.86)
P-value within Treatment	0.3567	0.0384
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.38 (-2.00, 4.75)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4219
Hedges' G (SE)		0.11 (0.13)
Hedges' 95% CI		(-0.15, 0.37)
Hedges' P-value		0.4207

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	78.98 (19.79)	81.96 (18.30)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	81.11 (2.12)	81.69 (2.23)
95% CI of LS mean	(76.92, 85.30)	(77.28, 86.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-5.51, 6.67)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	1.55 (1.34)	0.07 (1.43)
95% CI of LS mean	(-1.09, 4.20)	(-2.74, 2.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.48 (-5.35, 2.39)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	79.86 (2.03)	83.01 (2.13)
95% CI of LS mean	(75.84, 83.87)	(78.81, 87.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.16 (-2.67, 8.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	0.37 (1.41)	1.76 (1.49)
95% CI of LS mean	(-2.41, 3.15)	(-1.19, 4.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-2.67, 5.44)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	79.85 (2.08)	83.75 (2.19)
95% CI of LS mean	(75.74, 83.97)	(79.43, 88.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.90 (-2.08, 9.88)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	0.37 (1.58)	2.77 (1.68)
95% CI of LS mean	(-2.75, 3.49)	(-0.56, 6.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.40 (-2.16, 6.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	80	73
Mean (SD)	79.17 (20.57)	83.71 (18.34)
Absolute Change at Week 52		
n	80	70
Mean (SD)	-0.14 (14.31)	2.22 (13.85)
Week 52 (MMRM)		
n	79	69
LS mean (SE)	79.39 (2.17)	82.88 (2.29)
95% CI of LS mean	(75.11, 83.68)	(78.35, 87.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.48 (-2.77, 9.73)
Absolute Change at Week 52 (MMRM)		
n	79	67
LS mean (SE)	-0.09 (1.60)	1.54 (1.73)
95% CI of LS mean	(-3.26, 3.07)	(-1.88, 4.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-3.04, 6.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	0.21 (1.20)	2.02 (1.28)
95% CI of LS mean	(-2.17, 2.59)	(-0.52, 4.56)
P-value within Treatment	0.8592	0.1175
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.81 (-1.68, 5.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3072
Hedges' G (SE)		0.17 (0.16)
Hedges' 95% CI		(-0.15, 0.48)
Hedges' P-value		0.3069

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	78.66 (20.02)	79.61 (22.01)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	80.04 (2.17)	80.47 (2.23)
95% CI of LS mean	(75.75, 84.33)	(76.07, 84.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-5.72, 6.58)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	1.15 (1.44)	0.83 (1.48)
95% CI of LS mean	(-1.70, 4.00)	(-2.09, 3.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-4.40, 3.77)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	78.19 (2.32)	80.23 (2.37)
95% CI of LS mean	(73.61, 82.76)	(75.55, 84.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.04 (-4.51, 8.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	-0.48 (1.55)	0.78 (1.58)
95% CI of LS mean	(-3.54, 2.57)	(-2.35, 3.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.26 (-3.12, 5.63)
Week 24 (MMRM)		
n	89	84
LS mean (SE)	78.81 (2.28)	81.29 (2.33)
95% CI of LS mean	(74.32, 83.30)	(76.68, 85.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.48 (-3.96, 8.93)
Absolute Change at Week 24 (MMRM)		
n	87	82
LS mean (SE)	0.15 (1.62)	2.09 (1.67)
95% CI of LS mean	(-3.05, 3.36)	(-1.20, 5.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.94 (-2.66, 6.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	80.43 (19.43)	81.48 (20.31)
Absolute Change at Week 52		
n	86	76
Mean (SD)	1.29 (15.94)	0.73 (16.16)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	80.25 (2.16)	80.47 (2.24)
95% CI of LS mean	(75.98, 84.52)	(76.04, 84.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-5.94, 6.38)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	1.29 (1.79)	1.03 (1.88)
95% CI of LS mean	(-2.25, 4.84)	(-2.68, 4.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-5.40, 4.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	0.32 (1.40)	1.30 (1.44)
95% CI of LS mean	(-2.44, 3.08)	(-1.54, 4.14)
P-value within Treatment	0.8183	0.3675
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.98 (-2.99, 4.94)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6268
Hedges' G (SE)		0.07 (0.15)
Hedges' 95% CI		(-0.23, 0.38)
Hedges' P-value		0.6263

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	74.92 (23.20)	76.43 (23.78)
Week 8 (MMRM)		
n	109	105
LS mean (SE)	77.14 (2.16)	77.77 (2.20)
95% CI of LS mean	(72.87, 81.40)	(73.43, 82.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-5.45, 6.72)
Absolute Change at Week 8 (MMRM)		
n	107	104
LS mean (SE)	2.07 (1.23)	1.59 (1.25)
95% CI of LS mean	(-0.36, 4.49)	(-0.87, 4.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-3.93, 2.98)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	77.79 (2.03)	79.90 (2.06)
95% CI of LS mean	(73.79, 81.79)	(75.83, 83.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.11 (-3.59, 7.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	2.26 (1.29)	4.03 (1.30)
95% CI of LS mean	(-0.28, 4.79)	(1.47, 6.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.78 (-1.83, 5.38)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	74.88 (2.23)	77.66 (2.26)
95% CI of LS mean	(70.49, 79.27)	(73.19, 82.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.77 (-3.48, 9.03)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	-0.71 (1.54)	1.77 (1.55)
95% CI of LS mean	(-3.74, 2.32)	(-1.29, 4.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.48 (-1.83, 6.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	105	106
Mean (SD)	77.46 (21.71)	79.35 (20.94)
Absolute Change at Week 52		
n	103	104
Mean (SD)	2.27 (13.42)	3.31 (12.47)
Week 52 (MMRM)		
n	104	103
LS mean (SE)	77.53 (2.01)	79.23 (2.04)
95% CI of LS mean	(73.56, 81.49)	(75.21, 83.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.70 (-3.94, 7.35)
Absolute Change at Week 52 (MMRM)		
n	102	102
LS mean (SE)	2.11 (1.26)	3.22 (1.26)
95% CI of LS mean	(-0.37, 4.60)	(0.73, 5.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.11 (-2.41, 4.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	1.22 (1.08)	3.01 (1.09)
95% CI of LS mean	(-0.90, 3.34)	(0.86, 5.15)
P-value within Treatment	0.2586	0.0062
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.79 (-1.23, 4.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2442
Hedges' G (SE)		0.16 (0.14)
Hedges' 95% CI		(-0.11, 0.43)
Hedges' P-value		0.2449

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	98
Mean (SD)	83.63 (17.00)	85.94 (16.47)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	83.01 (1.57)	86.36 (1.68)
95% CI of LS mean	(79.92, 86.09)	(83.04, 89.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.35 (-1.19, 7.89)
Absolute Change at Week 8 (MMRM)		
n	110	95
LS mean (SE)	-1.30 (1.43)	1.24 (1.54)
95% CI of LS mean	(-4.13, 1.52)	(-1.80, 4.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.54 (-1.62, 6.71)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	82.51 (1.73)	84.11 (1.86)
95% CI of LS mean	(79.09, 85.92)	(80.44, 87.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.61 (-3.42, 6.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	95
LS mean (SE)	-1.81 (1.47)	-1.65 (1.58)
95% CI of LS mean	(-4.70, 1.08)	(-4.76, 1.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-4.09, 4.42)
Week 24 (MMRM)		
n	113	96
LS mean (SE)	84.19 (1.52)	84.90 (1.63)
95% CI of LS mean	(81.20, 87.18)	(81.67, 88.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.71 (-3.70, 5.12)
Absolute Change at Week 24 (MMRM)		
n	110	94
LS mean (SE)	-0.09 (1.42)	-0.41 (1.53)
95% CI of LS mean	(-2.89, 2.70)	(-3.42, 2.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.32 (-4.44, 3.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	84.72 (14.55)	83.45 (15.35)
Absolute Change at Week 52		
n	109	91
Mean (SD)	0.36 (16.22)	-2.44 (10.32)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	84.80 (1.39)	82.97 (1.51)
95% CI of LS mean	(82.06, 87.53)	(80.00, 85.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.83 (-5.88, 2.22)
Absolute Change at Week 52 (MMRM)		
n	109	90
LS mean (SE)	0.46 (1.31)	-2.28 (1.43)
95% CI of LS mean	(-2.11, 3.04)	(-5.09, 0.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.75 (-6.57, 1.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	95
LS mean (SE)	-0.48 (1.19)	-1.45 (1.29)
95% CI of LS mean	(-2.84, 1.88)	(-3.99, 1.10)
P-value within Treatment	0.6885	0.2633
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-4.44, 2.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5845
Hedges' G (SE)		-0.08 (0.14)
Hedges' 95% CI		(-0.35, 0.20)
Hedges' P-value		0.5832

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	81.44 (20.02)	83.76 (14.84)
Week 8 (MMRM)		
n	83	90
LS mean (SE)	80.33 (2.09)	85.99 (2.01)
95% CI of LS mean	(76.20, 84.47)	(82.02, 89.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.65 (-0.08, 11.38)
Absolute Change at Week 8 (MMRM)		
n	82	90
LS mean (SE)	-1.00 (1.68)	2.48 (1.61)
95% CI of LS mean	(-4.31, 2.32)	(-0.70, 5.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.47 (-1.12, 8.07)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	80.28 (2.17)	82.87 (2.08)
95% CI of LS mean	(75.98, 84.57)	(78.76, 86.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.59 (-3.35, 8.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	-1.09 (1.70)	-0.46 (1.62)
95% CI of LS mean	(-4.44, 2.25)	(-3.66, 2.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-4.00, 5.28)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	79.95 (1.92)	86.72 (1.85)
95% CI of LS mean	(76.15, 83.74)	(83.08, 90.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.78 (1.51, 12.05)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	-1.24 (1.44)	3.05 (1.38)
95% CI of LS mean	(-4.08, 1.60)	(0.32, 5.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.28 (0.35, 8.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	79	87
Mean (SD)	79.75 (22.35)	81.23 (19.56)
Absolute Change at Week 52		
n	78	86
Mean (SD)	-0.57 (16.88)	-1.94 (14.88)
Week 52 (MMRM)		
n	78	87
LS mean (SE)	80.63 (2.32)	81.51 (2.22)
95% CI of LS mean	(76.04, 85.21)	(77.13, 85.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.89 (-5.46, 7.23)
Absolute Change at Week 52 (MMRM)		
n	77	86
LS mean (SE)	-0.63 (1.78)	-1.84 (1.70)
95% CI of LS mean	(-4.15, 2.90)	(-5.19, 1.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.21 (-6.08, 3.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	-0.99 (1.35)	0.25 (1.29)
95% CI of LS mean	(-3.64, 1.67)	(-2.29, 2.79)
P-value within Treatment	0.4645	0.8458
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-2.44, 4.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5078
Hedges' G (SE)		0.10 (0.15)
Hedges' 95% CI		(-0.20, 0.40)
Hedges' P-value		0.5077

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	91.95 (14.21)	87.11 (14.59)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	89.03 (3.78)	83.77 (4.15)
95% CI of LS mean	(81.43, 96.62)	(75.44, 92.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.25 (-16.57, 6.07)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	-3.43 (2.79)	-0.99 (3.03)
95% CI of LS mean	(-9.03, 2.18)	(-7.08, 5.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.44 (-5.87, 10.74)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	86.35 (4.34)	81.68 (4.76)
95% CI of LS mean	(77.64, 95.07)	(72.12, 91.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.67 (-17.64, 8.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	-6.22 (3.12)	-2.34 (3.44)
95% CI of LS mean	(-12.49, 0.06)	(-9.27, 4.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.87 (-5.50, 13.24)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	91.91 (2.55)	88.74 (2.81)
95% CI of LS mean	(86.78, 97.05)	(83.09, 94.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.18 (-10.88, 4.52)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	-0.30 (2.54)	2.97 (2.80)
95% CI of LS mean	(-5.40, 4.80)	(-2.67, 8.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.27 (-4.37, 10.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	27	25
Mean (SD)	90.12 (17.52)	82.22 (20.79)
Absolute Change at Week 52		
n	26	24
Mean (SD)	-2.99 (13.90)	-3.70 (12.11)
Week 52 (MMRM)		
n	27	24
LS mean (SE)	90.34 (3.68)	79.62 (4.00)
95% CI of LS mean	(82.95, 97.73)	(71.59, 87.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.72 (-21.67, 0.24)
Absolute Change at Week 52 (MMRM)		
n	26	23
LS mean (SE)	-2.23 (2.52)	-4.61 (2.73)
95% CI of LS mean	(-7.31, 2.85)	(-10.10, 0.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.38 (-9.89, 5.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	-2.91 (2.15)	-1.33 (2.37)
95% CI of LS mean	(-7.24, 1.41)	(-6.09, 3.44)
P-value within Treatment	0.1820	0.5777
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.59 (-4.89, 8.07)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6244
Hedges' G (SE)		0.14 (0.28)
Hedges' 95% CI		(-0.42, 0.69)
Hedges' P-value		0.6227

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	166
Mean (SD)	81.05 (18.49)	84.74 (15.88)
Week 8 (MMRM)		
n	167	164
LS mean (SE)	80.55 (1.34)	86.54 (1.35)
95% CI of LS mean	(77.92, 83.19)	(83.88, 89.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.99 (2.24, 9.74)
Absolute Change at Week 8 (MMRM)		
n	164	161
LS mean (SE)	-0.78 (1.18)	2.25 (1.19)
95% CI of LS mean	(-3.10, 1.55)	(-0.10, 4.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.03 (-0.28, 6.33)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	80.66 (1.41)	83.78 (1.42)
95% CI of LS mean	(77.89, 83.44)	(80.98, 86.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.12 (-0.82, 7.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	162
LS mean (SE)	-0.67 (1.18)	-0.90 (1.19)
95% CI of LS mean	(-2.99, 1.65)	(-3.24, 1.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-3.53, 3.07)
Week 24 (MMRM)		
n	167	162
LS mean (SE)	80.66 (1.33)	85.44 (1.34)
95% CI of LS mean	(78.05, 83.27)	(82.80, 88.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.78 (1.07, 8.49)
Absolute Change at Week 24 (MMRM)		
n	164	160
LS mean (SE)	-0.60 (1.10)	1.05 (1.11)
95% CI of LS mean	(-2.77, 1.56)	(-1.14, 3.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.65 (-1.43, 4.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	81.41 (18.12)	82.39 (17.20)
Absolute Change at Week 52		
n	162	155
Mean (SD)	0.45 (16.78)	-1.94 (12.73)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	81.63 (1.35)	82.63 (1.37)
95% CI of LS mean	(78.98, 84.29)	(79.93, 85.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.00 (-2.79, 4.78)
Absolute Change at Week 52 (MMRM)		
n	160	153
LS mean (SE)	0.45 (1.18)	-1.74 (1.20)
95% CI of LS mean	(-1.87, 2.76)	(-4.10, 0.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.19 (-5.49, 1.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	162
LS mean (SE)	-0.28 (0.98)	-0.53 (0.99)
95% CI of LS mean	(-2.20, 1.64)	(-2.47, 1.41)
P-value within Treatment	0.7779	0.5895
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-2.99, 2.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8534
Hedges' G (SE)		-0.02 (0.11)
Hedges' 95% CI		(-0.24, 0.20)
Hedges' P-value		0.8533

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	81.87 (18.60)	81.94 (19.40)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	82.70 (4.13)	88.60 (4.51)
95% CI of LS mean	(74.29, 91.11)	(79.41, 97.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.90 (-6.74, 18.53)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	0.39 (4.08)	7.17 (4.45)
95% CI of LS mean	(-7.92, 8.70)	(-1.90, 16.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.78 (-5.69, 19.25)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	82.12 (4.65)	83.74 (5.08)
95% CI of LS mean	(72.62, 91.61)	(73.37, 94.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.62 (-12.60, 15.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-0.19 (4.21)	2.31 (4.60)
95% CI of LS mean	(-8.78, 8.40)	(-7.07, 11.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.50 (-10.37, 15.38)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	83.87 (3.76)	88.60 (4.11)
95% CI of LS mean	(76.20, 91.54)	(80.21, 96.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.73 (-6.84, 16.30)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	1.56 (3.23)	7.17 (3.53)
95% CI of LS mean	(-5.02, 8.15)	(-0.03, 14.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.61 (-4.37, 15.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	88.27 (11.09)	78.57 (21.11)
Absolute Change at Week 52		
n	18	13
Mean (SD)	5.56 (19.15)	1.71 (14.23)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	87.72 (3.49)	83.05 (3.93)
95% CI of LS mean	(80.59, 94.84)	(75.04, 91.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.66 (-15.59, 6.26)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	5.27 (3.87)	2.00 (4.35)
95% CI of LS mean	(-2.63, 13.17)	(-6.86, 10.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.26 (-15.31, 8.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	2.21 (3.37)	3.83 (3.70)
95% CI of LS mean	(-4.66, 9.09)	(-3.72, 11.37)
P-value within Treatment	0.5163	0.3088
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.62 (-8.80, 12.03)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7537
Hedges' G (SE)		0.11 (0.33)
Hedges' 95% CI		(-0.57, 0.78)
Hedges' P-value		0.7487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	173
Mean (SD)	82.77 (18.38)	85.16 (15.36)
Week 8 (MMRM)		
n	177	172
LS mean (SE)	81.62 (1.34)	86.12 (1.36)
95% CI of LS mean	(78.98, 84.26)	(83.44, 88.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.50 (0.73, 8.26)
Absolute Change at Week 8 (MMRM)		
n	173	169
LS mean (SE)	-1.46 (1.12)	1.45 (1.14)
95% CI of LS mean	(-3.67, 0.75)	(-0.79, 3.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.91 (-0.24, 6.06)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	81.33 (1.43)	83.65 (1.45)
95% CI of LS mean	(78.52, 84.14)	(80.80, 86.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.32 (-1.68, 6.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	169
LS mean (SE)	-1.76 (1.14)	-1.27 (1.15)
95% CI of LS mean	(-3.99, 0.48)	(-3.54, 0.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-2.70, 3.67)
Week 24 (MMRM)		
n	177	170
LS mean (SE)	82.07 (1.27)	85.68 (1.29)
95% CI of LS mean	(79.57, 84.58)	(83.13, 88.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (0.03, 7.18)
Absolute Change at Week 24 (MMRM)		
n	173	167
LS mean (SE)	-0.92 (1.06)	0.81 (1.08)
95% CI of LS mean	(-3.01, 1.16)	(-1.31, 2.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-1.24, 4.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	173	169
Mean (SD)	82.02 (18.81)	82.64 (17.43)
Absolute Change at Week 52		
n	169	165
Mean (SD)	-0.69 (16.07)	-2.42 (12.52)
Week 52 (MMRM)		
n	172	167
LS mean (SE)	82.32 (1.36)	82.25 (1.38)
95% CI of LS mean	(79.65, 85.00)	(79.54, 84.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-3.88, 3.74)
Absolute Change at Week 52 (MMRM)		
n	168	163
LS mean (SE)	-0.63 (1.11)	-2.42 (1.13)
95% CI of LS mean	(-2.81, 1.55)	(-4.64, -0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.79 (-4.90, 1.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	169
LS mean (SE)	-1.10 (0.91)	-0.96 (0.93)
95% CI of LS mean	(-2.90, 0.69)	(-2.78, 0.86)
P-value within Treatment	0.2274	0.2989
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-2.42, 2.70)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9136
Hedges' G (SE)		0.01 (0.11)
Hedges' 95% CI		(-0.20, 0.22)
Hedges' P-value		0.9136

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	114
Mean (SD)	84.31 (17.10)	86.35 (14.56)
Week 8 (MMRM)		
n	115	116
LS mean (SE)	82.92 (1.55)	88.24 (1.55)
95% CI of LS mean	(79.87, 85.97)	(85.19, 91.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.32 (0.99, 9.65)
Absolute Change at Week 8 (MMRM)		
n	111	114
LS mean (SE)	-1.69 (1.42)	1.70 (1.41)
95% CI of LS mean	(-4.49, 1.12)	(-1.07, 4.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.39 (-0.56, 7.34)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	82.87 (1.60)	85.94 (1.61)
95% CI of LS mean	(79.71, 86.03)	(82.77, 89.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.07 (-1.42, 7.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	113
LS mean (SE)	-1.73 (1.29)	-0.87 (1.28)
95% CI of LS mean	(-4.28, 0.81)	(-3.39, 1.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-2.73, 4.46)
Week 24 (MMRM)		
n	115	114
LS mean (SE)	83.84 (1.45)	86.69 (1.46)
95% CI of LS mean	(80.97, 86.70)	(83.82, 89.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.85 (-1.22, 6.92)
Absolute Change at Week 24 (MMRM)		
n	111	112
LS mean (SE)	-0.63 (1.20)	0.16 (1.19)
95% CI of LS mean	(-2.99, 1.72)	(-2.18, 2.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.79 (-2.54, 4.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	84.07 (15.42)	84.88 (15.12)
Absolute Change at Week 52		
n	109	109
Mean (SD)	-0.51 (14.22)	-1.12 (11.21)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	84.04 (1.42)	85.12 (1.42)
95% CI of LS mean	(81.25, 86.84)	(82.31, 87.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.08 (-2.90, 5.05)
Absolute Change at Week 52 (MMRM)		
n	108	109
LS mean (SE)	-0.36 (1.22)	-1.27 (1.21)
95% CI of LS mean	(-2.76, 2.04)	(-3.66, 1.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.91 (-4.31, 2.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	113
LS mean (SE)	-0.91 (1.05)	-0.66 (1.04)
95% CI of LS mean	(-2.97, 1.16)	(-2.71, 1.39)
P-value within Treatment	0.3864	0.5266
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-2.67, 3.17)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8664
Hedges' G (SE)		0.02 (0.13)
Hedges' 95% CI		(-0.24, 0.28)
Hedges' P-value		0.8659

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	80.39 (19.73)	83.12 (17.16)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	79.77 (2.15)	83.54 (2.26)
95% CI of LS mean	(75.52, 84.03)	(79.07, 88.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.77 (-2.42, 9.95)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	-0.55 (1.68)	2.11 (1.79)
95% CI of LS mean	(-3.87, 2.77)	(-1.42, 5.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.66 (-2.20, 7.52)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	79.07 (2.33)	80.48 (2.44)
95% CI of LS mean	(74.46, 83.69)	(75.66, 85.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-5.28, 8.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	-1.24 (1.96)	-1.29 (2.08)
95% CI of LS mean	(-5.12, 2.63)	(-5.40, 2.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-5.71, 5.61)
Week 24 (MMRM)		
n	81	72
LS mean (SE)	79.72 (2.06)	84.98 (2.17)
95% CI of LS mean	(75.64, 83.80)	(80.69, 89.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.26 (-0.67, 11.20)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	-0.56 (1.79)	3.04 (1.91)
95% CI of LS mean	(-4.09, 2.98)	(-0.72, 6.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (-1.57, 8.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	79	73
Mean (SD)	80.59 (21.61)	78.54 (20.48)
Absolute Change at Week 52		
n	79	70
Mean (SD)	0.63 (19.12)	-3.81 (14.52)
Week 52 (MMRM)		
n	78	69
LS mean (SE)	80.86 (2.32)	78.33 (2.44)
95% CI of LS mean	(76.28, 85.43)	(73.51, 83.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.52 (-9.18, 4.14)
Absolute Change at Week 52 (MMRM)		
n	78	67
LS mean (SE)	0.55 (1.93)	-3.42 (2.07)
95% CI of LS mean	(-3.26, 4.37)	(-7.51, 0.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.97 (-9.57, 1.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	-0.41 (1.57)	-0.55 (1.67)
95% CI of LS mean	(-3.52, 2.70)	(-3.86, 2.75)
P-value within Treatment	0.7928	0.7410
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-4.69, 4.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9516
Hedges' G (SE)		-0.01 (0.16)
Hedges' 95% CI		(-0.33, 0.31)
Hedges' P-value		0.9514

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	82.77 (18.20)	86.27 (14.51)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	78.70 (1.95)	88.23 (2.00)
95% CI of LS mean	(74.84, 82.55)	(84.28, 92.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.53 (4.01, 15.06)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	-4.25 (1.60)	2.62 (1.63)
95% CI of LS mean	(-7.40, -1.10)	(-0.60, 5.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.87 (2.36, 11.39)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	80.52 (2.11)	85.11 (2.15)
95% CI of LS mean	(76.36, 84.67)	(80.85, 89.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.59 (-1.36, 10.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	-2.54 (1.56)	-0.49 (1.60)
95% CI of LS mean	(-5.62, 0.55)	(-3.65, 2.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.05 (-2.37, 6.47)
Week 24 (MMRM)		
n	89	83
LS mean (SE)	82.89 (1.84)	87.13 (1.89)
95% CI of LS mean	(79.26, 86.51)	(83.40, 90.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.24 (-0.97, 9.44)
Absolute Change at Week 24 (MMRM)		
n	87	81
LS mean (SE)	0.02 (1.47)	1.43 (1.51)
95% CI of LS mean	(-2.88, 2.92)	(-1.57, 4.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-2.76, 5.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	81.31 (20.11)	82.76 (17.97)
Absolute Change at Week 52		
n	86	76
Mean (SD)	-1.36 (17.75)	-2.63 (12.15)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	81.46 (2.04)	82.97 (2.12)
95% CI of LS mean	(77.44, 85.48)	(78.79, 87.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-4.30, 7.32)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	-1.39 (1.65)	-2.26 (1.73)
95% CI of LS mean	(-4.65, 1.87)	(-5.69, 1.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.87 (-5.60, 3.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	-1.30 (1.29)	-0.44 (1.33)
95% CI of LS mean	(-3.84, 1.24)	(-3.06, 2.17)
P-value within Treatment	0.3129	0.7393
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-2.79, 4.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6425
Hedges' G (SE)		0.07 (0.15)
Hedges' 95% CI		(-0.23, 0.37)
Hedges' P-value		0.6421

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	106
Mean (SD)	82.57 (18.48)	84.07 (16.59)
Week 8 (MMRM)		
n	108	105
LS mean (SE)	84.26 (1.65)	84.77 (1.68)
95% CI of LS mean	(81.01, 87.52)	(81.46, 88.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-4.14, 5.14)
Absolute Change at Week 8 (MMRM)		
n	106	103
LS mean (SE)	1.39 (1.46)	1.14 (1.49)
95% CI of LS mean	(-1.49, 4.28)	(-1.79, 4.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-4.37, 3.86)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	82.17 (1.77)	82.43 (1.80)
95% CI of LS mean	(78.67, 85.67)	(78.87, 85.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-4.73, 5.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	102
LS mean (SE)	-0.63 (1.56)	-1.62 (1.59)
95% CI of LS mean	(-3.70, 2.45)	(-4.75, 1.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.00 (-5.38, 3.39)
Week 24 (MMRM)		
n	107	103
LS mean (SE)	81.75 (1.59)	84.86 (1.62)
95% CI of LS mean	(78.61, 84.89)	(81.66, 88.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.11 (-1.37, 7.59)
Absolute Change at Week 24 (MMRM)		
n	105	102
LS mean (SE)	-1.05 (1.42)	1.01 (1.44)
95% CI of LS mean	(-3.84, 1.75)	(-1.83, 3.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.06 (-1.92, 6.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	104	106
Mean (SD)	83.76 (16.53)	82.08 (17.52)
Absolute Change at Week 52		
n	102	103
Mean (SD)	1.09 (15.20)	-1.83 (13.03)
Week 52 (MMRM)		
n	103	103
LS mean (SE)	84.01 (1.61)	81.79 (1.63)
95% CI of LS mean	(80.83, 87.20)	(78.57, 85.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.23 (-6.75, 2.30)
Absolute Change at Week 52 (MMRM)		
n	101	101
LS mean (SE)	1.25 (1.40)	-2.08 (1.41)
95% CI of LS mean	(-1.51, 4.01)	(-4.86, 0.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.33 (-7.25, 0.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	102
LS mean (SE)	-0.14 (1.24)	-0.90 (1.26)
95% CI of LS mean	(-2.59, 2.31)	(-3.38, 1.59)
P-value within Treatment	0.9095	0.4784
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.75 (-4.24, 2.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6704
Hedges' G (SE)		-0.06 (0.14)
Hedges' 95% CI		(-0.33, 0.21)
Hedges' P-value		0.6705

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	93.09 (13.49)	90.24 (14.66)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	91.80 (1.44)	90.74 (1.55)
95% CI of LS mean	(88.95, 94.65)	(87.68, 93.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.05 (-5.24, 3.13)
Absolute Change at Week 8 (MMRM)		
n	110	96
LS mean (SE)	-1.72 (1.17)	0.53 (1.26)
95% CI of LS mean	(-4.04, 0.59)	(-1.95, 3.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.26 (-1.14, 5.66)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	91.16 (1.35)	91.17 (1.45)
95% CI of LS mean	(88.50, 93.82)	(88.32, 94.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-3.90, 3.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	-2.45 (1.19)	1.15 (1.27)
95% CI of LS mean	(-4.79, -0.11)	(-1.36, 3.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (0.17, 7.03)
Week 24 (MMRM)		
n	113	98
LS mean (SE)	93.69 (1.48)	89.26 (1.59)
95% CI of LS mean	(90.77, 96.61)	(86.12, 92.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.44 (-8.73, -0.14)
Absolute Change at Week 24 (MMRM)		
n	110	96
LS mean (SE)	0.18 (1.14)	-1.05 (1.22)
95% CI of LS mean	(-2.07, 2.43)	(-3.46, 1.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.23 (-4.53, 2.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	94.54 (11.93)	92.20 (15.01)
Absolute Change at Week 52		
n	109	92
Mean (SD)	0.92 (10.38)	1.57 (10.10)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	94.36 (1.27)	91.83 (1.37)
95% CI of LS mean	(91.86, 96.85)	(89.12, 94.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.53 (-6.22, 1.16)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	0.81 (1.00)	1.70 (1.09)
95% CI of LS mean	(-1.16, 2.77)	(-0.44, 3.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.89 (-2.02, 3.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	-0.49 (0.86)	0.60 (0.92)
95% CI of LS mean	(-2.19, 1.21)	(-1.22, 2.42)
P-value within Treatment	0.5700	0.5174
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-1.41, 3.59)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3912
Hedges' G (SE)		0.12 (0.14)
Hedges' 95% CI		(-0.15, 0.39)
Hedges' P-value		0.3899

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	92.42 (15.64)	91.82 (18.43)
Week 8 (MMRM)		
n	84	90
LS mean (SE)	93.02 (1.87)	90.49 (1.80)
95% CI of LS mean	(89.32, 96.71)	(86.93, 94.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.53 (-7.66, 2.60)
Absolute Change at Week 8 (MMRM)		
n	83	90
LS mean (SE)	0.00 (1.09)	-0.42 (1.04)
95% CI of LS mean	(-2.14, 2.15)	(-2.48, 1.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-3.40, 2.55)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	92.58 (1.81)	89.86 (1.74)
95% CI of LS mean	(89.00, 96.15)	(86.43, 93.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.72 (-7.68, 2.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	-0.49 (1.19)	-1.35 (1.14)
95% CI of LS mean	(-2.84, 1.86)	(-3.60, 0.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.86 (-4.11, 2.39)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	91.92 (1.85)	91.33 (1.78)
95% CI of LS mean	(88.26, 95.57)	(87.82, 94.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.59 (-5.66, 4.48)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	-1.16 (1.17)	0.36 (1.12)
95% CI of LS mean	(-3.46, 1.15)	(-1.85, 2.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.52 (-1.68, 4.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	80	87
Mean (SD)	92.50 (13.20)	89.91 (21.54)
Absolute Change at Week 52		
n	79	86
Mean (SD)	-0.14 (10.30)	-1.16 (13.95)
Week 52 (MMRM)		
n	79	87
LS mean (SE)	92.10 (1.95)	89.80 (1.87)
95% CI of LS mean	(88.25, 95.95)	(86.11, 93.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.30 (-7.64, 3.04)
Absolute Change at Week 52 (MMRM)		
n	78	86
LS mean (SE)	-0.95 (1.34)	-1.06 (1.28)
95% CI of LS mean	(-3.59, 1.70)	(-3.59, 1.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.12 (-3.78, 3.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	-0.86 (1.01)	-0.68 (0.96)
95% CI of LS mean	(-2.85, 1.12)	(-2.59, 1.22)
P-value within Treatment	0.3919	0.4781
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-2.57, 2.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8978
Hedges' G (SE)		0.02 (0.15)
Hedges' 95% CI		(-0.28, 0.32)
Hedges' P-value		0.8978

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	90.80 (16.01)	81.78 (29.90)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	88.55 (4.79)	78.67 (5.25)
95% CI of LS mean	(78.94, 98.16)	(68.12, 89.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.88 (-24.23, 4.47)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	-1.69 (2.63)	-0.77 (2.86)
95% CI of LS mean	(-6.96, 3.59)	(-6.51, 4.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-6.90, 8.74)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	87.37 (4.28)	81.30 (4.70)
95% CI of LS mean	(78.78, 95.96)	(71.87, 90.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.06 (-18.92, 6.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	-2.72 (2.45)	0.76 (2.70)
95% CI of LS mean	(-7.64, 2.21)	(-4.67, 6.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.47 (-3.89, 10.84)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	90.05 (4.23)	79.45 (4.65)
95% CI of LS mean	(81.55, 98.55)	(70.12, 88.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.60 (-23.32, 2.11)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	0.09 (2.26)	-0.29 (2.50)
95% CI of LS mean	(-4.46, 4.64)	(-5.32, 4.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-7.20, 6.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	28	25
Mean (SD)	90.87 (15.44)	79.11 (33.07)
Absolute Change at Week 52		
n	27	24
Mean (SD)	-0.82 (11.08)	0.46 (20.59)
Week 52 (MMRM)		
n	28	24
LS mean (SE)	88.96 (4.55)	80.39 (4.98)
95% CI of LS mean	(79.83, 98.10)	(70.40, 90.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.57 (-22.19, 5.05)
Absolute Change at Week 52 (MMRM)		
n	27	23
LS mean (SE)	-1.18 (3.16)	1.41 (3.45)
95% CI of LS mean	(-7.52, 5.16)	(-5.52, 8.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.59 (-6.83, 12.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	-1.27 (2.33)	0.63 (2.56)
95% CI of LS mean	(-5.95, 3.41)	(-4.53, 5.78)
P-value within Treatment	0.5885	0.8083
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.89 (-5.11, 8.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5891
Hedges' G (SE)		0.15 (0.28)
Hedges' 95% CI		(-0.41, 0.71)
Hedges' P-value		0.5877

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	93.19 (14.12)	92.48 (12.98)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	92.64 (1.06)	92.74 (1.07)
95% CI of LS mean	(90.55, 94.72)	(90.63, 94.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-2.86, 3.06)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	-0.83 (0.84)	0.18 (0.85)
95% CI of LS mean	(-2.49, 0.82)	(-1.49, 1.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-1.34, 3.37)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	92.23 (1.03)	92.31 (1.03)
95% CI of LS mean	(90.21, 94.25)	(90.28, 94.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-2.79, 2.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-1.40 (0.90)	-0.19 (0.91)
95% CI of LS mean	(-3.18, 0.38)	(-1.97, 1.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-1.31, 3.73)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	93.13 (1.12)	92.24 (1.13)
95% CI of LS mean	(90.92, 95.35)	(90.01, 94.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-4.04, 2.25)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	-0.45 (0.88)	-0.39 (0.89)
95% CI of LS mean	(-2.18, 1.28)	(-2.14, 1.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-2.40, 2.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
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- N/C: model does not converge.

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Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	94.21 (11.87)	93.08 (13.96)
Absolute Change at Week 52		
n	162	156
Mean (SD)	0.69 (10.19)	0.21 (10.29)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	93.89 (1.02)	92.81 (1.04)
95% CI of LS mean	(91.88, 95.90)	(90.77, 94.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.08 (-3.94, 1.79)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	0.33 (0.80)	0.22 (0.81)
95% CI of LS mean	(-1.23, 1.90)	(-1.37, 1.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-2.34, 2.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-0.50 (0.66)	-0.12 (0.66)
95% CI of LS mean	(-1.80, 0.80)	(-1.43, 1.19)
P-value within Treatment	0.4458	0.8579
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.39 (-1.46, 2.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6814
Hedges' G (SE)		0.05 (0.11)
Hedges' 95% CI		(-0.17, 0.26)
Hedges' P-value		0.6813

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	92.40 (16.99)	88.19 (17.44)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	90.16 (4.26)	90.16 (4.65)
95% CI of LS mean	(81.47, 98.85)	(80.67, 99.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-13.06, 13.06)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	-1.72 (2.69)	1.35 (2.94)
95% CI of LS mean	(-7.21, 3.77)	(-4.65, 7.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.06 (-5.17, 11.30)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	86.65 (3.77)	88.77 (4.12)
95% CI of LS mean	(78.95, 94.34)	(80.36, 97.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-9.50, 13.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-5.23 (3.20)	-0.04 (3.49)
95% CI of LS mean	(-11.74, 1.28)	(-7.15, 7.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.18 (-4.54, 14.91)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	90.74 (4.03)	89.46 (4.40)
95% CI of LS mean	(82.51, 98.97)	(80.47, 98.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.28 (-13.67, 11.11)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	-1.13 (3.33)	0.65 (3.63)
95% CI of LS mean	(-7.91, 5.65)	(-6.75, 8.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.79 (-8.33, 11.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	94.44 (12.20)	91.27 (23.94)
Absolute Change at Week 52		
n	18	13
Mean (SD)	0.62 (8.92)	0.00 (15.04)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	92.99 (4.07)	90.49 (4.68)
95% CI of LS mean	(84.62, 101.35)	(80.92, 100.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.50 (-15.38, 10.38)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	0.59 (2.85)	0.42 (3.39)
95% CI of LS mean	(-5.27, 6.45)	(-6.53, 7.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-9.32, 8.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	-1.92 (2.30)	0.34 (2.55)
95% CI of LS mean	(-6.67, 2.83)	(-4.92, 5.61)
P-value within Treatment	0.4111	0.8945
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.27 (-4.93, 9.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5222
Hedges' G (SE)		0.22 (0.33)
Hedges' 95% CI		(-0.46, 0.90)
Hedges' P-value		0.5147

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	93.09 (13.91)	91.44 (16.48)
Week 8 (MMRM)		
n	178	172
LS mean (SE)	92.42 (1.19)	90.77 (1.21)
95% CI of LS mean	(90.07, 94.77)	(88.39, 93.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.65 (-5.00, 1.69)
Absolute Change at Week 8 (MMRM)		
n	174	170
LS mean (SE)	-0.85 (0.85)	-0.10 (0.86)
95% CI of LS mean	(-2.53, 0.83)	(-1.80, 1.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-1.64, 3.14)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	92.21 (1.13)	90.82 (1.15)
95% CI of LS mean	(89.98, 94.44)	(88.56, 93.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.39 (-4.57, 1.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	-1.16 (0.88)	-0.12 (0.89)
95% CI of LS mean	(-2.89, 0.57)	(-1.86, 1.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-1.41, 3.50)
Week 24 (MMRM)		
n	177	172
LS mean (SE)	93.06 (1.22)	90.43 (1.24)
95% CI of LS mean	(90.67, 95.46)	(88.00, 92.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.63 (-6.05, 0.78)
Absolute Change at Week 24 (MMRM)		
n	173	169
LS mean (SE)	-0.26 (0.84)	-0.52 (0.85)
95% CI of LS mean	(-1.90, 1.39)	(-2.19, 1.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-2.61, 2.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	174	169
Mean (SD)	93.61 (12.54)	91.19 (17.89)
Absolute Change at Week 52		
n	170	166
Mean (SD)	0.20 (9.93)	0.20 (11.89)
Week 52 (MMRM)		
n	173	167
LS mean (SE)	93.39 (1.13)	91.03 (1.15)
95% CI of LS mean	(91.17, 95.62)	(88.77, 93.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.37 (-5.54, 0.81)
Absolute Change at Week 52 (MMRM)		
n	169	164
LS mean (SE)	0.07 (0.85)	0.29 (0.86)
95% CI of LS mean	(-1.59, 1.74)	(-1.40, 1.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-2.15, 2.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	-0.45 (0.68)	-0.12 (0.68)
95% CI of LS mean	(-1.78, 0.88)	(-1.46, 1.23)
P-value within Treatment	0.5080	0.8632
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-1.56, 2.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7315
Hedges' G (SE)		0.04 (0.11)
Hedges' 95% CI		(-0.17, 0.25)
Hedges' P-value		0.7314

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	92.98 (13.57)	92.85 (13.34)
Week 8 (MMRM)		
n	116	116
LS mean (SE)	91.56 (1.34)	92.87 (1.35)
95% CI of LS mean	(88.91, 94.21)	(90.21, 95.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.31 (-2.45, 5.06)
Absolute Change at Week 8 (MMRM)		
n	112	115
LS mean (SE)	-1.59 (1.08)	0.01 (1.06)
95% CI of LS mean	(-3.71, 0.53)	(-2.09, 2.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.59 (-1.39, 4.58)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	91.93 (1.22)	92.54 (1.22)
95% CI of LS mean	(89.53, 94.34)	(90.13, 94.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (-2.81, 4.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	-1.44 (1.07)	-0.50 (1.06)
95% CI of LS mean	(-3.55, 0.67)	(-2.58, 1.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.94 (-2.03, 3.92)
Week 24 (MMRM)		
n	115	115
LS mean (SE)	92.34 (1.34)	92.45 (1.34)
95% CI of LS mean	(89.71, 94.98)	(89.81, 95.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-3.64, 3.85)
Absolute Change at Week 24 (MMRM)		
n	111	114
LS mean (SE)	-0.94 (1.05)	-0.58 (1.04)
95% CI of LS mean	(-3.02, 1.13)	(-2.63, 1.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-2.57, 3.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	94.10 (12.07)	93.19 (13.83)
Absolute Change at Week 52		
n	109	110
Mean (SD)	0.61 (9.42)	0.10 (11.41)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	93.57 (1.22)	92.95 (1.23)
95% CI of LS mean	(91.16, 95.98)	(90.53, 95.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.62 (-4.04, 2.81)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	0.34 (1.01)	0.13 (1.00)
95% CI of LS mean	(-1.66, 2.34)	(-1.85, 2.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-3.02, 2.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	-0.68 (0.81)	-0.32 (0.80)
95% CI of LS mean	(-2.28, 0.92)	(-1.89, 1.26)
P-value within Treatment	0.4016	0.6939
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.37 (-1.89, 2.62)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7497
Hedges' G (SE)		0.04 (0.13)
Hedges' 95% CI		(-0.22, 0.30)
Hedges' P-value		0.7488

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	92.64 (15.55)	88.46 (20.11)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	92.39 (1.92)	88.34 (2.02)
95% CI of LS mean	(88.59, 96.18)	(84.35, 92.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.05 (-9.57, 1.47)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	-0.20 (1.22)	0.30 (1.30)
95% CI of LS mean	(-2.61, 2.21)	(-2.27, 2.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-3.03, 4.02)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	90.60 (1.94)	88.58 (2.03)
95% CI of LS mean	(86.77, 94.43)	(84.57, 92.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.02 (-7.58, 3.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	-1.94 (1.38)	0.68 (1.47)
95% CI of LS mean	(-4.67, 0.80)	(-2.22, 3.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.62 (-1.38, 6.61)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	92.79 (2.01)	87.94 (2.11)
95% CI of LS mean	(88.81, 96.77)	(83.77, 92.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.85 (-10.62, 0.93)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	0.29 (1.31)	0.07 (1.40)
95% CI of LS mean	(-2.31, 2.88)	(-2.70, 2.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-4.02, 3.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	80	73
Mean (SD)	93.19 (13.05)	88.13 (23.30)
Absolute Change at Week 52		
n	80	70
Mean (SD)	0.28 (11.45)	0.48 (13.17)
Week 52 (MMRM)		
n	79	69
LS mean (SE)	92.27 (1.95)	88.77 (2.05)
95% CI of LS mean	(88.42, 96.11)	(84.71, 92.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.50 (-9.10, 2.10)
Absolute Change at Week 52 (MMRM)		
n	79	67
LS mean (SE)	-0.30 (1.34)	0.93 (1.44)
95% CI of LS mean	(-2.95, 2.34)	(-1.92, 3.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-2.66, 5.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	-0.65 (1.09)	0.56 (1.16)
95% CI of LS mean	(-2.80, 1.50)	(-1.73, 2.85)
P-value within Treatment	0.5509	0.6299
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-1.94, 4.36)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4487
Hedges' G (SE)		0.12 (0.16)
Hedges' 95% CI		(-0.20, 0.44)
Hedges' P-value		0.4481

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	92.42 (16.03)	89.80 (15.92)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	91.79 (1.92)	89.17 (1.97)
95% CI of LS mean	(88.00, 95.58)	(85.29, 93.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.62 (-8.05, 2.81)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	-1.33 (1.26)	0.14 (1.29)
95% CI of LS mean	(-3.81, 1.16)	(-2.40, 2.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.47 (-2.09, 5.03)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	91.54 (1.69)	89.51 (1.73)
95% CI of LS mean	(88.20, 94.88)	(86.09, 92.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.03 (-6.81, 2.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	-1.57 (1.19)	0.17 (1.22)
95% CI of LS mean	(-3.92, 0.79)	(-2.24, 2.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-1.64, 5.11)
Week 24 (MMRM)		
n	89	84
LS mean (SE)	90.67 (1.96)	89.23 (2.01)
95% CI of LS mean	(86.80, 94.54)	(85.26, 93.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-6.99, 4.11)
Absolute Change at Week 24 (MMRM)		
n	87	82
LS mean (SE)	-2.46 (1.33)	0.17 (1.37)
95% CI of LS mean	(-5.08, 0.16)	(-2.53, 2.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-1.13, 6.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	92.80 (14.20)	89.89 (18.63)
Absolute Change at Week 52		
n	86	76
Mean (SD)	0.26 (9.33)	0.58 (10.25)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	93.05 (1.71)	89.18 (1.78)
95% CI of LS mean	(89.66, 96.43)	(85.67, 92.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.87 (-8.75, 1.01)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	-0.08 (1.00)	0.46 (1.06)
95% CI of LS mean	(-2.05, 1.90)	(-1.62, 2.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.54 (-2.33, 3.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	-1.37 (0.88)	0.27 (0.91)
95% CI of LS mean	(-3.11, 0.37)	(-1.52, 2.06)
P-value within Treatment	0.1221	0.7672
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-0.86, 4.14)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1976
Hedges' G (SE)		0.20 (0.15)
Hedges' 95% CI		(-0.10, 0.50)
Hedges' P-value		0.1980

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	93.17 (13.00)	92.11 (16.93)
Week 8 (MMRM)		
n	109	105
LS mean (SE)	92.75 (1.39)	91.77 (1.41)
95% CI of LS mean	(90.02, 95.49)	(88.98, 94.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.98 (-4.89, 2.92)
Absolute Change at Week 8 (MMRM)		
n	107	104
LS mean (SE)	-0.52 (1.04)	-0.15 (1.06)
95% CI of LS mean	(-2.57, 1.54)	(-2.23, 1.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.37 (-2.56, 3.30)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	91.96 (1.42)	91.36 (1.45)
95% CI of LS mean	(89.15, 94.76)	(88.51, 94.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.59 (-4.60, 3.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	-1.47 (1.18)	-0.42 (1.19)
95% CI of LS mean	(-3.80, 0.86)	(-2.77, 1.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.05 (-2.26, 4.36)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	94.85 (1.38)	91.05 (1.40)
95% CI of LS mean	(92.13, 97.56)	(88.29, 93.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.80 (-7.67, 0.07)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	1.51 (1.00)	-0.97 (1.01)
95% CI of LS mean	(-0.46, 3.47)	(-2.96, 1.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.48 (-5.27, 0.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	105	106
Mean (SD)	94.50 (10.80)	92.14 (18.08)
Absolute Change at Week 52		
n	103	104
Mean (SD)	0.65 (11.09)	0.00 (13.32)
Week 52 (MMRM)		
n	104	103
LS mean (SE)	93.72 (1.44)	92.12 (1.46)
95% CI of LS mean	(90.89, 96.56)	(89.25, 94.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.60 (-5.64, 2.43)
Absolute Change at Week 52 (MMRM)		
n	102	102
LS mean (SE)	0.32 (1.21)	0.14 (1.22)
95% CI of LS mean	(-2.07, 2.72)	(-2.27, 2.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-3.58, 3.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	0.12 (0.92)	-0.42 (0.93)
95% CI of LS mean	(-1.70, 1.94)	(-2.26, 1.42)
P-value within Treatment	0.8974	0.6551
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.54 (-3.13, 2.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6832
Hedges' G (SE)		-0.06 (0.14)
Hedges' 95% CI		(-0.33, 0.22)
Hedges' P-value		0.6832

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	80.17 (19.50)	79.87 (19.49)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	79.91 (1.67)	81.39 (1.79)
95% CI of LS mean	(76.62, 83.21)	(77.86, 84.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.48 (-3.37, 6.33)
Absolute Change at Week 8 (MMRM)		
n	110	96
LS mean (SE)	-0.64 (1.19)	1.67 (1.27)
95% CI of LS mean	(-2.99, 1.70)	(-0.84, 4.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.31 (-1.13, 5.76)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	80.63 (1.74)	81.10 (1.87)
95% CI of LS mean	(77.20, 84.07)	(77.42, 84.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.47 (-4.58, 5.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	0.14 (1.23)	1.49 (1.32)
95% CI of LS mean	(-2.28, 2.57)	(-1.11, 4.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-2.22, 4.91)
Week 24 (MMRM)		
n	113	98
LS mean (SE)	80.64 (1.67)	81.70 (1.79)
95% CI of LS mean	(77.35, 83.93)	(78.17, 85.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.06 (-3.78, 5.91)
Absolute Change at Week 24 (MMRM)		
n	110	96
LS mean (SE)	0.12 (1.37)	1.90 (1.47)
95% CI of LS mean	(-2.58, 2.83)	(-0.99, 4.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.78 (-2.19, 5.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	80.64 (18.68)	82.27 (17.01)
Absolute Change at Week 52		
n	109	92
Mean (SD)	-0.31 (13.16)	2.83 (14.26)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	80.32 (1.69)	82.43 (1.83)
95% CI of LS mean	(76.98, 83.66)	(78.82, 86.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.11 (-2.82, 7.04)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	-0.20 (1.31)	2.52 (1.42)
95% CI of LS mean	(-2.78, 2.38)	(-0.27, 5.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.72 (-1.08, 6.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	0.02 (1.14)	1.97 (1.23)
95% CI of LS mean	(-2.23, 2.28)	(-0.45, 4.39)
P-value within Treatment	0.9855	0.1096
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.95 (-1.37, 5.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2478
Hedges' G (SE)		0.16 (0.14)
Hedges' 95% CI		(-0.11, 0.44)
Hedges' P-value		0.2470

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	81.68 (16.76)	84.51 (14.73)
Week 8 (MMRM)		
n	84	90
LS mean (SE)	83.38 (1.73)	84.81 (1.67)
95% CI of LS mean	(79.96, 86.79)	(81.52, 88.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.44 (-3.31, 6.18)
Absolute Change at Week 8 (MMRM)		
n	83	90
LS mean (SE)	1.48 (1.02)	0.65 (0.98)
95% CI of LS mean	(-0.53, 3.50)	(-1.28, 2.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.83 (-3.63, 1.96)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	83.56 (1.79)	84.01 (1.71)
95% CI of LS mean	(80.03, 87.09)	(80.63, 87.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-4.44, 5.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	1.37 (1.28)	-0.12 (1.23)
95% CI of LS mean	(-1.17, 3.90)	(-2.54, 2.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.48 (-4.99, 2.02)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	82.83 (1.81)	83.47 (1.73)
95% CI of LS mean	(79.26, 86.39)	(80.05, 86.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-4.30, 5.59)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	1.12 (1.31)	-0.74 (1.26)
95% CI of LS mean	(-1.47, 3.71)	(-3.22, 1.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.86 (-5.45, 1.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	80	87
Mean (SD)	81.94 (18.65)	83.38 (15.09)
Absolute Change at Week 52		
n	79	86
Mean (SD)	1.00 (12.18)	-0.47 (12.22)
Week 52 (MMRM)		
n	79	87
LS mean (SE)	82.51 (1.85)	83.88 (1.77)
95% CI of LS mean	(78.86, 86.15)	(80.39, 87.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.37 (-3.68, 6.43)
Absolute Change at Week 52 (MMRM)		
n	78	86
LS mean (SE)	0.67 (1.39)	-0.30 (1.33)
95% CI of LS mean	(-2.08, 3.41)	(-2.93, 2.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-4.77, 2.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	1.05 (1.10)	-0.39 (1.05)
95% CI of LS mean	(-1.12, 3.22)	(-2.46, 1.69)
P-value within Treatment	0.3410	0.7142
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-4.44, 1.57)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3472
Hedges' G (SE)		-0.14 (0.15)
Hedges' 95% CI		(-0.44, 0.16)
Hedges' P-value		0.3474

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	77.76 (17.47)	86.03 (13.30)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	82.03 (2.54)	84.81 (2.79)
95% CI of LS mean	(76.94, 87.13)	(79.21, 90.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.77 (-4.85, 10.39)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	3.87 (1.84)	0.35 (2.00)
95% CI of LS mean	(0.18, 7.56)	(-3.68, 4.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.52 (-9.01, 1.97)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	83.46 (2.86)	82.48 (3.14)
95% CI of LS mean	(77.70, 89.21)	(76.17, 88.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-9.56, 7.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	5.12 (2.14)	-1.78 (2.36)
95% CI of LS mean	(0.82, 9.42)	(-6.52, 2.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.90 (-13.32, -0.47)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	84.90 (2.53)	84.59 (2.78)
95% CI of LS mean	(79.82, 89.98)	(79.01, 90.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-7.91, 7.30)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	6.68 (1.98)	0.04 (2.18)
95% CI of LS mean	(2.70, 10.66)	(-4.35, 4.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.64 (-12.59, -0.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	28	25
Mean (SD)	83.57 (15.30)	82.43 (17.05)
Absolute Change at Week 52		
n	27	24
Mean (SD)	5.12 (13.03)	-3.06 (12.60)
Week 52 (MMRM)		
n	28	24
LS mean (SE)	83.53 (3.03)	81.93 (3.31)
95% CI of LS mean	(77.46, 89.61)	(75.28, 88.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.60 (-10.65, 7.45)
Absolute Change at Week 52 (MMRM)		
n	27	23
LS mean (SE)	5.19 (2.49)	-2.77 (2.72)
95% CI of LS mean	(0.19, 10.19)	(-8.25, 2.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.96 (-15.40, -0.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	5.66 (1.93)	-1.50 (2.13)
95% CI of LS mean	(1.78, 9.55)	(-5.78, 2.78)
P-value within Treatment	0.0052	0.4832
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.17 (-12.98, -1.36)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0166
Hedges' G (SE)		-0.69 (0.29)
Hedges' 95% CI		(-1.26, -0.12)
Hedges' P-value		0.0193

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	81.31 (18.43)	81.68 (17.96)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	81.29 (1.34)	82.74 (1.36)
95% CI of LS mean	(78.65, 83.93)	(80.07, 85.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-2.31, 5.20)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	-0.45 (0.88)	1.38 (0.89)
95% CI of LS mean	(-2.18, 1.28)	(-0.37, 3.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.83 (-0.63, 4.29)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	81.64 (1.39)	82.48 (1.40)
95% CI of LS mean	(78.91, 84.37)	(79.73, 85.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.84 (-3.04, 4.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-0.17 (0.98)	1.16 (0.98)
95% CI of LS mean	(-2.09, 1.75)	(-0.77, 3.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.33 (-1.39, 4.05)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	81.00 (1.36)	82.23 (1.38)
95% CI of LS mean	(78.32, 83.69)	(79.53, 84.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-2.58, 5.04)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	-0.58 (1.07)	0.81 (1.07)
95% CI of LS mean	(-2.68, 1.52)	(-1.30, 2.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-1.59, 4.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	80.85 (19.12)	82.98 (15.92)
Absolute Change at Week 52		
n	162	156
Mean (SD)	-0.45 (12.61)	1.88 (13.33)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	80.85 (1.36)	83.34 (1.38)
95% CI of LS mean	(78.17, 83.53)	(80.62, 86.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.49 (-1.33, 6.31)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	-0.80 (1.02)	1.86 (1.04)
95% CI of LS mean	(-2.81, 1.21)	(-0.18, 3.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.66 (-0.20, 5.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-0.52 (0.87)	1.27 (0.88)
95% CI of LS mean	(-2.24, 1.20)	(-0.45, 3.00)
P-value within Treatment	0.5530	0.1479
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.79 (-0.65, 4.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1490
Hedges' G (SE)		0.16 (0.11)
Hedges' 95% CI		(-0.06, 0.38)
Hedges' P-value		0.1494

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	82.11 (17.51)	75.83 (23.71)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	84.08 (4.37)	80.99 (4.77)
95% CI of LS mean	(75.19, 92.97)	(71.27, 90.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.09 (-16.43, 10.25)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	1.42 (3.14)	5.81 (3.43)
95% CI of LS mean	(-4.98, 7.83)	(-1.19, 12.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.38 (-5.28, 14.05)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	84.08 (3.31)	77.66 (3.62)
95% CI of LS mean	(77.33, 90.83)	(70.27, 85.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.42 (-16.66, 3.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	1.42 (3.41)	2.47 (3.73)
95% CI of LS mean	(-5.53, 8.38)	(-5.13, 10.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.05 (-9.41, 11.51)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	87.59 (3.94)	76.82 (4.30)
95% CI of LS mean	(79.55, 95.63)	(68.04, 85.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.77 (-22.86, 1.32)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	4.93 (4.30)	1.64 (4.69)
95% CI of LS mean	(-3.81, 13.68)	(-7.91, 11.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.29 (-16.36, 9.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	83.70 (21.60)	76.67 (15.41)
Absolute Change at Week 52		
n	18	13
Mean (SD)	1.11 (16.37)	3.59 (17.77)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	83.76 (4.76)	77.54 (5.47)
95% CI of LS mean	(74.03, 93.50)	(66.39, 88.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.22 (-21.17, 8.73)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	1.09 (3.87)	2.36 (4.52)
95% CI of LS mean	(-6.86, 9.04)	(-6.90, 11.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.26 (-11.05, 13.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	2.48 (3.33)	2.16 (3.68)
95% CI of LS mean	(-4.31, 9.28)	(-5.34, 9.65)
P-value within Treatment	0.4613	0.5616
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-10.60, 9.94)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9488
Hedges' G (SE)		-0.02 (0.33)
Hedges' 95% CI		(-0.70, 0.65)
Hedges' P-value		0.9479

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	80.80 (18.35)	82.86 (16.70)
Week 8 (MMRM)		
n	178	172
LS mean (SE)	81.27 (1.25)	83.07 (1.27)
95% CI of LS mean	(78.82, 83.73)	(80.58, 85.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.80 (-1.70, 5.30)
Absolute Change at Week 8 (MMRM)		
n	174	170
LS mean (SE)	0.10 (0.83)	0.80 (0.84)
95% CI of LS mean	(-1.53, 1.72)	(-0.85, 2.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.70 (-1.61, 3.02)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	81.81 (1.34)	82.79 (1.35)
95% CI of LS mean	(79.18, 84.43)	(80.13, 85.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.99 (-2.75, 4.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	0.53 (0.93)	0.61 (0.94)
95% CI of LS mean	(-1.29, 2.35)	(-1.23, 2.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-2.51, 2.67)
Week 24 (MMRM)		
n	177	172
LS mean (SE)	81.07 (1.29)	82.94 (1.30)
95% CI of LS mean	(78.54, 83.60)	(80.37, 85.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.87 (-1.74, 5.47)
Absolute Change at Week 24 (MMRM)		
n	173	169
LS mean (SE)	0.01 (0.97)	0.60 (0.98)
95% CI of LS mean	(-1.89, 1.91)	(-1.32, 2.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-2.12, 3.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	174	169
Mean (SD)	81.15 (18.25)	83.48 (16.05)
Absolute Change at Week 52		
n	170	166
Mean (SD)	0.26 (12.45)	0.96 (12.95)
Week 52 (MMRM)		
n	173	167
LS mean (SE)	81.07 (1.30)	83.53 (1.32)
95% CI of LS mean	(78.52, 83.62)	(80.95, 86.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.46 (-1.17, 6.10)
Absolute Change at Week 52 (MMRM)		
n	169	164
LS mean (SE)	-0.05 (0.98)	1.15 (0.99)
95% CI of LS mean	(-1.97, 1.87)	(-0.80, 3.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.19 (-1.54, 3.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	0.17 (0.82)	0.78 (0.83)
95% CI of LS mean	(-1.45, 1.78)	(-0.85, 2.42)
P-value within Treatment	0.8405	0.3454
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-1.68, 2.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5966
Hedges' G (SE)		0.06 (0.11)
Hedges' 95% CI		(-0.15, 0.27)
Hedges' P-value		0.5965

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	81.77 (18.84)	82.10 (17.95)
Week 8 (MMRM)		
n	116	116
LS mean (SE)	81.60 (1.57)	83.97 (1.58)
95% CI of LS mean	(78.50, 84.70)	(80.86, 87.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-2.03, 6.79)
Absolute Change at Week 8 (MMRM)		
n	112	115
LS mean (SE)	-0.72 (1.13)	2.10 (1.11)
95% CI of LS mean	(-2.94, 1.51)	(-0.10, 4.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.82 (-0.32, 5.95)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	82.77 (1.69)	83.12 (1.69)
95% CI of LS mean	(79.44, 86.10)	(79.78, 86.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.35 (-4.38, 5.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	0.41 (1.21)	1.34 (1.20)
95% CI of LS mean	(-1.99, 2.80)	(-1.03, 3.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-2.44, 4.30)
Week 24 (MMRM)		
n	115	115
LS mean (SE)	81.30 (1.70)	82.25 (1.70)
95% CI of LS mean	(77.95, 84.65)	(78.89, 85.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.95 (-3.81, 5.71)
Absolute Change at Week 24 (MMRM)		
n	111	114
LS mean (SE)	-0.76 (1.31)	0.40 (1.30)
95% CI of LS mean	(-3.34, 1.82)	(-2.15, 2.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-2.48, 4.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	81.67 (17.78)	83.42 (16.55)
Absolute Change at Week 52		
n	109	110
Mean (SD)	-0.36 (11.70)	1.64 (12.62)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	81.19 (1.61)	83.66 (1.61)
95% CI of LS mean	(78.02, 84.36)	(80.48, 86.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.48 (-2.03, 6.98)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	-0.97 (1.17)	1.75 (1.16)
95% CI of LS mean	(-3.28, 1.33)	(-0.53, 4.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.73 (-0.52, 5.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	-0.44 (1.08)	1.16 (1.07)
95% CI of LS mean	(-2.57, 1.69)	(-0.94, 3.27)
P-value within Treatment	0.6831	0.2774
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.61 (-1.40, 4.61)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2937
Hedges' G (SE)		0.14 (0.13)
Hedges' 95% CI		(-0.12, 0.40)
Hedges' P-value		0.2926

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	79.44 (17.54)	82.46 (16.82)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	81.11 (1.90)	81.53 (1.99)
95% CI of LS mean	(77.36, 84.86)	(77.59, 85.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.42 (-5.03, 5.86)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	1.33 (1.09)	0.04 (1.17)
95% CI of LS mean	(-0.84, 3.49)	(-2.27, 2.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.29 (-4.46, 1.88)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	80.57 (1.86)	81.60 (1.95)
95% CI of LS mean	(76.88, 84.25)	(77.74, 85.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.03 (-4.31, 6.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	0.71 (1.30)	0.07 (1.37)
95% CI of LS mean	(-1.85, 3.27)	(-2.65, 2.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-4.38, 3.10)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	81.85 (1.73)	83.09 (1.82)
95% CI of LS mean	(78.43, 85.27)	(79.50, 86.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-3.74, 6.21)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	2.03 (1.39)	1.36 (1.48)
95% CI of LS mean	(-0.71, 4.77)	(-1.56, 4.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-4.68, 3.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	80	73
Mean (SD)	80.64 (19.80)	82.11 (15.29)
Absolute Change at Week 52		
n	80	70
Mean (SD)	1.30 (14.16)	0.57 (14.39)
Week 52 (MMRM)		
n	79	69
LS mean (SE)	81.12 (2.00)	82.41 (2.11)
95% CI of LS mean	(77.18, 85.07)	(78.24, 86.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.29 (-4.46, 7.04)
Absolute Change at Week 52 (MMRM)		
n	79	67
LS mean (SE)	1.31 (1.62)	0.62 (1.75)
95% CI of LS mean	(-1.89, 4.52)	(-2.83, 4.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.69 (-5.41, 4.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	1.35 (1.20)	0.68 (1.28)
95% CI of LS mean	(-1.02, 3.72)	(-1.84, 3.21)
P-value within Treatment	0.2627	0.5941
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-4.14, 2.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7047
Hedges' G (SE)		-0.06 (0.16)
Hedges' 95% CI		(-0.38, 0.26)
Hedges' P-value		0.7042

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	82.23 (17.24)	82.37 (17.56)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	81.93 (1.79)	82.61 (1.84)
95% CI of LS mean	(78.39, 85.47)	(78.98, 86.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.68 (-4.39, 5.76)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	-0.71 (1.21)	0.74 (1.24)
95% CI of LS mean	(-3.11, 1.68)	(-1.71, 3.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.46 (-1.98, 4.89)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	84.05 (1.90)	81.07 (1.94)
95% CI of LS mean	(80.31, 87.80)	(77.24, 84.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.99 (-8.35, 2.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	1.19 (1.35)	-0.48 (1.39)
95% CI of LS mean	(-1.48, 3.87)	(-3.21, 2.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.67 (-5.50, 2.15)
Week 24 (MMRM)		
n	89	84
LS mean (SE)	82.62 (1.93)	81.39 (1.98)
95% CI of LS mean	(78.81, 86.44)	(77.47, 85.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.24 (-6.71, 4.24)
Absolute Change at Week 24 (MMRM)		
n	87	82
LS mean (SE)	0.19 (1.50)	-0.32 (1.54)
95% CI of LS mean	(-2.77, 3.15)	(-3.36, 2.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.51 (-4.76, 3.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	82.34 (17.21)	81.91 (18.12)
Absolute Change at Week 52		
n	86	76
Mean (SD)	0.27 (10.46)	0.56 (13.00)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	82.86 (1.87)	82.44 (1.93)
95% CI of LS mean	(79.17, 86.54)	(78.63, 86.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-5.73, 4.88)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	0.28 (1.27)	0.58 (1.33)
95% CI of LS mean	(-2.24, 2.79)	(-2.04, 3.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-3.34, 3.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	0.55 (1.20)	-0.07 (1.23)
95% CI of LS mean	(-1.82, 2.92)	(-2.50, 2.36)
P-value within Treatment	0.6450	0.9538
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-4.03, 2.78)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7171
Hedges' G (SE)		-0.06 (0.15)
Hedges' 95% CI		(-0.36, 0.25)
Hedges' P-value		0.7167

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	79.63 (19.10)	82.14 (17.46)
Week 8 (MMRM)		
n	109	105
LS mean (SE)	81.12 (1.63)	83.24 (1.66)
95% CI of LS mean	(77.91, 84.33)	(79.96, 86.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-2.47, 6.70)
Absolute Change at Week 8 (MMRM)		
n	107	104
LS mean (SE)	0.97 (1.07)	1.62 (1.09)
95% CI of LS mean	(-1.14, 3.08)	(-0.52, 3.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-2.36, 3.66)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	80.27 (1.66)	83.49 (1.69)
95% CI of LS mean	(76.99, 83.55)	(80.16, 86.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-1.46, 7.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	0.13 (1.19)	1.76 (1.21)
95% CI of LS mean	(-2.22, 2.49)	(-0.62, 4.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-1.72, 4.98)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	80.87 (1.57)	83.34 (1.60)
95% CI of LS mean	(77.77, 83.96)	(80.19, 86.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.47 (-1.95, 6.88)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	0.75 (1.26)	1.48 (1.27)
95% CI of LS mean	(-1.73, 3.22)	(-1.03, 3.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.73 (-2.79, 4.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	105	106
Mean (SD)	80.33 (19.73)	83.63 (14.35)
Absolute Change at Week 52		
n	103	104
Mean (SD)	0.40 (14.50)	1.71 (13.57)
Week 52 (MMRM)		
n	104	103
LS mean (SE)	80.01 (1.67)	83.65 (1.70)
95% CI of LS mean	(76.71, 83.31)	(80.31, 87.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.64 (-1.06, 8.34)
Absolute Change at Week 52 (MMRM)		
n	102	102
LS mean (SE)	-0.13 (1.39)	1.81 (1.40)
95% CI of LS mean	(-2.87, 2.61)	(-0.94, 4.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.94 (-1.95, 5.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	0.25 (1.09)	1.68 (1.10)
95% CI of LS mean	(-1.90, 2.41)	(-0.49, 3.86)
P-value within Treatment	0.8188	0.1286
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.43 (-1.63, 4.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3571
Hedges' G (SE)		0.13 (0.14)
Hedges' 95% CI		(-0.15, 0.40)
Hedges' P-value		0.3575

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	79.65 (20.38)	77.73 (22.01)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	76.86 (2.10)	78.55 (2.26)
95% CI of LS mean	(72.72, 81.01)	(74.10, 83.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-4.41, 7.78)
Absolute Change at Week 8 (MMRM)		
n	110	96
LS mean (SE)	-2.93 (1.66)	0.60 (1.78)
95% CI of LS mean	(-6.20, 0.35)	(-2.90, 4.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.53 (-1.28, 8.33)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	76.26 (1.92)	80.70 (2.06)
95% CI of LS mean	(72.48, 80.04)	(76.64, 84.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.45 (-1.12, 10.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	-3.48 (1.38)	2.69 (1.47)
95% CI of LS mean	(-6.19, -0.76)	(-0.22, 5.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.16 (2.18, 10.15)
Week 24 (MMRM)		
n	113	98
LS mean (SE)	78.79 (2.10)	78.26 (2.26)
95% CI of LS mean	(74.65, 82.94)	(73.81, 82.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-6.63, 5.57)
Absolute Change at Week 24 (MMRM)		
n	110	96
LS mean (SE)	-0.98 (1.45)	0.25 (1.56)
95% CI of LS mean	(-3.85, 1.89)	(-2.82, 3.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-2.98, 5.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	80.19 (20.14)	80.37 (20.64)
Absolute Change at Week 52		
n	109	92
Mean (SD)	-0.32 (13.42)	3.00 (12.70)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	79.47 (1.91)	81.02 (2.06)
95% CI of LS mean	(75.71, 83.23)	(76.95, 85.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-4.00, 7.10)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	-0.29 (1.25)	3.05 (1.36)
95% CI of LS mean	(-2.75, 2.17)	(0.37, 5.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.34 (-0.30, 6.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	-1.58 (1.07)	2.00 (1.15)
95% CI of LS mean	(-3.69, 0.52)	(-0.26, 4.25)
P-value within Treatment	0.1398	0.0832
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.58 (0.48, 6.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0239
Hedges' G (SE)		0.32 (0.14)
Hedges' 95% CI		(0.04, 0.59)
Hedges' P-value		0.0242

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	85.97 (15.36)	89.02 (15.26)
Week 8 (MMRM)		
n	84	90
LS mean (SE)	85.01 (1.96)	87.85 (1.88)
95% CI of LS mean	(81.15, 88.88)	(84.13, 91.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-2.53, 8.21)
Absolute Change at Week 8 (MMRM)		
n	83	90
LS mean (SE)	-1.01 (1.29)	-0.54 (1.24)
95% CI of LS mean	(-3.56, 1.55)	(-2.99, 1.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.46 (-3.08, 4.01)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	86.03 (2.10)	86.77 (2.01)
95% CI of LS mean	(81.89, 90.17)	(82.81, 90.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.74 (-5.00, 6.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	0.05 (1.68)	-1.88 (1.61)
95% CI of LS mean	(-3.28, 3.37)	(-5.06, 1.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.93 (-6.53, 2.68)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	86.88 (1.76)	89.79 (1.69)
95% CI of LS mean	(83.42, 90.35)	(86.46, 93.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.91 (-1.90, 7.72)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	0.93 (1.24)	1.17 (1.19)
95% CI of LS mean	(-1.52, 3.38)	(-1.18, 3.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-3.16, 3.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	80	87
Mean (SD)	88.75 (14.96)	89.26 (16.16)
Absolute Change at Week 52		
n	79	86
Mean (SD)	3.12 (11.15)	0.92 (11.54)
Week 52 (MMRM)		
n	79	87
LS mean (SE)	88.68 (1.70)	89.65 (1.63)
95% CI of LS mean	(85.32, 92.04)	(86.43, 92.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-3.69, 5.63)
Absolute Change at Week 52 (MMRM)		
n	78	86
LS mean (SE)	2.86 (1.28)	1.10 (1.23)
95% CI of LS mean	(0.32, 5.40)	(-1.32, 3.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.76 (-5.27, 1.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	1.28 (1.12)	0.13 (1.07)
95% CI of LS mean	(-0.93, 3.49)	(-1.99, 2.24)
P-value within Treatment	0.2545	0.9052
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.15 (-4.21, 1.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4586
Hedges' G (SE)		-0.11 (0.15)
Hedges' 95% CI		(-0.41, 0.19)
Hedges' P-value		0.4586

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	86.90 (15.96)	85.81 (14.90)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	88.33 (2.62)	87.87 (2.88)
95% CI of LS mean	(83.05, 93.61)	(82.08, 93.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-8.35, 7.43)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	0.97 (2.22)	4.22 (2.43)
95% CI of LS mean	(-3.49, 5.43)	(-0.65, 9.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.26 (-3.38, 9.89)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	88.74 (2.98)	87.21 (3.27)
95% CI of LS mean	(82.76, 94.71)	(80.65, 93.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.53 (-10.46, 7.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	1.32 (1.91)	3.75 (2.10)
95% CI of LS mean	(-2.51, 5.15)	(-0.48, 7.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.43 (-3.31, 8.17)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	87.20 (3.27)	84.58 (3.59)
95% CI of LS mean	(80.64, 93.76)	(77.37, 91.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.62 (-12.41, 7.17)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	-0.30 (2.33)	1.03 (2.57)
95% CI of LS mean	(-4.98, 4.38)	(-4.13, 6.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.33 (-5.66, 8.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	28	25
Mean (SD)	89.73 (16.26)	87.44 (16.58)
Absolute Change at Week 52		
n	27	24
Mean (SD)	1.73 (13.75)	3.55 (12.93)
Week 52 (MMRM)		
n	28	24
LS mean (SE)	88.88 (3.27)	87.53 (3.57)
95% CI of LS mean	(82.31, 95.46)	(80.35, 94.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.35 (-11.13, 8.43)
Absolute Change at Week 52 (MMRM)		
n	27	23
LS mean (SE)	1.42 (2.61)	4.40 (2.85)
95% CI of LS mean	(-3.82, 6.66)	(-1.33, 10.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.98 (-4.80, 10.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	0.81 (1.95)	3.06 (2.15)
95% CI of LS mean	(-3.11, 4.74)	(-1.26, 7.38)
P-value within Treatment	0.6790	0.1610
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.25 (-3.63, 8.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4454
Hedges' G (SE)		0.21 (0.28)
Hedges' 95% CI		(-0.34, 0.77)
Hedges' P-value		0.4442

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	81.69 (18.93)	82.77 (20.41)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	79.28 (1.63)	82.02 (1.64)
95% CI of LS mean	(76.08, 82.48)	(78.79, 85.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.74 (-1.81, 7.29)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	-2.57 (1.20)	-0.60 (1.21)
95% CI of LS mean	(-4.94, -0.20)	(-2.99, 1.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.97 (-1.40, 5.33)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	79.33 (1.57)	82.72 (1.58)
95% CI of LS mean	(76.25, 82.42)	(79.61, 85.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.38 (-1.00, 7.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-2.49 (1.21)	-0.05 (1.22)
95% CI of LS mean	(-4.87, -0.10)	(-2.45, 2.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.43 (-0.95, 5.82)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	81.78 (1.54)	83.33 (1.56)
95% CI of LS mean	(78.74, 84.81)	(80.27, 86.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-2.76, 5.86)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	-0.10 (1.07)	0.61 (1.08)
95% CI of LS mean	(-2.21, 2.01)	(-1.51, 2.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.71 (-2.28, 3.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	82.77 (18.78)	84.23 (19.30)
Absolute Change at Week 52		
n	162	156
Mean (SD)	0.97 (12.43)	1.76 (12.01)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	82.78 (1.42)	84.45 (1.44)
95% CI of LS mean	(79.98, 85.57)	(81.62, 87.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.68 (-2.30, 5.65)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	1.02 (0.96)	1.75 (0.98)
95% CI of LS mean	(-0.87, 2.91)	(-0.17, 3.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.73 (-1.97, 3.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-0.52 (0.85)	0.77 (0.85)
95% CI of LS mean	(-2.19, 1.14)	(-0.90, 2.44)
P-value within Treatment	0.5381	0.3656
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.29 (-1.07, 3.65)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2824
Hedges' G (SE)		0.12 (0.11)
Hedges' 95% CI		(-0.10, 0.34)
Hedges' P-value		0.2826

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	80.92 (21.03)	73.40 (25.25)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	83.53 (4.34)	77.82 (4.74)
95% CI of LS mean	(74.67, 92.39)	(68.14, 87.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.72 (-19.04, 7.61)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	2.82 (3.28)	4.17 (3.58)
95% CI of LS mean	(-3.88, 9.52)	(-3.14, 11.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-8.66, 11.36)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	79.36 (4.09)	76.89 (4.48)
95% CI of LS mean	(71.00, 87.73)	(67.74, 86.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.48 (-15.10, 10.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-1.35 (2.78)	3.24 (3.04)
95% CI of LS mean	(-7.03, 4.33)	(-2.96, 9.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.59 (-3.94, 13.11)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	79.80 (3.96)	80.68 (4.33)
95% CI of LS mean	(71.71, 87.89)	(71.83, 89.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-11.34, 13.10)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	-0.91 (3.21)	7.03 (3.51)
95% CI of LS mean	(-7.46, 5.64)	(-0.12, 14.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.94 (-1.86, 17.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	85.19 (15.67)	75.89 (22.66)
Absolute Change at Week 52		
n	18	13
Mean (SD)	2.78 (13.63)	5.82 (11.88)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	84.37 (4.41)	77.68 (5.06)
95% CI of LS mean	(75.32, 93.41)	(67.33, 88.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.69 (-20.60, 7.22)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	3.05 (3.05)	5.47 (3.60)
95% CI of LS mean	(-3.19, 9.30)	(-1.90, 12.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.42 (-7.31, 12.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	0.26 (2.28)	5.25 (2.54)
95% CI of LS mean	(-4.40, 4.93)	(0.07, 10.43)
P-value within Treatment	0.9085	0.0473
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.98 (-2.12, 12.09)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1627
Hedges' G (SE)		0.48 (0.34)
Hedges' 95% CI		(-0.20, 1.17)
Hedges' P-value		0.1597

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	82.60 (18.40)	84.18 (19.11)
Week 8 (MMRM)		
n	178	172
LS mean (SE)	80.34 (1.53)	83.18 (1.56)
95% CI of LS mean	(77.33, 83.36)	(80.12, 86.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-1.46, 7.14)
Absolute Change at Week 8 (MMRM)		
n	174	170
LS mean (SE)	-2.61 (1.14)	-0.37 (1.15)
95% CI of LS mean	(-4.85, -0.36)	(-2.64, 1.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.24 (-0.95, 5.43)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	80.89 (1.50)	83.87 (1.52)
95% CI of LS mean	(77.94, 83.84)	(80.88, 86.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.98 (-1.22, 7.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	-1.99 (1.15)	0.16 (1.17)
95% CI of LS mean	(-4.27, 0.28)	(-2.13, 2.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.15 (-1.08, 5.38)
Week 24 (MMRM)		
n	177	172
LS mean (SE)	82.89 (1.50)	83.73 (1.52)
95% CI of LS mean	(79.95, 85.84)	(80.74, 86.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.84 (-3.36, 5.03)
Absolute Change at Week 24 (MMRM)		
n	173	169
LS mean (SE)	-0.05 (1.02)	0.05 (1.03)
95% CI of LS mean	(-2.05, 1.96)	(-1.97, 2.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-2.75, 2.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	174	169
Mean (SD)	83.66 (18.92)	85.57 (18.40)
Absolute Change at Week 52		
n	170	166
Mean (SD)	0.95 (12.52)	1.84 (12.02)
Week 52 (MMRM)		
n	173	167
LS mean (SE)	83.73 (1.37)	85.43 (1.39)
95% CI of LS mean	(81.04, 86.42)	(82.70, 88.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.70 (-2.13, 5.53)
Absolute Change at Week 52 (MMRM)		
n	169	164
LS mean (SE)	0.90 (0.94)	1.76 (0.96)
95% CI of LS mean	(-0.95, 2.76)	(-0.12, 3.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.85 (-1.79, 3.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	-0.38 (0.82)	0.66 (0.83)
95% CI of LS mean	(-1.99, 1.24)	(-0.97, 2.29)
P-value within Treatment	0.6450	0.4284
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-1.26, 3.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3754
Hedges' G (SE)		0.10 (0.11)
Hedges' 95% CI		(-0.12, 0.31)
Hedges' P-value		0.3755

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	84.67 (18.30)	84.91 (18.63)
Week 8 (MMRM)		
n	116	116
LS mean (SE)	81.76 (1.83)	85.26 (1.84)
95% CI of LS mean	(78.15, 85.37)	(81.64, 88.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.49 (-1.64, 8.62)
Absolute Change at Week 8 (MMRM)		
n	112	115
LS mean (SE)	-3.20 (1.45)	0.65 (1.44)
95% CI of LS mean	(-6.07, -0.34)	(-2.18, 3.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.86 (-0.18, 7.89)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	83.14 (1.71)	84.91 (1.71)
95% CI of LS mean	(79.77, 86.52)	(81.53, 88.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.76 (-3.03, 6.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	-1.75 (1.26)	0.03 (1.24)
95% CI of LS mean	(-4.22, 0.73)	(-2.41, 2.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.78 (-1.71, 5.27)
Week 24 (MMRM)		
n	115	115
LS mean (SE)	84.61 (1.66)	85.89 (1.66)
95% CI of LS mean	(81.35, 87.88)	(82.61, 89.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.27 (-3.37, 5.91)
Absolute Change at Week 24 (MMRM)		
n	111	114
LS mean (SE)	-0.38 (1.20)	1.13 (1.19)
95% CI of LS mean	(-2.75, 1.99)	(-1.21, 3.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-1.83, 4.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	85.47 (17.98)	86.30 (18.57)
Absolute Change at Week 52		
n	109	110
Mean (SD)	0.51 (9.87)	1.80 (10.53)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	85.17 (1.62)	86.88 (1.63)
95% CI of LS mean	(81.98, 88.37)	(83.68, 90.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-2.83, 6.25)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	0.39 (0.98)	1.98 (0.97)
95% CI of LS mean	(-1.54, 2.32)	(0.07, 3.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.59 (-1.14, 4.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	-0.58 (0.90)	1.05 (0.89)
95% CI of LS mean	(-2.36, 1.20)	(-0.71, 2.80)
P-value within Treatment	0.5214	0.2418
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-0.88, 4.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2030
Hedges' G (SE)		0.17 (0.13)
Hedges' 95% CI		(-0.09, 0.43)
Hedges' P-value		0.2021

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	79.42 (18.63)	80.56 (21.24)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	78.96 (2.32)	78.93 (2.44)
95% CI of LS mean	(74.38, 83.54)	(74.12, 83.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-6.68, 6.63)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	-0.72 (1.61)	-0.72 (1.72)
95% CI of LS mean	(-3.91, 2.46)	(-4.11, 2.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-4.65, 4.66)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	77.22 (2.38)	80.90 (2.49)
95% CI of LS mean	(72.52, 81.93)	(75.98, 85.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.68 (-3.15, 10.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	-2.42 (1.91)	1.27 (2.02)
95% CI of LS mean	(-6.19, 1.35)	(-2.73, 5.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.69 (-1.81, 9.19)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	79.64 (2.42)	79.88 (2.54)
95% CI of LS mean	(74.85, 84.43)	(74.85, 84.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-6.72, 7.19)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	-0.02 (1.66)	0.14 (1.77)
95% CI of LS mean	(-3.30, 3.26)	(-3.36, 3.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-4.64, 4.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	80	73
Mean (SD)	81.39 (19.22)	82.17 (19.37)
Absolute Change at Week 52		
n	80	70
Mean (SD)	1.85 (15.58)	2.32 (14.33)
Week 52 (MMRM)		
n	79	69
LS mean (SE)	81.58 (2.14)	81.79 (2.26)
95% CI of LS mean	(77.34, 85.82)	(77.32, 86.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.21 (-5.96, 6.39)
Absolute Change at Week 52 (MMRM)		
n	79	67
LS mean (SE)	1.86 (1.69)	2.29 (1.82)
95% CI of LS mean	(-1.48, 5.20)	(-1.30, 5.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-4.48, 5.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	-0.19 (1.39)	1.23 (1.48)
95% CI of LS mean	(-2.94, 2.55)	(-1.68, 4.15)
P-value within Treatment	0.8885	0.4051
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.43 (-2.58, 5.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4831
Hedges' G (SE)		0.11 (0.16)
Hedges' 95% CI		(-0.21, 0.43)
Hedges' P-value		0.4824

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	82.45 (17.92)	83.43 (20.91)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	79.26 (2.33)	82.90 (2.39)
95% CI of LS mean	(74.66, 83.86)	(78.18, 87.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.65 (-2.95, 10.24)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	-3.51 (1.63)	0.22 (1.67)
95% CI of LS mean	(-6.73, -0.30)	(-3.07, 3.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.74 (-0.86, 8.34)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	81.62 (2.18)	82.87 (2.24)
95% CI of LS mean	(77.31, 85.93)	(78.46, 87.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.25 (-4.92, 7.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	-1.11 (1.62)	-0.07 (1.65)
95% CI of LS mean	(-4.30, 2.08)	(-3.34, 3.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-3.53, 5.61)
Week 24 (MMRM)		
n	89	84
LS mean (SE)	81.99 (2.34)	81.21 (2.40)
95% CI of LS mean	(77.37, 86.62)	(76.46, 85.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.79 (-7.42, 5.84)
Absolute Change at Week 24 (MMRM)		
n	87	82
LS mean (SE)	-0.73 (1.49)	-1.60 (1.54)
95% CI of LS mean	(-3.68, 2.22)	(-4.64, 1.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.87 (-5.11, 3.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	83.43 (18.79)	83.69 (21.21)
Absolute Change at Week 52		
n	86	76
Mean (SD)	0.76 (12.57)	1.24 (11.91)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	83.51 (2.06)	84.06 (2.14)
95% CI of LS mean	(79.44, 87.58)	(79.84, 88.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.54 (-5.33, 6.41)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	0.88 (1.32)	1.36 (1.39)
95% CI of LS mean	(-1.72, 3.48)	(-1.38, 4.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-3.30, 4.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	-0.32 (1.16)	-0.10 (1.19)
95% CI of LS mean	(-2.61, 1.97)	(-2.46, 2.25)
P-value within Treatment	0.7823	0.9307
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-3.07, 3.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8966
Hedges' G (SE)		0.02 (0.15)
Hedges' 95% CI		(-0.28, 0.32)
Hedges' P-value		0.8964

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	82.47 (19.17)	82.95 (18.92)
Week 8 (MMRM)		
n	109	105
LS mean (SE)	81.75 (1.79)	82.70 (1.82)
95% CI of LS mean	(78.22, 85.27)	(79.11, 86.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.95 (-4.08, 5.99)
Absolute Change at Week 8 (MMRM)		
n	107	104
LS mean (SE)	-0.94 (1.43)	-0.06 (1.45)
95% CI of LS mean	(-3.77, 1.88)	(-2.93, 2.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-3.14, 4.90)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	79.93 (1.85)	83.67 (1.88)
95% CI of LS mean	(76.28, 83.58)	(79.96, 87.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.74 (-1.47, 8.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	-2.66 (1.46)	0.86 (1.48)
95% CI of LS mean	(-5.54, 0.22)	(-2.05, 3.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.52 (-0.57, 7.62)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	83.01 (1.65)	85.36 (1.67)
95% CI of LS mean	(79.77, 86.26)	(82.06, 88.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.34 (-2.29, 6.97)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	0.32 (1.26)	2.52 (1.27)
95% CI of LS mean	(-2.16, 2.80)	(0.01, 5.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.20 (-1.33, 5.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	105	106
Mean (SD)	84.07 (18.45)	85.38 (17.16)
Absolute Change at Week 52		
n	103	104
Mean (SD)	1.34 (12.66)	2.55 (12.29)
Week 52 (MMRM)		
n	104	103
LS mean (SE)	83.83 (1.65)	85.49 (1.67)
95% CI of LS mean	(80.57, 87.08)	(82.19, 88.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.67 (-2.97, 6.31)
Absolute Change at Week 52 (MMRM)		
n	102	102
LS mean (SE)	1.23 (1.23)	2.66 (1.23)
95% CI of LS mean	(-1.19, 3.65)	(0.23, 5.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.43 (-2.00, 4.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	-0.37 (1.04)	2.01 (1.05)
95% CI of LS mean	(-2.42, 1.68)	(-0.05, 4.08)
P-value within Treatment	0.7228	0.0563
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-0.53, 5.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1082
Hedges' G (SE)		0.22 (0.14)
Hedges' 95% CI		(-0.05, 0.50)
Hedges' P-value		0.1092

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	71.53 (17.81)	72.28 (18.71)
Week 8 (MMRM)		
n	113	98
LS mean (SE)	74.46 (1.62)	73.79 (1.73)
95% CI of LS mean	(71.27, 77.64)	(70.37, 77.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-5.35, 4.02)
Absolute Change at Week 8 (MMRM)		
n	110	96
LS mean (SE)	2.82 (1.20)	1.54 (1.28)
95% CI of LS mean	(0.47, 5.18)	(-0.98, 4.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.28 (-4.75, 2.18)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	73.21 (1.82)	71.99 (1.95)
95% CI of LS mean	(69.63, 76.80)	(68.13, 75.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.23 (-6.50, 4.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	1.45 (1.41)	-0.12 (1.51)
95% CI of LS mean	(-1.34, 4.23)	(-3.10, 2.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.56 (-5.65, 2.52)
Week 24 (MMRM)		
n	113	98
LS mean (SE)	75.35 (1.69)	73.52 (1.82)
95% CI of LS mean	(72.01, 78.69)	(69.93, 77.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.83 (-6.74, 3.07)
Absolute Change at Week 24 (MMRM)		
n	110	96
LS mean (SE)	3.64 (1.23)	1.39 (1.32)
95% CI of LS mean	(1.22, 6.07)	(-1.21, 3.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.26 (-5.82, 1.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	76.45 (16.36)	74.88 (18.70)
Absolute Change at Week 52		
n	109	92
Mean (SD)	4.27 (13.36)	2.84 (15.02)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	76.13 (1.65)	75.25 (1.79)
95% CI of LS mean	(72.87, 79.39)	(71.72, 78.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-5.70, 3.93)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	4.35 (1.35)	2.79 (1.47)
95% CI of LS mean	(1.68, 7.02)	(-0.10, 5.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.56 (-5.51, 2.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	3.15 (1.16)	1.35 (1.24)
95% CI of LS mean	(0.86, 5.44)	(-1.10, 3.81)
P-value within Treatment	0.0072	0.2780
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.79 (-5.16, 1.57)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2943
Hedges' G (SE)		-0.15 (0.14)
Hedges' 95% CI		(-0.42, 0.13)
Hedges' P-value		0.2934

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	77.56 (15.64)	77.68 (17.57)
Week 8 (MMRM)		
n	84	90
LS mean (SE)	76.71 (1.86)	78.03 (1.80)
95% CI of LS mean	(73.04, 80.39)	(74.49, 81.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.32 (-3.79, 6.43)
Absolute Change at Week 8 (MMRM)		
n	83	90
LS mean (SE)	-1.13 (1.62)	0.61 (1.56)
95% CI of LS mean	(-4.34, 2.07)	(-2.47, 3.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.74 (-2.71, 6.19)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	76.63 (1.88)	77.30 (1.80)
95% CI of LS mean	(72.91, 80.34)	(73.74, 80.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.68 (-4.47, 5.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	-1.44 (1.57)	-0.22 (1.51)
95% CI of LS mean	(-4.55, 1.67)	(-3.19, 2.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-3.08, 5.53)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	77.73 (1.77)	80.37 (1.69)
95% CI of LS mean	(74.25, 81.22)	(77.02, 83.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.64 (-2.20, 7.47)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	-0.30 (1.47)	2.86 (1.41)
95% CI of LS mean	(-3.20, 2.61)	(0.07, 5.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.15 (-0.88, 7.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	80	87
Mean (SD)	79.19 (15.72)	79.97 (15.85)
Absolute Change at Week 52		
n	79	86
Mean (SD)	1.66 (13.56)	2.76 (13.43)
Week 52 (MMRM)		
n	79	87
LS mean (SE)	79.61 (1.72)	80.25 (1.65)
95% CI of LS mean	(76.22, 83.00)	(77.00, 83.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-4.06, 5.34)
Absolute Change at Week 52 (MMRM)		
n	78	86
LS mean (SE)	1.66 (1.50)	2.91 (1.43)
95% CI of LS mean	(-1.29, 4.61)	(0.09, 5.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-2.84, 5.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	-0.03 (1.24)	1.85 (1.19)
95% CI of LS mean	(-2.47, 2.42)	(-0.49, 4.19)
P-value within Treatment	0.9836	0.1211
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.87 (-1.52, 5.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2767
Hedges' G (SE)		0.17 (0.15)
Hedges' 95% CI		(-0.13, 0.47)
Hedges' P-value		0.2770

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	72.50 (15.29)	77.65 (13.56)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	73.35 (2.83)	76.91 (3.10)
95% CI of LS mean	(67.67, 79.02)	(70.68, 83.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.56 (-4.90, 12.02)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	0.53 (2.63)	0.69 (2.87)
95% CI of LS mean	(-4.76, 5.82)	(-5.08, 6.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-7.70, 8.03)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	74.37 (2.57)	75.54 (2.82)
95% CI of LS mean	(69.21, 79.53)	(69.87, 81.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-6.54, 8.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	1.13 (2.50)	-1.13 (2.76)
95% CI of LS mean	(-3.91, 6.16)	(-6.68, 4.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.25 (-9.79, 5.28)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	75.29 (2.36)	77.69 (2.59)
95% CI of LS mean	(70.55, 80.03)	(72.48, 82.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.40 (-4.69, 9.49)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	2.91 (2.51)	0.88 (2.76)
95% CI of LS mean	(-2.13, 7.95)	(-4.67, 6.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.03 (-9.56, 5.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	28	25
Mean (SD)	78.49 (12.60)	76.76 (15.87)
Absolute Change at Week 52		
n	27	24
Mean (SD)	5.29 (14.94)	-0.54 (15.04)
Week 52 (MMRM)		
n	28	24
LS mean (SE)	78.33 (2.60)	75.74 (2.82)
95% CI of LS mean	(73.11, 83.54)	(70.06, 81.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.59 (-10.33, 5.15)
Absolute Change at Week 52 (MMRM)		
n	27	23
LS mean (SE)	5.68 (2.87)	-0.56 (3.13)
95% CI of LS mean	(-0.08, 11.43)	(-6.84, 5.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.24 (-14.79, 2.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	3.24 (2.19)	-0.27 (2.41)
95% CI of LS mean	(-1.16, 7.64)	(-5.12, 4.58)
P-value within Treatment	0.1458	0.9121
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.51 (-10.10, 3.08)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2903
Hedges' G (SE)		-0.30 (0.28)
Hedges' 95% CI		(-0.86, 0.26)
Hedges' P-value		0.2901

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	74.58 (17.51)	74.72 (18.99)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	75.87 (1.34)	75.60 (1.35)
95% CI of LS mean	(73.23, 78.51)	(72.93, 78.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-4.02, 3.48)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	1.19 (1.07)	1.18 (1.08)
95% CI of LS mean	(-0.91, 3.30)	(-0.94, 3.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-3.00, 2.98)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	74.79 (1.47)	74.34 (1.48)
95% CI of LS mean	(71.90, 77.68)	(71.43, 77.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-4.55, 3.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	0.07 (1.16)	-0.02 (1.17)
95% CI of LS mean	(-2.22, 2.36)	(-2.32, 2.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-3.33, 3.15)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	76.62 (1.38)	76.63 (1.39)
95% CI of LS mean	(73.92, 79.33)	(73.90, 79.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-3.84, 3.85)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	1.80 (1.03)	2.27 (1.04)
95% CI of LS mean	(-0.22, 3.83)	(0.23, 4.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.46 (-2.42, 3.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	77.58 (16.71)	77.50 (17.78)
Absolute Change at Week 52		
n	162	156
Mean (SD)	2.80 (13.19)	3.21 (14.03)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	77.58 (1.32)	77.87 (1.34)
95% CI of LS mean	(74.98, 80.18)	(75.24, 80.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-3.41, 3.99)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	2.78 (1.07)	3.33 (1.08)
95% CI of LS mean	(0.68, 4.88)	(1.20, 5.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-2.45, 3.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	1.55 (0.93)	1.86 (0.93)
95% CI of LS mean	(-0.27, 3.38)	(0.02, 3.69)
P-value within Treatment	0.0954	0.0473
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-2.28, 2.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8161
Hedges' G (SE)		0.03 (0.11)
Hedges' 95% CI		(-0.19, 0.24)
Hedges' P-value		0.8160

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	73.68 (13.96)	71.88 (23.26)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	76.57 (4.36)	77.47 (4.77)
95% CI of LS mean	(67.68, 85.47)	(67.74, 87.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.90 (-12.56, 14.37)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	2.28 (2.34)	6.32 (2.56)
95% CI of LS mean	(-2.50, 7.06)	(1.10, 11.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.04 (-3.13, 11.21)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	73.94 (4.69)	75.04 (5.13)
95% CI of LS mean	(64.34, 83.54)	(64.55, 85.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.10 (-13.37, 15.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-0.35 (2.37)	3.89 (2.59)
95% CI of LS mean	(-5.20, 4.50)	(-1.41, 9.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.24 (-3.03, 11.52)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	76.57 (4.45)	78.17 (4.87)
95% CI of LS mean	(67.49, 85.66)	(68.23, 88.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.60 (-12.14, 15.33)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	2.28 (2.74)	7.02 (2.99)
95% CI of LS mean	(-3.29, 7.85)	(0.93, 13.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.74 (-3.59, 13.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	78.09 (18.42)	72.78 (22.64)
Absolute Change at Week 52		
n	18	13
Mean (SD)	3.70 (10.78)	1.88 (14.01)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	78.33 (4.79)	73.34 (5.41)
95% CI of LS mean	(68.55, 88.11)	(62.33, 84.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.99 (-19.96, 9.97)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	3.85 (2.73)	2.00 (3.24)
95% CI of LS mean	(-1.75, 9.45)	(-4.63, 8.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.85 (-10.59, 6.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	1.93 (1.96)	4.30 (2.18)
95% CI of LS mean	(-2.08, 5.93)	(-0.16, 8.76)
P-value within Treatment	0.3341	0.0580
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-3.72, 8.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4324
Hedges' G (SE)		0.27 (0.33)
Hedges' 95% CI		(-0.41, 0.95)
Hedges' P-value		0.4253

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	74.35 (17.57)	75.30 (17.91)
Week 8 (MMRM)		
n	178	172
LS mean (SE)	75.49 (1.27)	75.48 (1.29)
95% CI of LS mean	(72.99, 77.99)	(72.95, 78.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-3.57, 3.55)
Absolute Change at Week 8 (MMRM)		
n	174	170
LS mean (SE)	1.00 (1.06)	0.62 (1.07)
95% CI of LS mean	(-1.08, 3.09)	(-1.50, 2.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-3.36, 2.58)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	74.97 (1.37)	74.27 (1.38)
95% CI of LS mean	(72.28, 77.66)	(71.55, 76.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-4.52, 3.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	0.30 (1.14)	-0.55 (1.15)
95% CI of LS mean	(-1.94, 2.55)	(-2.82, 1.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.86 (-4.05, 2.34)
Week 24 (MMRM)		
n	177	172
LS mean (SE)	76.56 (1.28)	76.47 (1.30)
95% CI of LS mean	(74.04, 79.09)	(73.91, 79.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-3.69, 3.50)
Absolute Change at Week 24 (MMRM)		
n	173	169
LS mean (SE)	1.94 (1.01)	1.63 (1.02)
95% CI of LS mean	(-0.05, 3.93)	(-0.38, 3.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-3.14, 2.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	174	169
Mean (SD)	77.83 (15.87)	77.78 (17.08)
Absolute Change at Week 52		
n	170	166
Mean (SD)	3.25 (13.61)	2.72 (14.26)
Week 52 (MMRM)		
n	173	167
LS mean (SE)	77.75 (1.23)	77.74 (1.25)
95% CI of LS mean	(75.33, 80.17)	(75.28, 80.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-3.46, 3.44)
Absolute Change at Week 52 (MMRM)		
n	169	164
LS mean (SE)	3.11 (1.07)	2.82 (1.08)
95% CI of LS mean	(1.01, 5.21)	(0.69, 4.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-3.28, 2.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	1.78 (0.92)	1.30 (0.93)
95% CI of LS mean	(-0.02, 3.59)	(-0.53, 3.13)
P-value within Treatment	0.0531	0.1632
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.49 (-3.06, 2.09)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7105
Hedges' G (SE)		-0.04 (0.11)
Hedges' 95% CI		(-0.25, 0.17)
Hedges' P-value		0.7104

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	74.86 (18.00)	75.32 (19.28)
Week 8 (MMRM)		
n	116	116
LS mean (SE)	75.52 (1.63)	75.76 (1.64)
95% CI of LS mean	(72.31, 78.74)	(72.54, 78.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-4.33, 4.81)
Absolute Change at Week 8 (MMRM)		
n	112	115
LS mean (SE)	0.63 (1.24)	0.46 (1.23)
95% CI of LS mean	(-1.81, 3.07)	(-1.95, 2.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-3.61, 3.28)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	74.14 (1.71)	73.90 (1.72)
95% CI of LS mean	(70.76, 77.52)	(70.52, 77.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-5.04, 4.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	-0.98 (1.37)	-1.42 (1.35)
95% CI of LS mean	(-3.67, 1.71)	(-4.08, 1.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-4.24, 3.35)
Week 24 (MMRM)		
n	115	115
LS mean (SE)	76.86 (1.64)	77.23 (1.65)
95% CI of LS mean	(73.62, 80.09)	(73.99, 80.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.38 (-4.22, 4.97)
Absolute Change at Week 24 (MMRM)		
n	111	114
LS mean (SE)	1.83 (1.21)	1.94 (1.20)
95% CI of LS mean	(-0.56, 4.22)	(-0.42, 4.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-3.26, 3.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	77.69 (16.01)	77.23 (18.35)
Absolute Change at Week 52		
n	109	110
Mean (SD)	2.38 (11.20)	1.82 (14.61)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	77.36 (1.60)	77.31 (1.60)
95% CI of LS mean	(74.21, 80.50)	(74.15, 80.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-4.52, 4.42)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	2.27 (1.25)	1.81 (1.24)
95% CI of LS mean	(-0.20, 4.74)	(-0.64, 4.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-3.95, 3.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	1.04 (1.09)	0.78 (1.08)
95% CI of LS mean	(-1.10, 3.18)	(-1.34, 2.89)
P-value within Treatment	0.3406	0.4716
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-3.29, 2.76)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8639
Hedges' G (SE)		-0.02 (0.13)
Hedges' 95% CI		(-0.28, 0.24)
Hedges' P-value		0.8634

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	73.47 (16.06)	74.77 (17.03)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	75.24 (1.82)	76.03 (1.92)
95% CI of LS mean	(71.63, 78.84)	(72.23, 79.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.79 (-4.46, 6.03)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	1.88 (1.63)	2.14 (1.74)
95% CI of LS mean	(-1.34, 5.10)	(-1.29, 5.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-4.45, 4.98)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	75.47 (2.05)	75.41 (2.14)
95% CI of LS mean	(71.43, 79.51)	(71.19, 79.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-5.91, 5.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	1.99 (1.66)	1.71 (1.76)
95% CI of LS mean	(-1.29, 5.28)	(-1.78, 5.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-5.09, 4.51)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	75.72 (1.85)	76.04 (1.94)
95% CI of LS mean	(72.07, 79.37)	(72.21, 79.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-4.98, 5.62)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	2.26 (1.55)	2.23 (1.65)
95% CI of LS mean	(-0.81, 5.33)	(-1.04, 5.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-4.52, 4.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	80	73
Mean (SD)	77.74 (16.46)	77.66 (16.22)
Absolute Change at Week 52		
n	80	70
Mean (SD)	4.22 (16.00)	4.10 (13.45)
Week 52 (MMRM)		
n	79	69
LS mean (SE)	78.04 (1.82)	78.07 (1.92)
95% CI of LS mean	(74.45, 81.64)	(74.27, 81.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-5.21, 5.28)
Absolute Change at Week 52 (MMRM)		
n	79	67
LS mean (SE)	4.58 (1.66)	4.40 (1.79)
95% CI of LS mean	(1.29, 7.86)	(0.87, 7.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-5.00, 4.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	2.94 (1.38)	2.78 (1.47)
95% CI of LS mean	(0.21, 5.68)	(-0.13, 5.69)
P-value within Treatment	0.0350	0.0609
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.16 (-4.16, 3.84)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9353
Hedges' G (SE)		-0.01 (0.16)
Hedges' 95% CI		(-0.33, 0.31)
Hedges' P-value		0.9352

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	76.70 (15.66)	75.04 (18.41)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	76.76 (1.69)	76.44 (1.73)
95% CI of LS mean	(73.42, 80.09)	(73.02, 79.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-5.09, 4.47)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	-0.24 (1.37)	1.77 (1.41)
95% CI of LS mean	(-2.95, 2.48)	(-1.01, 4.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.01 (-1.88, 5.90)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	76.96 (1.92)	73.65 (1.96)
95% CI of LS mean	(73.17, 80.74)	(69.78, 77.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.30 (-8.73, 2.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	-0.26 (1.47)	-0.90 (1.51)
95% CI of LS mean	(-3.17, 2.65)	(-3.88, 2.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-4.81, 3.52)
Week 24 (MMRM)		
n	89	84
LS mean (SE)	78.35 (1.77)	75.34 (1.81)
95% CI of LS mean	(74.85, 81.84)	(71.75, 78.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.01 (-8.02, 2.00)
Absolute Change at Week 24 (MMRM)		
n	87	82
LS mean (SE)	1.42 (1.37)	0.78 (1.40)
95% CI of LS mean	(-1.28, 4.12)	(-1.99, 3.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-4.51, 3.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	78.88 (15.17)	76.72 (16.39)
Absolute Change at Week 52		
n	86	76
Mean (SD)	2.20 (12.58)	2.45 (13.44)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	79.50 (1.64)	76.99 (1.71)
95% CI of LS mean	(76.25, 82.74)	(73.62, 80.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.51 (-7.19, 2.17)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	2.52 (1.38)	2.39 (1.44)
95% CI of LS mean	(-0.20, 5.23)	(-0.46, 5.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-4.07, 3.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	1.22 (1.16)	0.75 (1.19)
95% CI of LS mean	(-1.07, 3.52)	(-1.60, 3.11)
P-value within Treatment	0.2928	0.5282
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-3.76, 2.82)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7785
Hedges' G (SE)		-0.04 (0.15)
Hedges' 95% CI		(-0.34, 0.26)
Hedges' P-value		0.7781

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	72.32 (18.15)	75.14 (18.42)
Week 8 (MMRM)		
n	109	105
LS mean (SE)	74.58 (1.73)	75.13 (1.76)
95% CI of LS mean	(71.18, 77.98)	(71.67, 78.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-4.30, 5.41)
Absolute Change at Week 8 (MMRM)		
n	107	104
LS mean (SE)	2.29 (1.39)	0.52 (1.41)
95% CI of LS mean	(-0.44, 5.03)	(-2.25, 3.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.77 (-5.67, 2.13)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	73.09 (1.80)	74.97 (1.83)
95% CI of LS mean	(69.54, 76.63)	(71.36, 78.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.88 (-3.18, 6.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	0.71 (1.51)	0.36 (1.52)
95% CI of LS mean	(-2.26, 3.68)	(-2.64, 3.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-4.58, 3.88)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	75.04 (1.71)	77.71 (1.73)
95% CI of LS mean	(71.67, 78.40)	(74.29, 81.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.67 (-2.13, 7.47)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	2.49 (1.32)	3.08 (1.34)
95% CI of LS mean	(-0.12, 5.10)	(0.44, 5.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-3.13, 4.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	105	106
Mean (SD)	76.73 (16.94)	77.90 (18.32)
Absolute Change at Week 52		
n	103	104
Mean (SD)	3.95 (14.12)	2.89 (14.76)
Week 52 (MMRM)		
n	104	103
LS mean (SE)	76.34 (1.69)	77.84 (1.72)
95% CI of LS mean	(73.00, 79.68)	(74.46, 81.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.50 (-3.25, 6.25)
Absolute Change at Week 52 (MMRM)		
n	102	102
LS mean (SE)	3.84 (1.42)	3.10 (1.43)
95% CI of LS mean	(1.04, 6.64)	(0.29, 5.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-4.71, 3.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	2.35 (1.23)	2.18 (1.24)
95% CI of LS mean	(-0.07, 4.76)	(-0.26, 4.62)
P-value within Treatment	0.0569	0.0799
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-3.60, 3.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9241
Hedges' G (SE)		-0.01 (0.14)
Hedges' 95% CI		(-0.29, 0.26)
Hedges' P-value		0.9241

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Baseline		
n	111	99
Mean (SD)	70.17 (19.53)	70.03 (18.54)
Week 8 (MMRM)		
n	112	98
LS mean (SE)	68.79 (1.89)	70.13 (2.03)
95% CI of LS mean	(65.06, 72.52)	(66.12, 74.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.34 (-4.15, 6.83)
Absolute Change at Week 8 (MMRM)		
n	109	96
LS mean (SE)	-1.29 (1.16)	0.17 (1.24)
95% CI of LS mean	(-3.58, 1.01)	(-2.28, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-1.91, 4.82)
Week 16 (MMRM)		
n	113	98
LS mean (SE)	68.78 (1.93)	70.89 (2.07)
95% CI of LS mean	(64.99, 72.58)	(66.81, 74.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.11 (-3.48, 7.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	110	96
LS mean (SE)	-1.70 (1.30)	1.38 (1.39)
95% CI of LS mean	(-4.25, 0.86)	(-1.36, 4.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.07 (-0.68, 6.82)
Week 24 (MMRM)		
n	113	98
LS mean (SE)	71.25 (1.93)	70.55 (2.07)
95% CI of LS mean	(67.45, 75.05)	(66.47, 74.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-6.29, 4.89)
Absolute Change at Week 24 (MMRM)		
n	110	96
LS mean (SE)	0.83 (1.36)	0.68 (1.46)
95% CI of LS mean	(-1.86, 3.52)	(-2.20, 3.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-4.09, 3.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Week 52		
n	112	94
Mean (SD)	71.73 (19.67)	74.11 (19.58)
Absolute Change at Week 52		
n	109	92
Mean (SD)	1.12 (14.10)	4.47 (15.01)
Week 52 (MMRM)		
n	112	93
LS mean (SE)	71.39 (1.84)	73.99 (2.00)
95% CI of LS mean	(67.75, 75.03)	(70.05, 77.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.60 (-2.77, 7.97)
Absolute Change at Week 52 (MMRM)		
n	109	91
LS mean (SE)	0.96 (1.41)	4.12 (1.54)
95% CI of LS mean	(-1.83, 3.75)	(1.09, 7.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.16 (-0.97, 7.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	110	96
LS mean (SE)	0.03 (1.13)	2.06 (1.21)
95% CI of LS mean	(-2.19, 2.25)	(-0.32, 4.44)
P-value within Treatment	0.9793	0.0899
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.03 (-1.24, 5.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2219
Hedges' G (SE)		0.17 (0.14)
Hedges' 95% CI		(-0.10, 0.45)
Hedges' P-value		0.2212

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Baseline		
n	85	91
Mean (SD)	70.59 (20.98)	74.36 (20.87)
Week 8 (MMRM)		
n	84	90
LS mean (SE)	73.44 (2.05)	76.50 (1.98)
95% CI of LS mean	(69.39, 77.50)	(72.60, 80.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.06 (-2.58, 8.69)
Absolute Change at Week 8 (MMRM)		
n	83	90
LS mean (SE)	3.00 (1.71)	2.36 (1.64)
95% CI of LS mean	(-0.37, 6.38)	(-0.87, 5.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-5.32, 4.04)
Week 16 (MMRM)		
n	83	91
LS mean (SE)	72.70 (2.27)	75.33 (2.18)
95% CI of LS mean	(68.21, 77.18)	(71.03, 79.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-3.59, 8.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change at Week 16 (MMRM)		
n	82	90
LS mean (SE)	2.28 (1.80)	1.38 (1.72)
95% CI of LS mean	(-1.27, 5.83)	(-2.02, 4.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.90 (-5.82, 4.03)
Week 24 (MMRM)		
n	83	90
LS mean (SE)	73.64 (2.18)	75.92 (2.09)
95% CI of LS mean	(69.33, 77.94)	(71.78, 80.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.28 (-3.69, 8.25)
Absolute Change at Week 24 (MMRM)		
n	82	89
LS mean (SE)	3.28 (1.59)	1.69 (1.53)
95% CI of LS mean	(0.14, 6.42)	(-1.32, 4.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-5.94, 2.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Week 52		
n	80	87
Mean (SD)	76.53 (20.16)	78.54 (18.23)
Absolute Change at Week 52		
n	79	86
Mean (SD)	6.19 (18.03)	4.52 (16.11)
Week 52 (MMRM)		
n	79	87
LS mean (SE)	75.96 (2.13)	78.78 (2.04)
95% CI of LS mean	(71.75, 80.17)	(74.75, 82.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.82 (-3.01, 8.65)
Absolute Change at Week 52 (MMRM)		
n	78	86
LS mean (SE)	5.46 (1.90)	4.47 (1.81)
95% CI of LS mean	(1.72, 9.21)	(0.89, 8.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.99 (-6.18, 4.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87	VNZ/TEZ/D-IVA N = 92
Absolute Change through Week 52 (MMRM)		
n	82	90
LS mean (SE)	3.67 (1.55)	2.52 (1.48)
95% CI of LS mean	(0.62, 6.73)	(-0.41, 5.44)
P-value within Treatment	0.0186	0.0915
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.16 (-5.39, 3.07)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5900
Hedges' G (SE)		-0.08 (0.15)
Hedges' 95% CI		(-0.38, 0.22)
Hedges' P-value		0.5899

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Baseline		
n	29	25
Mean (SD)	70.11 (19.04)	72.89 (22.70)
Week 8 (MMRM)		
n	29	24
LS mean (SE)	69.45 (3.40)	77.03 (3.73)
95% CI of LS mean	(62.62, 76.28)	(69.53, 84.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.58 (-2.62, 17.78)
Absolute Change at Week 8 (MMRM)		
n	28	24
LS mean (SE)	-1.16 (3.59)	6.62 (3.92)
95% CI of LS mean	(-8.38, 6.05)	(-1.26, 14.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.79 (-2.95, 18.52)
Week 16 (MMRM)		
n	29	24
LS mean (SE)	68.41 (4.07)	76.01 (4.48)
95% CI of LS mean	(60.23, 76.59)	(67.02, 85.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.60 (-4.60, 19.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	28	23
LS mean (SE)	-3.07 (4.08)	6.53 (4.49)
95% CI of LS mean	(-11.26, 5.13)	(-2.49, 15.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.60 (-2.64, 21.83)
Week 24 (MMRM)		
n	29	24
LS mean (SE)	71.70 (3.81)	74.75 (4.19)
95% CI of LS mean	(64.05, 79.34)	(66.34, 83.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.05 (-8.38, 14.48)
Absolute Change at Week 24 (MMRM)		
n	28	23
LS mean (SE)	0.89 (3.72)	4.37 (4.11)
95% CI of LS mean	(-6.60, 8.37)	(-3.89, 12.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.48 (-7.72, 14.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Week 52		
n	28	25
Mean (SD)	72.62 (19.24)	80.00 (18.98)
Absolute Change at Week 52		
n	27	24
Mean (SD)	2.47 (19.57)	7.87 (26.11)
Week 52 (MMRM)		
n	28	24
LS mean (SE)	72.63 (3.58)	78.91 (3.91)
95% CI of LS mean	(65.44, 79.82)	(71.06, 86.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.28 (-4.42, 16.98)
Absolute Change at Week 52 (MMRM)		
n	27	23
LS mean (SE)	1.72 (4.34)	7.98 (4.75)
95% CI of LS mean	(-6.99, 10.43)	(-1.56, 17.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.26 (-6.70, 19.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	28	23
LS mean (SE)	-0.15 (3.59)	6.29 (3.96)
95% CI of LS mean	(-7.37, 7.07)	(-1.65, 14.24)
P-value within Treatment	0.9665	0.1180
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.45 (-4.34, 17.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2358
Hedges' G (SE)		0.33 (0.28)
Hedges' 95% CI		(-0.23, 0.89)
Hedges' P-value		0.2369

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	70.44 (20.30)	72.19 (19.36)
Week 8 (MMRM)		
n	167	164
LS mean (SE)	71.14 (1.51)	72.52 (1.53)
95% CI of LS mean	(68.16, 74.12)	(69.52, 75.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-2.85, 5.62)
Absolute Change at Week 8 (MMRM)		
n	164	162
LS mean (SE)	0.85 (0.99)	0.45 (0.99)
95% CI of LS mean	(-1.09, 2.80)	(-1.51, 2.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-3.17, 2.35)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	70.93 (1.57)	72.46 (1.58)
95% CI of LS mean	(67.85, 74.01)	(69.36, 75.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-2.85, 5.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	0.55 (1.05)	0.62 (1.06)
95% CI of LS mean	(-1.52, 2.62)	(-1.46, 2.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-2.87, 3.00)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	72.47 (1.56)	72.76 (1.57)
95% CI of LS mean	(69.40, 75.54)	(69.66, 75.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-4.07, 4.65)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	2.05 (1.05)	0.70 (1.06)
95% CI of LS mean	(-0.02, 4.11)	(-1.38, 2.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.35 (-4.28, 1.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	73.87 (20.08)	75.75 (18.95)
Absolute Change at Week 52		
n	162	156
Mean (SD)	3.29 (15.41)	3.92 (13.10)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	73.58 (1.51)	75.79 (1.53)
95% CI of LS mean	(70.60, 76.56)	(72.77, 78.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.20 (-2.03, 6.44)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	3.12 (1.14)	3.73 (1.15)
95% CI of LS mean	(0.88, 5.36)	(1.46, 6.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.61 (-2.58, 3.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	1.91 (0.91)	1.68 (0.91)
95% CI of LS mean	(0.12, 3.69)	(-0.11, 3.48)
P-value within Treatment	0.0365	0.0664
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-2.76, 2.31)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8622
Hedges' G (SE)		-0.02 (0.11)
Hedges' 95% CI		(-0.24, 0.20)
Hedges' P-value		0.8621

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	70.18 (18.90)	72.92 (15.70)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	75.53 (4.10)	70.73 (4.49)
95% CI of LS mean	(67.15, 83.91)	(61.56, 79.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.80 (-17.50, 7.89)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	5.13 (2.49)	-1.93 (2.72)
95% CI of LS mean	(0.06, 10.20)	(-7.46, 3.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.06 (-14.66, 0.55)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	70.27 (4.48)	66.56 (4.90)
95% CI of LS mean	(61.12, 79.42)	(56.56, 76.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.71 (-17.51, 10.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-0.13 (3.13)	-6.09 (3.42)
95% CI of LS mean	(-6.51, 6.24)	(-13.05, 0.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.96 (-15.46, 3.55)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	74.36 (4.46)	67.95 (4.88)
95% CI of LS mean	(65.26, 83.46)	(58.00, 77.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.41 (-20.15, 7.32)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	3.96 (3.12)	-4.70 (3.40)
95% CI of LS mean	(-2.38, 10.30)	(-11.62, 2.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.66 (-18.12, 0.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	74.69 (18.98)	68.25 (20.37)
Absolute Change at Week 52		
n	18	13
Mean (SD)	4.32 (6.75)	-3.42 (13.13)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	73.86 (4.70)	67.39 (5.32)
95% CI of LS mean	(64.26, 83.46)	(56.56, 78.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.47 (-21.17, 8.23)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	3.91 (2.38)	-3.60 (2.84)
95% CI of LS mean	(-0.96, 8.78)	(-9.42, 2.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.52 (-15.15, 0.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	2.58 (2.19)	-4.80 (2.43)
95% CI of LS mean	(-1.94, 7.10)	(-9.79, 0.19)
P-value within Treatment	0.2504	0.0588
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.38 (-14.21, -0.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0352
Hedges' G (SE)		-0.75 (0.34)
Hedges' 95% CI		(-1.45, -0.05)
Hedges' P-value		0.0364

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Baseline		
n	177	174
Mean (SD)	70.31 (20.26)	72.29 (20.19)
Week 8 (MMRM)		
n	177	172
LS mean (SE)	70.43 (1.47)	73.26 (1.49)
95% CI of LS mean	(67.53, 73.33)	(70.32, 76.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.83 (-1.30, 6.96)
Absolute Change at Week 8 (MMRM)		
n	173	170
LS mean (SE)	0.07 (1.07)	1.48 (1.08)
95% CI of LS mean	(-2.03, 2.17)	(-0.64, 3.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-1.57, 4.39)
Week 16 (MMRM)		
n	177	173
LS mean (SE)	70.63 (1.55)	73.47 (1.57)
95% CI of LS mean	(67.59, 73.68)	(70.39, 76.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-1.50, 7.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change at Week 16 (MMRM)		
n	173	170
LS mean (SE)	0.09 (1.13)	2.04 (1.14)
95% CI of LS mean	(-2.14, 2.32)	(-0.21, 4.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.95 (-1.22, 5.12)
Week 24 (MMRM)		
n	177	172
LS mean (SE)	72.21 (1.52)	73.44 (1.54)
95% CI of LS mean	(69.21, 75.21)	(70.41, 76.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-3.04, 5.50)
Absolute Change at Week 24 (MMRM)		
n	173	169
LS mean (SE)	1.70 (1.10)	1.67 (1.11)
95% CI of LS mean	(-0.45, 3.86)	(-0.51, 3.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-3.10, 3.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Week 52		
n	174	169
Mean (SD)	73.44 (20.02)	76.92 (18.78)
Absolute Change at Week 52		
n	170	166
Mean (SD)	3.01 (16.74)	5.02 (15.50)
Week 52 (MMRM)		
n	173	167
LS mean (SE)	73.43 (1.46)	76.88 (1.48)
95% CI of LS mean	(70.56, 76.30)	(73.97, 79.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.45 (-0.64, 7.54)
Absolute Change at Week 52 (MMRM)		
n	169	164
LS mean (SE)	2.88 (1.23)	5.05 (1.24)
95% CI of LS mean	(0.47, 5.30)	(2.60, 7.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.17 (-1.27, 5.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182	VNZ/TEZ/D-IVA N = 177
Absolute Change through Week 52 (MMRM)		
n	173	170
LS mean (SE)	1.56 (0.98)	2.92 (0.99)
95% CI of LS mean	(-0.38, 3.49)	(0.96, 4.87)
P-value within Treatment	0.1143	0.0036
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.36 (-1.39, 4.11)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3320
Hedges' G (SE)		0.10 (0.11)
Hedges' 95% CI		(-0.11, 0.32)
Hedges' P-value		0.3321

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Baseline		
n	114	115
Mean (SD)	71.73 (20.86)	73.53 (20.10)
Week 8 (MMRM)		
n	115	116
LS mean (SE)	71.49 (1.83)	73.68 (1.84)
95% CI of LS mean	(67.88, 75.11)	(70.07, 77.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-2.94, 7.32)
Absolute Change at Week 8 (MMRM)		
n	111	115
LS mean (SE)	-0.21 (1.25)	0.23 (1.24)
95% CI of LS mean	(-2.68, 2.26)	(-2.21, 2.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.44 (-3.04, 3.92)
Week 16 (MMRM)		
n	115	115
LS mean (SE)	71.89 (1.88)	74.42 (1.89)
95% CI of LS mean	(68.18, 75.59)	(70.70, 78.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.53 (-2.74, 7.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change at Week 16 (MMRM)		
n	111	114
LS mean (SE)	-0.15 (1.33)	1.09 (1.32)
95% CI of LS mean	(-2.77, 2.48)	(-1.50, 3.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-2.46, 4.94)
Week 24 (MMRM)		
n	115	115
LS mean (SE)	72.87 (1.87)	74.62 (1.87)
95% CI of LS mean	(69.20, 76.55)	(70.93, 78.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.74 (-3.48, 6.97)
Absolute Change at Week 24 (MMRM)		
n	111	114
LS mean (SE)	0.87 (1.33)	1.30 (1.32)
95% CI of LS mean	(-1.76, 3.49)	(-1.30, 3.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-3.27, 4.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Week 52		
n	113	111
Mean (SD)	74.73 (21.63)	76.18 (19.87)
Absolute Change at Week 52		
n	109	110
Mean (SD)	2.34 (15.43)	3.03 (14.89)
Week 52 (MMRM)		
n	112	111
LS mean (SE)	74.25 (1.94)	76.41 (1.94)
95% CI of LS mean	(70.43, 78.06)	(72.59, 80.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.17 (-3.25, 7.59)
Absolute Change at Week 52 (MMRM)		
n	108	110
LS mean (SE)	2.19 (1.45)	3.11 (1.44)
95% CI of LS mean	(-0.66, 5.05)	(0.28, 5.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-3.12, 4.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 116
Absolute Change through Week 52 (MMRM)		
n	111	114
LS mean (SE)	0.97 (1.17)	1.83 (1.16)
95% CI of LS mean	(-1.34, 3.28)	(-0.45, 4.11)
P-value within Treatment	0.4077	0.1150
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-2.40, 4.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6031
Hedges' G (SE)		0.07 (0.13)
Hedges' 95% CI		(-0.19, 0.33)
Hedges' P-value		0.6019

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Baseline		
n	83	77
Mean (SD)	68.54 (18.92)	70.42 (19.21)
Week 8 (MMRM)		
n	81	72
LS mean (SE)	70.20 (2.12)	72.02 (2.23)
95% CI of LS mean	(66.01, 74.39)	(67.62, 76.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.82 (-4.27, 7.91)
Absolute Change at Week 8 (MMRM)		
n	81	71
LS mean (SE)	1.87 (1.64)	2.52 (1.75)
95% CI of LS mean	(-1.37, 5.11)	(-0.93, 5.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-4.09, 5.39)
Week 16 (MMRM)		
n	81	74
LS mean (SE)	68.87 (2.32)	70.40 (2.43)
95% CI of LS mean	(64.28, 73.46)	(65.60, 75.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-5.12, 8.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change at Week 16 (MMRM)		
n	81	72
LS mean (SE)	0.56 (1.80)	1.49 (1.91)
95% CI of LS mean	(-2.99, 4.12)	(-2.28, 5.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-4.27, 6.12)
Week 24 (MMRM)		
n	81	73
LS mean (SE)	71.87 (2.24)	70.29 (2.35)
95% CI of LS mean	(67.45, 76.30)	(65.64, 74.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.59 (-8.02, 4.84)
Absolute Change at Week 24 (MMRM)		
n	81	71
LS mean (SE)	3.59 (1.64)	0.57 (1.74)
95% CI of LS mean	(0.36, 6.82)	(-2.87, 4.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.02 (-7.75, 1.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Week 52		
n	80	73
Mean (SD)	72.22 (17.23)	76.56 (17.62)
Absolute Change at Week 52		
n	80	70
Mean (SD)	4.31 (16.82)	6.67 (16.10)
Week 52 (MMRM)		
n	79	69
LS mean (SE)	72.38 (1.93)	75.71 (2.04)
95% CI of LS mean	(68.56, 76.21)	(71.67, 79.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.33 (-2.25, 8.90)
Absolute Change at Week 52 (MMRM)		
n	79	67
LS mean (SE)	4.17 (1.87)	5.86 (2.01)
95% CI of LS mean	(0.47, 7.87)	(1.89, 9.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-3.75, 7.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 83	VNZ/TEZ/D-IVA N = 80
Absolute Change through Week 52 (MMRM)		
n	81	72
LS mean (SE)	2.78 (1.51)	2.64 (1.61)
95% CI of LS mean	(-0.21, 5.76)	(-0.54, 5.82)
P-value within Treatment	0.0684	0.1027
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-4.51, 4.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9515
Hedges' G (SE)		-0.01 (0.16)
Hedges' 95% CI		(-0.33, 0.31)
Hedges' P-value		0.9514

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Baseline		
n	88	85
Mean (SD)	69.70 (18.81)	72.16 (18.28)
Week 8 (MMRM)		
n	88	83
LS mean (SE)	71.34 (1.98)	72.74 (2.03)
95% CI of LS mean	(67.44, 75.24)	(68.74, 76.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.40 (-4.19, 7.00)
Absolute Change at Week 8 (MMRM)		
n	86	82
LS mean (SE)	1.61 (1.29)	0.67 (1.32)
95% CI of LS mean	(-0.93, 4.16)	(-1.94, 3.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-4.60, 2.70)
Week 16 (MMRM)		
n	89	85
LS mean (SE)	71.30 (2.24)	71.89 (2.29)
95% CI of LS mean	(66.87, 75.72)	(67.36, 76.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-5.75, 6.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change at Week 16 (MMRM)		
n	87	83
LS mean (SE)	1.29 (1.55)	0.25 (1.59)
95% CI of LS mean	(-1.78, 4.36)	(-2.89, 3.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.04 (-5.44, 3.36)
Week 24 (MMRM)		
n	89	84
LS mean (SE)	72.29 (2.07)	71.53 (2.12)
95% CI of LS mean	(68.21, 76.38)	(67.34, 75.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.76 (-6.62, 5.10)
Absolute Change at Week 24 (MMRM)		
n	87	82
LS mean (SE)	2.44 (1.48)	-0.43 (1.52)
95% CI of LS mean	(-0.47, 5.36)	(-3.42, 2.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.87 (-7.05, 1.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Week 52		
n	88	78
Mean (SD)	75.25 (18.59)	74.93 (18.47)
Absolute Change at Week 52		
n	86	76
Mean (SD)	5.81 (15.50)	3.22 (12.28)
Week 52 (MMRM)		
n	87	77
LS mean (SE)	75.33 (1.96)	74.80 (2.03)
95% CI of LS mean	(71.46, 79.19)	(70.79, 78.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-6.10, 5.04)
Absolute Change at Week 52 (MMRM)		
n	85	75
LS mean (SE)	5.54 (1.55)	2.86 (1.63)
95% CI of LS mean	(2.48, 8.61)	(-0.35, 6.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.68 (-7.13, 1.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 91	VNZ/TEZ/D-IVA N = 87
Absolute Change through Week 52 (MMRM)		
n	87	83
LS mean (SE)	3.09 (1.27)	0.90 (1.31)
95% CI of LS mean	(0.59, 5.60)	(-1.68, 3.47)
P-value within Treatment	0.0159	0.4930
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.19 (-5.79, 1.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2303
Hedges' G (SE)		-0.18 (0.15)
Hedges' 95% CI		(-0.49, 0.12)
Hedges' P-value		0.2305

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Baseline		
n	109	107
Mean (SD)	70.95 (21.11)	72.38 (20.95)
Week 8 (MMRM)		
n	108	105
LS mean (SE)	70.42 (1.94)	73.45 (1.97)
95% CI of LS mean	(66.60, 74.25)	(69.56, 77.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.03 (-2.43, 8.49)
Absolute Change at Week 8 (MMRM)		
n	106	104
LS mean (SE)	-0.34 (1.46)	1.63 (1.48)
95% CI of LS mean	(-3.22, 2.55)	(-1.29, 4.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.97 (-2.14, 6.07)
Week 16 (MMRM)		
n	107	104
LS mean (SE)	69.90 (1.93)	73.83 (1.97)
95% CI of LS mean	(66.09, 73.71)	(69.96, 77.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.93 (-1.50, 9.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change at Week 16 (MMRM)		
n	105	103
LS mean (SE)	-0.99 (1.47)	2.24 (1.49)
95% CI of LS mean	(-3.89, 1.91)	(-0.70, 5.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.23 (-0.90, 7.35)
Week 24 (MMRM)		
n	107	104
LS mean (SE)	72.40 (2.00)	74.26 (2.03)
95% CI of LS mean	(68.46, 76.34)	(70.25, 78.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.86 (-3.76, 7.48)
Absolute Change at Week 24 (MMRM)		
n	105	103
LS mean (SE)	1.46 (1.45)	2.37 (1.46)
95% CI of LS mean	(-1.39, 4.31)	(-0.51, 5.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-3.14, 4.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Week 52		
n	105	106
Mean (SD)	72.38 (20.96)	77.36 (19.33)
Absolute Change at Week 52		
n	103	104
Mean (SD)	0.97 (16.18)	5.34 (17.38)
Week 52 (MMRM)		
n	104	103
LS mean (SE)	71.78 (1.95)	77.34 (1.98)
95% CI of LS mean	(67.93, 75.64)	(73.44, 81.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.56 (0.07, 11.05)
Absolute Change at Week 52 (MMRM)		
n	102	102
LS mean (SE)	0.76 (1.64)	5.37 (1.65)
95% CI of LS mean	(-2.48, 4.00)	(2.11, 8.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.61 (0.01, 9.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 111	VNZ/TEZ/D-IVA N = 109
Absolute Change through Week 52 (MMRM)		
n	105	103
LS mean (SE)	0.41 (1.32)	3.33 (1.33)
95% CI of LS mean	(-2.19, 3.01)	(0.70, 5.95)
P-value within Treatment	0.7550	0.0134
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.91 (-0.78, 6.61)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1217
Hedges' G (SE)		0.21 (0.14)
Hedges' 95% CI		(-0.06, 0.49)
Hedges' P-value		0.1228

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Baseline		
n	108	99
Mean (SD)	69.03 (20.50)	71.38 (21.30)
Week 8 (MMRM)		
n	109	98
LS mean (SE)	66.74 (2.02)	69.77 (2.13)
95% CI of LS mean	(62.77, 70.72)	(65.58, 73.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.03 (-2.76, 8.82)
Absolute Change at Week 8 (MMRM)		
n	107	96
LS mean (SE)	-2.17 (1.45)	-2.02 (1.53)
95% CI of LS mean	(-5.02, 0.68)	(-5.03, 0.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-4.01, 4.30)
Week 16 (MMRM)		
n	109	98
LS mean (SE)	68.28 (2.00)	70.37 (2.11)
95% CI of LS mean	(64.33, 72.23)	(66.21, 74.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.10 (-3.66, 7.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	107	96
LS mean (SE)	-0.75 (1.40)	-1.28 (1.48)
95% CI of LS mean	(-3.50, 2.01)	(-4.20, 1.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.54 (-4.56, 3.48)
Week 24 (MMRM)		
n	109	98
LS mean (SE)	68.56 (2.05)	70.51 (2.16)
95% CI of LS mean	(64.51, 72.60)	(66.24, 74.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.95 (-3.94, 7.84)
Absolute Change at Week 24 (MMRM)		
n	107	96
LS mean (SE)	-0.43 (1.28)	-1.63 (1.35)
95% CI of LS mean	(-2.96, 2.09)	(-4.30, 1.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.20 (-4.87, 2.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Week 52		
n	108	94
Mean (SD)	70.27 (20.87)	71.99 (21.72)
Absolute Change at Week 52		
n	106	92
Mean (SD)	0.42 (12.64)	0.48 (15.88)
Week 52 (MMRM)		
n	108	93
LS mean (SE)	69.65 (2.03)	72.50 (2.15)
95% CI of LS mean	(65.66, 73.65)	(68.25, 76.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-3.00, 8.69)
Absolute Change at Week 52 (MMRM)		
n	106	91
LS mean (SE)	0.55 (1.39)	0.31 (1.49)
95% CI of LS mean	(-2.20, 3.29)	(-2.63, 3.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-4.27, 3.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	107	96
LS mean (SE)	-0.21 (1.09)	-0.87 (1.15)
95% CI of LS mean	(-2.36, 1.93)	(-3.14, 1.40)
P-value within Treatment	0.8464	0.4521
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.66 (-3.79, 2.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6797
Hedges' G (SE)		-0.06 (0.14)
Hedges' 95% CI		(-0.33, 0.22)
Hedges' P-value		0.6788

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Baseline		
n	80	86
Mean (SD)	74.17 (17.12)	76.36 (16.94)
Week 8 (MMRM)		
n	80	85
LS mean (SE)	75.06 (1.84)	77.00 (1.78)
95% CI of LS mean	(71.42, 78.70)	(73.48, 80.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.94 (-3.13, 7.01)
Absolute Change at Week 8 (MMRM)		
n	79	85
LS mean (SE)	0.65 (1.44)	0.66 (1.39)
95% CI of LS mean	(-2.20, 3.49)	(-2.08, 3.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-3.94, 3.97)
Week 16 (MMRM)		
n	78	86
LS mean (SE)	75.37 (2.11)	75.98 (2.02)
95% CI of LS mean	(71.19, 79.54)	(71.98, 79.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.61 (-5.17, 6.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Absolute Change at Week 16 (MMRM)		
n	77	86
LS mean (SE)	0.44 (1.64)	-0.40 (1.55)
95% CI of LS mean	(-2.79, 3.67)	(-3.47, 2.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.84 (-5.29, 3.62)
Week 24 (MMRM)		
n	78	85
LS mean (SE)	72.36 (2.16)	78.49 (2.08)
95% CI of LS mean	(68.08, 76.63)	(74.38, 82.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.13 (0.20, 12.06)
Absolute Change at Week 24 (MMRM)		
n	77	85
LS mean (SE)	-2.35 (1.71)	2.14 (1.63)
95% CI of LS mean	(-5.73, 1.03)	(-1.07, 5.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.50 (-0.17, 9.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Week 52		
n	75	82
Mean (SD)	76.37 (18.18)	78.32 (17.62)
Absolute Change at Week 52		
n	74	82
Mean (SD)	2.33 (13.33)	2.03 (13.98)
Week 52 (MMRM)		
n	74	82
LS mean (SE)	77.43 (2.00)	78.61 (1.91)
95% CI of LS mean	(73.48, 81.39)	(74.83, 82.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-4.30, 6.64)
Absolute Change at Week 52 (MMRM)		
n	73	82
LS mean (SE)	2.83 (1.59)	2.20 (1.50)
95% CI of LS mean	(-0.32, 5.97)	(-0.77, 5.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-4.95, 3.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Absolute Change through Week 52 (MMRM)		
n	77	86
LS mean (SE)	0.30 (1.30)	1.31 (1.23)
95% CI of LS mean	(-2.26, 2.87)	(-1.12, 3.75)
P-value within Treatment	0.8158	0.2881
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-2.53, 4.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5732
Hedges' G (SE)		0.09 (0.16)
Hedges' 95% CI		(-0.22, 0.40)
Hedges' P-value		0.5732

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Baseline		
n	21	20
Mean (SD)	71.43 (13.87)	81.67 (14.98)
Week 8 (MMRM)		
n	21	19
LS mean (SE)	73.22 (3.56)	78.72 (3.74)
95% CI of LS mean	(66.00, 80.44)	(71.13, 86.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.50 (-5.01, 16.01)
Absolute Change at Week 8 (MMRM)		
n	21	19
LS mean (SE)	2.03 (2.81)	-2.25 (2.95)
95% CI of LS mean	(-3.66, 7.72)	(-8.23, 3.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.28 (-12.56, 4.00)
Week 16 (MMRM)		
n	20	19
LS mean (SE)	72.28 (3.77)	74.63 (3.91)
95% CI of LS mean	(64.63, 79.94)	(66.69, 82.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.35 (-8.71, 13.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 16 (MMRM)		
n	20	19
LS mean (SE)	1.00 (3.03)	-6.34 (3.12)
95% CI of LS mean	(-5.13, 7.14)	(-12.67, -0.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.34 (-16.18, 1.49)
Week 24 (MMRM)		
n	20	19
LS mean (SE)	69.13 (4.31)	76.97 (4.44)
95% CI of LS mean	(60.38, 77.88)	(67.97, 85.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.84 (-4.75, 20.42)
Absolute Change at Week 24 (MMRM)		
n	20	19
LS mean (SE)	-2.09 (3.94)	-4.00 (4.04)
95% CI of LS mean	(-10.08, 5.90)	(-12.19, 4.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.91 (-13.37, 9.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Week 52		
n	19	20
Mean (SD)	74.27 (17.78)	79.44 (15.41)
Absolute Change at Week 52		
n	19	20
Mean (SD)	2.92 (12.75)	-2.22 (15.12)
Week 52 (MMRM)		
n	19	19
LS mean (SE)	74.57 (3.78)	78.72 (3.82)
95% CI of LS mean	(66.91, 82.23)	(70.97, 86.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.16 (-6.77, 15.09)
Absolute Change at Week 52 (MMRM)		
n	19	19
LS mean (SE)	3.25 (3.31)	-2.25 (3.31)
95% CI of LS mean	(-3.45, 9.95)	(-8.96, 4.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.50 (-15.00, 4.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change through Week 52 (MMRM)		
n	20	19
LS mean (SE)	0.72 (2.30)	-4.20 (2.35)
95% CI of LS mean	(-3.94, 5.38)	(-8.97, 0.58)
P-value within Treatment	0.7555	0.0832
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.92 (-11.62, 1.78)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1452
Hedges' G (SE)		-0.47 (0.32)
Hedges' 95% CI		(-1.11, 0.18)
Hedges' P-value		0.1487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	71.10 (19.84)	72.99 (19.83)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	70.04 (1.49)	72.34 (1.51)
95% CI of LS mean	(67.11, 72.97)	(69.38, 75.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.30 (-1.87, 6.47)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	-1.43 (1.10)	-0.51 (1.11)
95% CI of LS mean	(-3.61, 0.74)	(-2.71, 1.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-2.17, 4.01)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	71.26 (1.57)	72.64 (1.58)
95% CI of LS mean	(68.17, 74.34)	(69.53, 75.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.38 (-3.00, 5.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-0.47 (1.13)	-0.15 (1.13)
95% CI of LS mean	(-2.69, 1.74)	(-2.37, 2.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-2.81, 3.46)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	70.38 (1.59)	73.74 (1.61)
95% CI of LS mean	(67.24, 73.52)	(70.57, 76.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.36 (-1.10, 7.81)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	-1.22 (1.07)	0.70 (1.07)
95% CI of LS mean	(-3.32, 0.88)	(-1.41, 2.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.92 (-1.06, 4.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	72.49 (20.25)	74.42 (20.53)
Absolute Change at Week 52		
n	162	156
Mean (SD)	0.99 (12.93)	1.50 (14.99)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	72.78 (1.55)	74.80 (1.57)
95% CI of LS mean	(69.74, 75.82)	(71.72, 77.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.02 (-2.31, 6.36)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	1.15 (1.10)	1.70 (1.12)
95% CI of LS mean	(-1.02, 3.32)	(-0.50, 3.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-2.54, 3.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-0.18 (0.89)	0.75 (0.89)
95% CI of LS mean	(-1.93, 1.57)	(-1.01, 2.51)
P-value within Treatment	0.8400	0.4020
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-1.55, 3.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4615
Hedges' G (SE)		0.08 (0.11)
Hedges' 95% CI		(-0.14, 0.30)
Hedges' P-value		0.4615

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	71.93 (20.41)	67.36 (24.50)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	67.88 (4.49)	71.48 (4.91)
95% CI of LS mean	(58.71, 77.05)	(61.45, 81.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (-10.23, 17.42)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	-4.43 (3.10)	4.57 (3.39)
95% CI of LS mean	(-10.76, 1.90)	(-2.34, 11.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.01 (-0.47, 18.48)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	66.71 (4.14)	71.48 (4.53)
95% CI of LS mean	(58.26, 75.16)	(62.23, 80.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.77 (-8.02, 17.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-5.60 (3.86)	4.57 (4.21)
95% CI of LS mean	(-13.49, 2.28)	(-4.03, 13.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.18 (-1.57, 21.92)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	63.79 (4.87)	69.39 (5.32)
95% CI of LS mean	(53.86, 73.71)	(58.55, 80.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.61 (-9.31, 20.52)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	-8.53 (4.55)	2.49 (4.96)
95% CI of LS mean	(-17.81, 0.76)	(-7.64, 12.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.02 (-2.79, 24.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	74.07 (22.55)	66.67 (22.22)
Absolute Change at Week 52		
n	18	13
Mean (SD)	1.85 (10.26)	1.71 (12.71)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	73.64 (4.98)	67.84 (5.71)
95% CI of LS mean	(63.42, 83.86)	(56.18, 79.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.80 (-21.49, 9.89)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	1.33 (2.56)	2.31 (3.03)
95% CI of LS mean	(-3.91, 6.57)	(-3.89, 8.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.98 (-7.21, 9.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	-4.27 (2.87)	3.12 (3.16)
95% CI of LS mean	(-10.15, 1.61)	(-3.34, 9.59)
P-value within Treatment	0.1481	0.3308
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.39 (-1.44, 16.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0976
Hedges' G (SE)		0.58 (0.34)
Hedges' 95% CI		(-0.11, 1.26)
Hedges' P-value		0.0989

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Baseline		
n	169	169
Mean (SD)	71.20 (19.11)	74.62 (18.91)
Week 8 (MMRM)		
n	170	167
LS mean (SE)	70.69 (1.45)	73.13 (1.46)
95% CI of LS mean	(67.84, 73.55)	(70.25, 76.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.44 (-1.62, 6.49)
Absolute Change at Week 8 (MMRM)		
n	167	165
LS mean (SE)	-0.75 (1.09)	-1.11 (1.10)
95% CI of LS mean	(-2.90, 1.41)	(-3.28, 1.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-3.42, 2.68)
Week 16 (MMRM)		
n	168	168
LS mean (SE)	71.92 (1.55)	72.96 (1.55)
95% CI of LS mean	(68.87, 74.96)	(69.91, 76.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-3.27, 5.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Absolute Change at Week 16 (MMRM)		
n	165	166
LS mean (SE)	0.19 (1.11)	-1.22 (1.10)
95% CI of LS mean	(-1.99, 2.36)	(-3.39, 0.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.41 (-4.49, 1.66)
Week 24 (MMRM)		
n	168	167
LS mean (SE)	71.05 (1.57)	74.50 (1.58)
95% CI of LS mean	(67.96, 74.15)	(71.40, 77.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.44 (-0.94, 7.83)
Absolute Change at Week 24 (MMRM)		
n	165	165
LS mean (SE)	-0.56 (1.05)	0.08 (1.05)
95% CI of LS mean	(-2.63, 1.51)	(-1.99, 2.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-2.29, 3.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Week 52		
n	165	164
Mean (SD)	72.83 (19.41)	75.88 (19.68)
Absolute Change at Week 52		
n	162	162
Mean (SD)	1.27 (13.08)	1.03 (15.26)
Week 52 (MMRM)		
n	164	162
LS mean (SE)	72.96 (1.51)	75.84 (1.51)
95% CI of LS mean	(70.00, 75.93)	(72.86, 78.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.88 (-1.33, 7.08)
Absolute Change at Week 52 (MMRM)		
n	161	160
LS mean (SE)	1.33 (1.12)	1.33 (1.12)
95% CI of LS mean	(-0.87, 3.54)	(-0.88, 3.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-3.12, 3.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Absolute Change through Week 52 (MMRM)		
n	165	166
LS mean (SE)	0.32 (0.88)	0.06 (0.88)
95% CI of LS mean	(-1.40, 2.04)	(-1.66, 1.79)
P-value within Treatment	0.7148	0.9431
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-2.70, 2.18)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8353
Hedges' G (SE)		-0.02 (0.11)
Hedges' 95% CI		(-0.24, 0.19)
Hedges' P-value		0.8352

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Baseline		
n	109	114
Mean (SD)	71.36 (20.25)	73.78 (20.96)
Week 8 (MMRM)		
n	110	115
LS mean (SE)	69.96 (1.89)	74.24 (1.86)
95% CI of LS mean	(66.23, 73.69)	(70.58, 77.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.28 (-0.96, 9.51)
Absolute Change at Week 8 (MMRM)		
n	107	114
LS mean (SE)	-1.62 (1.37)	0.52 (1.33)
95% CI of LS mean	(-4.32, 1.08)	(-2.09, 3.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.15 (-1.62, 5.91)
Week 16 (MMRM)		
n	109	115
LS mean (SE)	72.24 (1.97)	73.17 (1.93)
95% CI of LS mean	(68.35, 76.13)	(69.37, 76.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-4.51, 6.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Absolute Change at Week 16 (MMRM)		
n	106	114
LS mean (SE)	0.29 (1.33)	-0.55 (1.28)
95% CI of LS mean	(-2.33, 2.91)	(-3.08, 1.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.83 (-4.48, 2.81)
Week 24 (MMRM)		
n	109	115
LS mean (SE)	71.00 (2.00)	74.24 (1.96)
95% CI of LS mean	(67.05, 74.95)	(70.38, 78.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.24 (-2.29, 8.77)
Absolute Change at Week 24 (MMRM)		
n	106	114
LS mean (SE)	-0.76 (1.23)	0.52 (1.19)
95% CI of LS mean	(-3.19, 1.66)	(-1.82, 2.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.29 (-2.09, 4.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Week 52		
n	107	111
Mean (SD)	73.57 (19.15)	74.07 (21.52)
Absolute Change at Week 52		
n	104	110
Mean (SD)	1.44 (10.98)	0.30 (14.71)
Week 52 (MMRM)		
n	106	111
LS mean (SE)	73.28 (1.95)	74.19 (1.91)
95% CI of LS mean	(69.44, 77.12)	(70.43, 77.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-4.47, 6.30)
Absolute Change at Week 52 (MMRM)		
n	103	110
LS mean (SE)	1.47 (1.28)	0.36 (1.24)
95% CI of LS mean	(-1.05, 3.99)	(-2.08, 2.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.11 (-4.62, 2.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Absolute Change through Week 52 (MMRM)		
n	106	114
LS mean (SE)	0.33 (1.04)	0.11 (1.00)
95% CI of LS mean	(-1.71, 2.37)	(-1.86, 2.09)
P-value within Treatment	0.7504	0.9109
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-3.06, 2.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8801
Hedges' G (SE)		-0.02 (0.13)
Hedges' 95% CI		(-0.29, 0.24)
Hedges' P-value		0.8799

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Baseline		
n	80	73
Mean (SD)	70.83 (17.89)	74.12 (17.18)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	71.06 (2.00)	70.83 (2.14)
95% CI of LS mean	(67.11, 75.01)	(66.61, 75.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-6.02, 5.55)
Absolute Change at Week 8 (MMRM)		
n	79	67
LS mean (SE)	-0.30 (1.55)	-2.71 (1.67)
95% CI of LS mean	(-3.36, 2.76)	(-6.02, 0.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.42 (-6.93, 2.09)
Week 16 (MMRM)		
n	78	69
LS mean (SE)	70.27 (2.17)	72.24 (2.30)
95% CI of LS mean	(65.99, 74.55)	(67.69, 76.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.97 (-4.29, 8.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Absolute Change at Week 16 (MMRM)		
n	78	68
LS mean (SE)	-1.14 (1.75)	-1.09 (1.88)
95% CI of LS mean	(-4.61, 2.33)	(-4.81, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-5.04, 5.13)
Week 24 (MMRM)		
n	78	68
LS mean (SE)	69.40 (2.24)	73.72 (2.39)
95% CI of LS mean	(64.97, 73.84)	(68.99, 78.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.32 (-2.17, 10.81)
Absolute Change at Week 24 (MMRM)		
n	78	67
LS mean (SE)	-2.01 (1.83)	-0.22 (1.97)
95% CI of LS mean	(-5.62, 1.59)	(-4.11, 3.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.79 (-3.52, 7.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Week 52		
n	77	68
Mean (SD)	71.43 (21.13)	76.47 (17.44)
Absolute Change at Week 52		
n	77	66
Mean (SD)	0.87 (15.16)	2.36 (15.53)
Week 52 (MMRM)		
n	76	64
LS mean (SE)	72.71 (2.14)	76.96 (2.31)
95% CI of LS mean	(68.48, 76.94)	(72.40, 81.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.25 (-1.98, 10.48)
Absolute Change at Week 52 (MMRM)		
n	76	63
LS mean (SE)	1.32 (1.77)	3.02 (1.93)
95% CI of LS mean	(-2.18, 4.83)	(-0.81, 6.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-3.50, 6.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	-0.61 (1.39)	0.57 (1.50)
95% CI of LS mean	(-3.36, 2.14)	(-2.40, 3.53)
P-value within Treatment	0.6619	0.7059
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.18 (-2.87, 5.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5665
Hedges' G (SE)		0.09 (0.17)
Hedges' 95% CI		(-0.23, 0.42)
Hedges' P-value		0.5661

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Baseline		
n	83	84
Mean (SD)	72.82 (18.05)	74.74 (19.00)
Week 8 (MMRM)		
n	83	82
LS mean (SE)	71.10 (2.08)	73.26 (2.08)
95% CI of LS mean	(67.00, 75.20)	(69.15, 77.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.16 (-3.65, 7.97)
Absolute Change at Week 8 (MMRM)		
n	82	81
LS mean (SE)	-1.77 (1.49)	-1.79 (1.50)
95% CI of LS mean	(-4.71, 1.16)	(-4.75, 1.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-4.19, 4.15)
Week 16 (MMRM)		
n	83	83
LS mean (SE)	73.04 (2.20)	72.34 (2.20)
95% CI of LS mean	(68.70, 77.38)	(68.00, 76.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-6.84, 5.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Absolute Change at Week 16 (MMRM)		
n	82	82
LS mean (SE)	-0.22 (1.58)	-2.63 (1.58)
95% CI of LS mean	(-3.33, 2.90)	(-5.74, 0.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.41 (-6.82, 1.99)
Week 24 (MMRM)		
n	83	82
LS mean (SE)	71.97 (2.17)	74.66 (2.18)
95% CI of LS mean	(67.68, 76.26)	(70.36, 78.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.69 (-3.39, 8.78)
Absolute Change at Week 24 (MMRM)		
n	82	81
LS mean (SE)	-1.03 (1.44)	-0.24 (1.45)
95% CI of LS mean	(-3.87, 1.81)	(-3.10, 2.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.78 (-3.25, 4.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Week 52		
n	82	76
Mean (SD)	72.70 (19.99)	76.32 (19.23)
Absolute Change at Week 52		
n	81	75
Mean (SD)	0.34 (12.62)	1.78 (14.27)
Week 52 (MMRM)		
n	81	75
LS mean (SE)	73.58 (2.07)	76.54 (2.10)
95% CI of LS mean	(69.50, 77.66)	(72.40, 80.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.96 (-2.86, 8.78)
Absolute Change at Week 52 (MMRM)		
n	80	74
LS mean (SE)	0.66 (1.49)	1.53 (1.53)
95% CI of LS mean	(-2.27, 3.60)	(-1.49, 4.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-3.35, 5.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Absolute Change through Week 52 (MMRM)		
n	82	82
LS mean (SE)	-0.19 (1.17)	-0.45 (1.18)
95% CI of LS mean	(-2.51, 2.12)	(-2.78, 1.88)
P-value within Treatment	0.8693	0.7052
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-3.54, 3.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8790
Hedges' G (SE)		-0.02 (0.16)
Hedges' 95% CI		(-0.33, 0.28)
Hedges' P-value		0.8789

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Baseline		
n	106	103
Mean (SD)	69.81 (20.10)	73.25 (20.01)
Week 8 (MMRM)		
n	106	101
LS mean (SE)	69.85 (1.88)	72.74 (1.92)
95% CI of LS mean	(66.15, 73.56)	(68.95, 76.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.89 (-2.41, 8.19)
Absolute Change at Week 8 (MMRM)		
n	104	100
LS mean (SE)	-0.41 (1.43)	0.11 (1.45)
95% CI of LS mean	(-3.22, 2.40)	(-2.75, 2.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-3.50, 4.53)
Week 16 (MMRM)		
n	104	101
LS mean (SE)	70.08 (1.96)	73.25 (2.00)
95% CI of LS mean	(66.21, 73.94)	(69.30, 77.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.17 (-2.36, 8.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Absolute Change at Week 16 (MMRM)		
n	102	100
LS mean (SE)	-0.33 (1.42)	0.64 (1.43)
95% CI of LS mean	(-3.12, 2.47)	(-2.19, 3.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-3.01, 4.94)
Week 24 (MMRM)		
n	104	101
LS mean (SE)	69.01 (2.07)	73.57 (2.11)
95% CI of LS mean	(64.93, 73.10)	(69.41, 77.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.56 (-1.27, 10.38)
Absolute Change at Week 24 (MMRM)		
n	102	100
LS mean (SE)	-1.44 (1.48)	0.51 (1.49)
95% CI of LS mean	(-4.35, 1.47)	(-2.44, 3.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.95 (-2.20, 6.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Week 52		
n	102	103
Mean (SD)	72.66 (20.06)	74.00 (20.67)
Absolute Change at Week 52		
n	100	101
Mean (SD)	1.89 (13.12)	0.55 (15.59)
Week 52 (MMRM)		
n	101	100
LS mean (SE)	72.64 (2.00)	74.20 (2.03)
95% CI of LS mean	(68.69, 76.59)	(70.20, 78.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.56 (-4.06, 7.19)
Absolute Change at Week 52 (MMRM)		
n	99	99
LS mean (SE)	2.08 (1.45)	1.08 (1.46)
95% CI of LS mean	(-0.79, 4.95)	(-1.80, 3.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.00 (-5.07, 3.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Absolute Change through Week 52 (MMRM)		
n	102	100
LS mean (SE)	0.10 (1.16)	0.74 (1.17)
95% CI of LS mean	(-2.19, 2.40)	(-1.57, 3.06)
P-value within Treatment	0.9287	0.5284
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-2.62, 3.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7000
Hedges' G (SE)		0.05 (0.14)
Hedges' 95% CI		(-0.22, 0.33)
Hedges' P-value		0.7000

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Baseline		
n	108	98
Mean (SD)	85.49 (19.81)	84.27 (18.34)
Week 8 (MMRM)		
n	109	98
LS mean (SE)	84.78 (1.59)	86.36 (1.68)
95% CI of LS mean	(81.65, 87.92)	(83.05, 89.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.57 (-3.00, 6.14)
Absolute Change at Week 8 (MMRM)		
n	107	95
LS mean (SE)	-0.80 (1.31)	2.13 (1.39)
95% CI of LS mean	(-3.38, 1.79)	(-0.61, 4.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.93 (-0.85, 6.71)
Week 16 (MMRM)		
n	109	98
LS mean (SE)	84.25 (1.61)	88.25 (1.70)
95% CI of LS mean	(81.07, 87.42)	(84.91, 91.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.01 (-0.61, 8.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	107	95
LS mean (SE)	-1.22 (1.49)	4.89 (1.59)
95% CI of LS mean	(-4.17, 1.72)	(1.77, 8.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.12 (1.81, 10.42)
Week 24 (MMRM)		
n	109	97
LS mean (SE)	86.14 (1.61)	87.06 (1.70)
95% CI of LS mean	(82.97, 89.30)	(83.72, 90.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-3.69, 5.54)
Absolute Change at Week 24 (MMRM)		
n	107	94
LS mean (SE)	0.35 (1.44)	3.22 (1.53)
95% CI of LS mean	(-2.48, 3.18)	(0.21, 6.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.87 (-1.27, 7.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Week 52		
n	108	94
Mean (SD)	87.58 (15.97)	88.12 (14.89)
Absolute Change at Week 52		
n	106	91
Mean (SD)	1.34 (12.76)	4.49 (14.61)
Week 52 (MMRM)		
n	108	93
LS mean (SE)	87.20 (1.47)	88.33 (1.57)
95% CI of LS mean	(84.29, 90.11)	(85.24, 91.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.13 (-3.12, 5.39)
Absolute Change at Week 52 (MMRM)		
n	106	90
LS mean (SE)	1.47 (1.33)	4.32 (1.43)
95% CI of LS mean	(-1.15, 4.10)	(1.50, 7.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.85 (-1.01, 6.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	107	95
LS mean (SE)	0.20 (1.23)	4.15 (1.30)
95% CI of LS mean	(-2.22, 2.62)	(1.58, 6.72)
P-value within Treatment	0.8707	0.0017
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.95 (0.41, 7.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0290
Hedges' G (SE)		0.31 (0.14)
Hedges' 95% CI		(0.03, 0.59)
Hedges' P-value		0.0294

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Baseline		
n	80	86
Mean (SD)	90.52 (11.62)	90.70 (11.53)
Week 8 (MMRM)		
n	79	85
LS mean (SE)	89.96 (1.44)	89.53 (1.39)
95% CI of LS mean	(87.12, 92.80)	(86.80, 92.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-4.37, 3.52)
Absolute Change at Week 8 (MMRM)		
n	78	85
LS mean (SE)	-0.63 (1.33)	-1.07 (1.27)
95% CI of LS mean	(-3.25, 1.99)	(-3.58, 1.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-4.08, 3.18)
Week 16 (MMRM)		
n	78	86
LS mean (SE)	87.98 (1.64)	89.69 (1.57)
95% CI of LS mean	(84.75, 91.22)	(86.60, 92.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-2.77, 6.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Absolute Change at Week 16 (MMRM)		
n	77	86
LS mean (SE)	-2.43 (1.43)	-0.97 (1.36)
95% CI of LS mean	(-5.26, 0.40)	(-3.65, 1.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.46 (-2.44, 5.37)
Week 24 (MMRM)		
n	78	85
LS mean (SE)	87.66 (1.49)	89.72 (1.43)
95% CI of LS mean	(84.72, 90.60)	(86.90, 92.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.05 (-2.02, 6.13)
Absolute Change at Week 24 (MMRM)		
n	77	85
LS mean (SE)	-2.76 (1.39)	-0.92 (1.32)
95% CI of LS mean	(-5.51, -0.02)	(-3.53, 1.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.85 (-1.94, 5.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Week 52		
n	74	82
Mean (SD)	90.43 (12.77)	89.13 (14.85)
Absolute Change at Week 52		
n	73	82
Mean (SD)	0.57 (11.73)	-1.12 (14.33)
Week 52 (MMRM)		
n	73	82
LS mean (SE)	90.49 (1.59)	89.42 (1.52)
95% CI of LS mean	(87.34, 93.64)	(86.43, 92.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.06 (-5.41, 3.28)
Absolute Change at Week 52 (MMRM)		
n	72	82
LS mean (SE)	0.22 (1.53)	-1.15 (1.45)
95% CI of LS mean	(-2.81, 3.25)	(-4.01, 1.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.37 (-5.53, 2.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Absolute Change through Week 52 (MMRM)		
n	77	86
LS mean (SE)	-1.66 (1.16)	-1.01 (1.11)
95% CI of LS mean	(-3.96, 0.64)	(-3.20, 1.17)
P-value within Treatment	0.1558	0.3619
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-2.53, 3.82)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6875
Hedges' G (SE)		0.06 (0.16)
Hedges' 95% CI		(-0.25, 0.37)
Hedges' P-value		0.6874

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Baseline		
n	21	20
Mean (SD)	86.90 (12.79)	88.75 (10.57)
Week 8 (MMRM)		
n	21	19
LS mean (SE)	87.08 (2.77)	89.28 (2.91)
95% CI of LS mean	(81.47, 92.70)	(83.37, 95.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-5.98, 10.36)
Absolute Change at Week 8 (MMRM)		
n	21	19
LS mean (SE)	0.18 (3.53)	0.68 (3.71)
95% CI of LS mean	(-6.98, 7.34)	(-6.85, 8.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-9.92, 10.91)
Week 16 (MMRM)		
n	20	19
LS mean (SE)	86.35 (2.84)	89.72 (2.93)
95% CI of LS mean	(80.59, 92.11)	(83.77, 95.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.37 (-4.94, 11.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 16 (MMRM)		
n	20	19
LS mean (SE)	-0.48 (3.27)	1.12 (3.39)
95% CI of LS mean	(-7.11, 6.14)	(-5.75, 7.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.60 (-7.97, 11.17)
Week 24 (MMRM)		
n	20	19
LS mean (SE)	83.81 (3.16)	87.08 (3.27)
95% CI of LS mean	(77.41, 90.21)	(80.46, 93.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.28 (-5.96, 12.51)
Absolute Change at Week 24 (MMRM)		
n	20	19
LS mean (SE)	-3.05 (3.70)	-1.52 (3.85)
95% CI of LS mean	(-10.55, 4.44)	(-9.31, 6.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.54 (-9.30, 12.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Week 52		
n	18	20
Mean (SD)	85.19 (17.04)	90.42 (13.04)
Absolute Change at Week 52		
n	18	20
Mean (SD)	-1.85 (16.06)	1.67 (11.97)
Week 52 (MMRM)		
n	18	19
LS mean (SE)	84.85 (3.51)	89.72 (3.49)
95% CI of LS mean	(77.75, 91.95)	(82.64, 96.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.87 (-5.17, 14.91)
Absolute Change at Week 52 (MMRM)		
n	18	19
LS mean (SE)	-1.84 (3.32)	1.12 (3.31)
95% CI of LS mean	(-8.55, 4.88)	(-5.61, 7.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.95 (-6.58, 12.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change through Week 52 (MMRM)		
n	20	19
LS mean (SE)	-1.79 (2.79)	0.24 (2.90)
95% CI of LS mean	(-7.45, 3.86)	(-5.64, 6.11)
P-value within Treatment	0.5249	0.9349
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.03 (-6.16, 10.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6184
Hedges' G (SE)		0.16 (0.31)
Hedges' 95% CI		(-0.48, 0.80)
Hedges' P-value		0.6173

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	166
Mean (SD)	87.75 (17.40)	87.20 (16.30)
Week 8 (MMRM)		
n	167	164
LS mean (SE)	87.10 (1.18)	87.54 (1.19)
95% CI of LS mean	(84.78, 89.41)	(85.20, 89.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.44 (-2.85, 3.73)
Absolute Change at Week 8 (MMRM)		
n	164	161
LS mean (SE)	-0.71 (0.97)	0.47 (0.98)
95% CI of LS mean	(-2.62, 1.21)	(-1.46, 2.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-1.55, 3.89)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	85.89 (1.25)	88.69 (1.25)
95% CI of LS mean	(83.44, 88.34)	(86.22, 91.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.80 (-0.68, 6.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	162
LS mean (SE)	-1.74 (1.13)	2.08 (1.14)
95% CI of LS mean	(-3.96, 0.48)	(-0.15, 4.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.82 (0.67, 6.97)
Week 24 (MMRM)		
n	167	163
LS mean (SE)	87.29 (1.19)	88.30 (1.20)
95% CI of LS mean	(84.95, 89.62)	(85.94, 90.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-2.31, 4.34)
Absolute Change at Week 24 (MMRM)		
n	164	160
LS mean (SE)	-0.57 (1.05)	1.45 (1.06)
95% CI of LS mean	(-2.63, 1.49)	(-0.63, 3.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.02 (-0.91, 4.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	89.19 (14.50)	88.52 (14.99)
Absolute Change at Week 52		
n	162	155
Mean (SD)	1.39 (11.83)	1.83 (14.99)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	89.16 (1.14)	88.57 (1.16)
95% CI of LS mean	(86.92, 91.40)	(86.29, 90.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.60 (-3.79, 2.59)
Absolute Change at Week 52 (MMRM)		
n	160	153
LS mean (SE)	1.43 (1.06)	1.60 (1.08)
95% CI of LS mean	(-0.67, 3.52)	(-0.52, 3.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-2.81, 3.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	162
LS mean (SE)	-0.29 (0.91)	1.71 (0.92)
95% CI of LS mean	(-2.09, 1.51)	(-0.11, 3.53)
P-value within Treatment	0.7479	0.0648
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.00 (-0.55, 4.56)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1241
Hedges' G (SE)		0.17 (0.11)
Hedges' 95% CI		(-0.05, 0.39)
Hedges' P-value		0.1246

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	88.16 (15.29)	82.81 (17.34)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	88.26 (3.32)	88.42 (3.62)
95% CI of LS mean	(81.50, 95.02)	(81.04, 95.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-9.93, 10.25)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	-1.72 (2.34)	7.78 (2.56)
95% CI of LS mean	(-6.50, 3.05)	(2.56, 12.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.50 (2.35, 16.65)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	80.37 (3.72)	85.82 (4.06)
95% CI of LS mean	(72.79, 87.94)	(77.55, 94.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.45 (-5.85, 16.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-9.62 (3.10)	5.17 (3.39)
95% CI of LS mean	(-15.94, -3.30)	(-1.72, 12.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.79 (5.38, 24.20)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	87.38 (2.95)	84.25 (3.22)
95% CI of LS mean	(81.37, 93.39)	(77.69, 90.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.13 (-12.13, 5.87)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	-2.60 (3.77)	3.61 (4.11)
95% CI of LS mean	(-10.29, 5.09)	(-4.77, 11.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.21 (-5.21, 17.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	90.74 (10.26)	87.50 (9.10)
Absolute Change at Week 52		
n	18	13
Mean (SD)	1.39 (8.69)	6.41 (13.24)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	91.06 (2.21)	86.25 (2.53)
95% CI of LS mean	(86.54, 95.59)	(81.09, 91.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.81 (-11.78, 2.16)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	0.57 (2.52)	6.61 (2.87)
95% CI of LS mean	(-4.59, 5.73)	(0.74, 12.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.04 (-1.83, 13.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	-3.88 (2.59)	5.13 (2.84)
95% CI of LS mean	(-9.17, 1.41)	(-0.67, 10.93)
P-value within Treatment	0.1444	0.0810
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.01 (1.10, 16.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0269
Hedges' G (SE)		0.78 (0.34)
Hedges' 95% CI		(0.08, 1.48)
Hedges' P-value		0.0307

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Baseline		
n	169	168
Mean (SD)	87.52 (17.16)	87.75 (15.66)
Week 8 (MMRM)		
n	169	167
LS mean (SE)	86.99 (1.16)	87.62 (1.16)
95% CI of LS mean	(84.72, 89.27)	(85.33, 89.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-2.60, 3.85)
Absolute Change at Week 8 (MMRM)		
n	166	164
LS mean (SE)	-0.65 (1.01)	-0.06 (1.02)
95% CI of LS mean	(-2.64, 1.33)	(-2.06, 1.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (-2.23, 3.42)
Week 16 (MMRM)		
n	168	168
LS mean (SE)	86.60 (1.22)	89.05 (1.22)
95% CI of LS mean	(84.20, 88.99)	(86.65, 91.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.45 (-0.94, 5.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Absolute Change at Week 16 (MMRM)		
n	165	165
LS mean (SE)	-0.85 (1.12)	1.85 (1.12)
95% CI of LS mean	(-3.04, 1.35)	(-0.36, 4.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.69 (-0.42, 5.81)
Week 24 (MMRM)		
n	168	166
LS mean (SE)	86.89 (1.19)	88.52 (1.20)
95% CI of LS mean	(84.55, 89.23)	(86.17, 90.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-1.69, 4.95)
Absolute Change at Week 24 (MMRM)		
n	165	163
LS mean (SE)	-0.79 (1.06)	1.07 (1.06)
95% CI of LS mean	(-2.87, 1.29)	(-1.02, 3.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.87 (-1.08, 4.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Week 52		
n	164	164
Mean (SD)	88.52 (15.20)	88.87 (15.20)
Absolute Change at Week 52		
n	161	161
Mean (SD)	1.04 (12.70)	1.45 (14.78)
Week 52 (MMRM)		
n	163	162
LS mean (SE)	88.50 (1.17)	88.89 (1.18)
95% CI of LS mean	(86.19, 90.81)	(86.57, 91.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.39 (-2.89, 3.66)
Absolute Change at Week 52 (MMRM)		
n	160	159
LS mean (SE)	0.94 (1.08)	1.31 (1.09)
95% CI of LS mean	(-1.19, 3.08)	(-0.84, 3.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-2.66, 3.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Absolute Change through Week 52 (MMRM)		
n	165	165
LS mean (SE)	-0.23 (0.92)	1.41 (0.92)
95% CI of LS mean	(-2.04, 1.58)	(-0.41, 3.23)
P-value within Treatment	0.8011	0.1279
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-0.93, 4.21)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2094
Hedges' G (SE)		0.14 (0.11)
Hedges' 95% CI		(-0.08, 0.35)
Hedges' P-value		0.2095

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Baseline		
n	109	113
Mean (SD)	88.07 (17.36)	89.16 (13.81)
Week 8 (MMRM)		
n	109	115
LS mean (SE)	88.80 (1.39)	88.53 (1.36)
95% CI of LS mean	(86.07, 91.54)	(85.85, 91.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-4.11, 3.55)
Absolute Change at Week 8 (MMRM)		
n	106	113
LS mean (SE)	0.64 (1.23)	-0.65 (1.19)
95% CI of LS mean	(-1.78, 3.07)	(-3.00, 1.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.29 (-4.67, 2.09)
Week 16 (MMRM)		
n	109	115
LS mean (SE)	86.12 (1.53)	89.61 (1.49)
95% CI of LS mean	(83.11, 89.13)	(86.67, 92.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.49 (-0.72, 7.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Absolute Change at Week 16 (MMRM)		
n	106	113
LS mean (SE)	-1.84 (1.24)	0.61 (1.21)
95% CI of LS mean	(-4.29, 0.61)	(-1.77, 2.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.45 (-0.97, 5.87)
Week 24 (MMRM)		
n	109	114
LS mean (SE)	88.65 (1.37)	89.53 (1.34)
95% CI of LS mean	(85.94, 91.36)	(86.88, 92.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-2.92, 4.67)
Absolute Change at Week 24 (MMRM)		
n	106	112
LS mean (SE)	0.37 (1.24)	0.61 (1.21)
95% CI of LS mean	(-2.08, 2.82)	(-1.77, 3.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-3.18, 3.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Week 52		
n	107	111
Mean (SD)	89.64 (14.29)	88.96 (15.50)
Absolute Change at Week 52		
n	104	109
Mean (SD)	1.36 (10.71)	0.08 (12.24)
Week 52 (MMRM)		
n	106	111
LS mean (SE)	89.50 (1.42)	89.24 (1.39)
95% CI of LS mean	(86.70, 92.30)	(86.50, 91.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-4.19, 3.66)
Absolute Change at Week 52 (MMRM)		
n	103	109
LS mean (SE)	1.36 (1.13)	0.09 (1.10)
95% CI of LS mean	(-0.87, 3.59)	(-2.08, 2.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.27 (-4.39, 1.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Absolute Change through Week 52 (MMRM)		
n	106	113
LS mean (SE)	-0.04 (1.01)	0.44 (0.98)
95% CI of LS mean	(-2.02, 1.95)	(-1.49, 2.37)
P-value within Treatment	0.9709	0.6552
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.47 (-2.30, 3.25)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7364
Hedges' G (SE)		0.05 (0.13)
Hedges' 95% CI		(-0.22, 0.31)
Hedges' P-value		0.7359

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Baseline		
n	80	73
Mean (SD)	87.08 (16.40)	84.59 (18.14)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	84.60 (1.76)	86.49 (1.88)
95% CI of LS mean	(81.13, 88.07)	(82.77, 90.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.89 (-3.20, 6.98)
Absolute Change at Week 8 (MMRM)		
n	79	67
LS mean (SE)	-2.43 (1.45)	2.53 (1.57)
95% CI of LS mean	(-5.30, 0.44)	(-0.56, 5.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.96 (0.74, 9.19)
Week 16 (MMRM)		
n	78	69
LS mean (SE)	85.59 (1.78)	87.49 (1.89)
95% CI of LS mean	(82.08, 89.11)	(83.75, 91.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.90 (-3.24, 7.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Absolute Change at Week 16 (MMRM)		
n	78	68
LS mean (SE)	-1.41 (1.87)	4.36 (2.00)
95% CI of LS mean	(-5.10, 2.28)	(0.41, 8.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.77 (0.36, 11.18)
Week 24 (MMRM)		
n	78	68
LS mean (SE)	84.42 (1.85)	85.98 (1.97)
95% CI of LS mean	(80.77, 88.07)	(82.09, 89.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.56 (-3.78, 6.91)
Absolute Change at Week 24 (MMRM)		
n	78	67
LS mean (SE)	-2.59 (1.71)	2.07 (1.84)
95% CI of LS mean	(-5.97, 0.79)	(-1.56, 5.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.66 (-0.30, 9.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Week 52		
n	76	68
Mean (SD)	87.61 (15.43)	88.36 (13.59)
Absolute Change at Week 52		
n	76	66
Mean (SD)	0.66 (14.26)	4.67 (17.67)
Week 52 (MMRM)		
n	75	64
LS mean (SE)	87.54 (1.68)	88.00 (1.80)
95% CI of LS mean	(84.23, 90.86)	(84.43, 91.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-4.42, 5.33)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	0.57 (1.83)	4.12 (1.98)
95% CI of LS mean	(-3.06, 4.19)	(0.20, 8.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.55 (-1.79, 8.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	-1.14 (1.53)	3.52 (1.65)
95% CI of LS mean	(-4.18, 1.89)	(0.26, 6.77)
P-value within Treatment	0.4570	0.0344
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.66 (0.21, 9.11)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0403
Hedges' G (SE)		0.34 (0.17)
Hedges' 95% CI		(0.01, 0.67)
Hedges' P-value		0.0416

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Baseline		
n	83	84
Mean (SD)	92.07 (12.13)	88.19 (14.18)
Week 8 (MMRM)		
n	83	82
LS mean (SE)	88.59 (1.65)	87.05 (1.65)
95% CI of LS mean	(85.34, 91.84)	(83.79, 90.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.54 (-6.15, 3.07)
Absolute Change at Week 8 (MMRM)		
n	82	81
LS mean (SE)	-3.34 (1.20)	-1.36 (1.21)
95% CI of LS mean	(-5.72, -0.96)	(-3.76, 1.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.98 (-1.40, 5.35)
Week 16 (MMRM)		
n	83	83
LS mean (SE)	89.49 (1.60)	88.72 (1.60)
95% CI of LS mean	(86.33, 92.66)	(85.56, 91.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.77 (-5.25, 3.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Absolute Change at Week 16 (MMRM)		
n	82	82
LS mean (SE)	-2.32 (1.28)	0.59 (1.28)
95% CI of LS mean	(-4.84, 0.20)	(-1.92, 3.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.92 (-0.65, 6.48)
Week 24 (MMRM)		
n	83	81
LS mean (SE)	87.89 (1.79)	87.35 (1.80)
95% CI of LS mean	(84.35, 91.42)	(83.79, 90.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.54 (-5.56, 4.48)
Absolute Change at Week 24 (MMRM)		
n	82	80
LS mean (SE)	-3.95 (1.31)	-0.65 (1.33)
95% CI of LS mean	(-6.54, -1.36)	(-3.27, 1.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.30 (-0.39, 6.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Week 52		
n	82	76
Mean (SD)	91.77 (12.11)	87.83 (15.12)
Absolute Change at Week 52		
n	81	75
Mean (SD)	-0.10 (9.46)	0.33 (10.29)
Week 52 (MMRM)		
n	81	75
LS mean (SE)	91.74 (1.48)	88.18 (1.51)
95% CI of LS mean	(88.81, 94.67)	(85.20, 91.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.56 (-7.74, 0.62)
Absolute Change at Week 52 (MMRM)		
n	80	74
LS mean (SE)	-0.04 (1.11)	0.16 (1.14)
95% CI of LS mean	(-2.22, 2.15)	(-2.09, 2.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-2.94, 3.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Absolute Change through Week 52 (MMRM)		
n	82	82
LS mean (SE)	-2.10 (0.95)	0.03 (0.95)
95% CI of LS mean	(-3.97, -0.23)	(-1.85, 1.92)
P-value within Treatment	0.0279	0.9709
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.14 (-0.52, 4.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1141
Hedges' G (SE)		0.25 (0.16)
Hedges' 95% CI		(-0.06, 0.56)
Hedges' P-value		0.1151

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Baseline		
n	106	102
Mean (SD)	84.20 (19.24)	86.68 (17.00)
Week 8 (MMRM)		
n	105	101
LS mean (SE)	85.86 (1.44)	88.45 (1.48)
95% CI of LS mean	(83.02, 88.71)	(85.54, 91.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.59 (-1.49, 6.66)
Absolute Change at Week 8 (MMRM)		
n	103	99
LS mean (SE)	1.53 (1.37)	2.13 (1.40)
95% CI of LS mean	(-1.17, 4.24)	(-0.64, 4.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (-3.28, 4.47)
Week 16 (MMRM)		
n	104	101
LS mean (SE)	83.00 (1.63)	88.98 (1.66)
95% CI of LS mean	(79.79, 86.21)	(85.71, 92.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.98 (1.40, 10.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Absolute Change at Week 16 (MMRM)		
n	102	99
LS mean (SE)	-1.10 (1.63)	3.20 (1.66)
95% CI of LS mean	(-4.32, 2.11)	(-0.07, 6.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.31 (-0.28, 8.89)
Week 24 (MMRM)		
n	104	101
LS mean (SE)	86.04 (1.40)	88.99 (1.43)
95% CI of LS mean	(83.28, 88.80)	(86.17, 91.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.95 (-0.99, 6.89)
Absolute Change at Week 24 (MMRM)		
n	102	99
LS mean (SE)	1.61 (1.47)	2.69 (1.50)
95% CI of LS mean	(-1.29, 4.50)	(-0.26, 5.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-3.05, 5.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Week 52		
n	101	103
Mean (SD)	86.39 (16.28)	89.40 (14.54)
Absolute Change at Week 52		
n	99	100
Mean (SD)	2.02 (14.19)	2.92 (17.18)
Week 52 (MMRM)		
n	100	100
LS mean (SE)	86.13 (1.53)	89.30 (1.54)
95% CI of LS mean	(83.12, 89.14)	(86.26, 92.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.17 (-1.11, 7.45)
Absolute Change at Week 52 (MMRM)		
n	98	98
LS mean (SE)	1.78 (1.58)	2.95 (1.60)
95% CI of LS mean	(-1.33, 4.89)	(-0.20, 6.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-3.26, 5.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Absolute Change through Week 52 (MMRM)		
n	102	99
LS mean (SE)	0.76 (1.36)	2.95 (1.38)
95% CI of LS mean	(-1.92, 3.44)	(0.22, 5.68)
P-value within Treatment	0.5761	0.0343
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-1.64, 6.01)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2604
Hedges' G (SE)		0.16 (0.14)
Hedges' 95% CI		(-0.12, 0.44)
Hedges' P-value		0.2610

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Baseline		
n	108	99
Mean (SD)	66.74 (18.49)	67.68 (20.46)
Week 8 (MMRM)		
n	109	98
LS mean (SE)	64.19 (1.89)	68.44 (1.99)
95% CI of LS mean	(60.47, 67.91)	(64.52, 72.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.25 (-1.16, 9.67)
Absolute Change at Week 8 (MMRM)		
n	107	96
LS mean (SE)	-2.96 (1.72)	0.69 (1.81)
95% CI of LS mean	(-6.34, 0.43)	(-2.89, 4.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.64 (-1.29, 8.57)
Week 16 (MMRM)		
n	109	98
LS mean (SE)	64.28 (1.97)	68.82 (2.08)
95% CI of LS mean	(60.40, 68.16)	(64.72, 72.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.54 (-1.11, 10.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	107	96
LS mean (SE)	-2.58 (1.53)	1.49 (1.62)
95% CI of LS mean	(-5.59, 0.44)	(-1.69, 4.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.07 (-0.32, 8.47)
Week 24 (MMRM)		
n	109	98
LS mean (SE)	64.02 (2.10)	66.11 (2.21)
95% CI of LS mean	(59.89, 68.16)	(61.75, 70.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.08 (-3.94, 8.11)
Absolute Change at Week 24 (MMRM)		
n	107	96
LS mean (SE)	-3.04 (1.62)	-1.88 (1.71)
95% CI of LS mean	(-6.24, 0.16)	(-5.26, 1.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-3.50, 5.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Week 52		
n	108	94
Mean (SD)	66.28 (18.87)	68.17 (20.00)
Absolute Change at Week 52		
n	106	92
Mean (SD)	-1.34 (13.71)	0.63 (16.86)
Week 52 (MMRM)		
n	108	93
LS mean (SE)	65.99 (1.84)	68.64 (1.96)
95% CI of LS mean	(62.36, 69.62)	(64.76, 72.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.65 (-2.67, 7.97)
Absolute Change at Week 52 (MMRM)		
n	106	91
LS mean (SE)	-1.18 (1.50)	0.60 (1.61)
95% CI of LS mean	(-4.13, 1.77)	(-2.57, 3.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.78 (-2.56, 6.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	107	96
LS mean (SE)	-2.27 (1.25)	0.07 (1.32)
95% CI of LS mean	(-4.72, 0.19)	(-2.53, 2.67)
P-value within Treatment	0.0704	0.9561
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.34 (-1.25, 5.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2003
Hedges' G (SE)		0.18 (0.14)
Hedges' 95% CI		(-0.10, 0.46)
Hedges' P-value		0.1997

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Baseline		
n	80	86
Mean (SD)	66.84 (16.83)	71.41 (19.45)
Week 8 (MMRM)		
n	80	85
LS mean (SE)	66.12 (2.16)	67.21 (2.09)
95% CI of LS mean	(61.85, 70.38)	(63.08, 71.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-4.85, 7.03)
Absolute Change at Week 8 (MMRM)		
n	79	85
LS mean (SE)	-0.77 (1.92)	-4.28 (1.85)
95% CI of LS mean	(-4.56, 3.02)	(-7.92, -0.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.51 (-8.77, 1.75)
Week 16 (MMRM)		
n	78	86
LS mean (SE)	64.99 (2.28)	66.69 (2.18)
95% CI of LS mean	(60.49, 69.49)	(62.38, 71.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-4.53, 7.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Absolute Change at Week 16 (MMRM)		
n	77	86
LS mean (SE)	-1.76 (1.92)	-4.79 (1.82)
95% CI of LS mean	(-5.55, 2.03)	(-8.39, -1.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.03 (-8.26, 2.20)
Week 24 (MMRM)		
n	78	85
LS mean (SE)	64.54 (2.17)	69.37 (2.08)
95% CI of LS mean	(60.25, 68.83)	(65.25, 73.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.83 (-1.12, 10.77)
Absolute Change at Week 24 (MMRM)		
n	77	85
LS mean (SE)	-2.20 (1.91)	-2.17 (1.82)
95% CI of LS mean	(-5.97, 1.58)	(-5.76, 1.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-5.19, 5.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Week 52		
n	75	82
Mean (SD)	67.78 (18.45)	69.31 (20.15)
Absolute Change at Week 52		
n	74	82
Mean (SD)	1.28 (16.44)	-2.03 (19.67)
Week 52 (MMRM)		
n	74	82
LS mean (SE)	67.70 (2.22)	69.57 (2.13)
95% CI of LS mean	(63.30, 72.09)	(65.37, 73.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.87 (-4.21, 7.96)
Absolute Change at Week 52 (MMRM)		
n	73	82
LS mean (SE)	0.79 (2.08)	-1.92 (1.97)
95% CI of LS mean	(-3.32, 4.89)	(-5.81, 1.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.70 (-8.37, 2.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Absolute Change through Week 52 (MMRM)		
n	77	86
LS mean (SE)	-1.06 (1.63)	-2.96 (1.56)
95% CI of LS mean	(-4.28, 2.17)	(-6.03, 0.11)
P-value within Treatment	0.5190	0.0590
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.90 (-6.36, 2.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4005
Hedges' G (SE)		-0.13 (0.16)
Hedges' 95% CI		(-0.44, 0.18)
Hedges' P-value		0.4008

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Baseline		
n	21	20
Mean (SD)	66.27 (16.97)	72.08 (19.36)
Week 8 (MMRM)		
n	21	19
LS mean (SE)	68.89 (3.71)	72.10 (3.90)
95% CI of LS mean	(61.37, 76.42)	(64.19, 80.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.21 (-7.74, 14.16)
Absolute Change at Week 8 (MMRM)		
n	21	19
LS mean (SE)	3.12 (3.75)	0.94 (3.94)
95% CI of LS mean	(-4.49, 10.72)	(-7.05, 8.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.17 (-13.23, 8.89)
Week 16 (MMRM)		
n	20	19
LS mean (SE)	65.86 (4.35)	65.52 (4.50)
95% CI of LS mean	(57.04, 74.68)	(56.41, 74.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.34 (-13.05, 12.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 16 (MMRM)		
n	20	19
LS mean (SE)	0.27 (4.08)	-5.64 (4.21)
95% CI of LS mean	(-7.99, 8.53)	(-14.16, 2.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.90 (-17.80, 5.99)
Week 24 (MMRM)		
n	20	19
LS mean (SE)	63.74 (3.78)	72.54 (3.90)
95% CI of LS mean	(56.07, 71.40)	(64.63, 80.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.80 (-2.25, 19.85)
Absolute Change at Week 24 (MMRM)		
n	20	19
LS mean (SE)	-1.79 (3.35)	1.38 (3.45)
95% CI of LS mean	(-8.58, 5.00)	(-5.62, 8.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.17 (-6.62, 12.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Week 52		
n	19	20
Mean (SD)	64.04 (22.40)	72.92 (19.28)
Absolute Change at Week 52		
n	19	20
Mean (SD)	-2.63 (17.14)	0.83 (18.91)
Week 52 (MMRM)		
n	19	19
LS mean (SE)	63.71 (4.68)	71.66 (4.75)
95% CI of LS mean	(54.23, 73.20)	(62.03, 81.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.95 (-5.59, 21.49)
Absolute Change at Week 52 (MMRM)		
n	19	19
LS mean (SE)	-2.11 (4.20)	0.50 (4.24)
95% CI of LS mean	(-10.62, 6.40)	(-8.10, 9.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.62 (-9.51, 14.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change through Week 52 (MMRM)		
n	20	19
LS mean (SE)	-1.21 (3.07)	-1.25 (3.17)
95% CI of LS mean	(-7.44, 5.02)	(-7.68, 5.18)
P-value within Treatment	0.6956	0.6956
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-9.03, 8.95)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9933
Hedges' G (SE)		0.00 (0.31)
Hedges' 95% CI		(-0.64, 0.63)
Hedges' P-value		0.9932

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	66.85 (17.85)	69.36 (20.19)
Week 8 (MMRM)		
n	168	164
LS mean (SE)	64.54 (1.51)	67.37 (1.53)
95% CI of LS mean	(61.56, 67.52)	(64.36, 70.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.82 (-1.41, 7.06)
Absolute Change at Week 8 (MMRM)		
n	165	162
LS mean (SE)	-2.63 (1.37)	-1.98 (1.38)
95% CI of LS mean	(-5.33, 0.06)	(-4.70, 0.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-3.17, 4.48)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	64.44 (1.59)	68.04 (1.60)
95% CI of LS mean	(61.32, 67.56)	(64.90, 71.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (-0.82, 8.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-2.51 (1.25)	-1.02 (1.26)
95% CI of LS mean	(-4.97, -0.05)	(-3.49, 1.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.49 (-2.00, 4.97)
Week 24 (MMRM)		
n	167	164
LS mean (SE)	64.34 (1.63)	67.00 (1.65)
95% CI of LS mean	(61.12, 67.55)	(63.75, 70.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.66 (-1.91, 7.23)
Absolute Change at Week 24 (MMRM)		
n	164	162
LS mean (SE)	-2.76 (1.32)	-2.47 (1.33)
95% CI of LS mean	(-5.35, -0.17)	(-5.08, 0.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-3.39, 3.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	67.22 (18.18)	68.45 (20.12)
Absolute Change at Week 52		
n	162	156
Mean (SD)	0.02 (14.61)	-0.80 (18.08)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	67.08 (1.48)	68.73 (1.50)
95% CI of LS mean	(64.16, 70.00)	(65.77, 71.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.65 (-2.51, 5.80)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	-0.09 (1.30)	-0.79 (1.32)
95% CI of LS mean	(-2.65, 2.46)	(-3.38, 1.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.69 (-4.33, 2.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-1.79 (1.06)	-1.43 (1.06)
95% CI of LS mean	(-3.86, 0.29)	(-3.52, 0.67)
P-value within Treatment	0.0918	0.1808
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-2.59, 3.31)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8099
Hedges' G (SE)		0.03 (0.11)
Hedges' 95% CI		(-0.19, 0.24)
Hedges' P-value		0.8098

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	69.30 (20.23)	59.90 (26.91)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	69.03 (4.46)	65.43 (4.87)
95% CI of LS mean	(59.94, 78.12)	(55.50, 75.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.60 (-17.25, 10.05)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	0.12 (4.13)	5.07 (4.51)
95% CI of LS mean	(-8.29, 8.52)	(-4.11, 14.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.95 (-7.63, 17.53)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	64.64 (5.04)	64.39 (5.51)
95% CI of LS mean	(54.36, 74.92)	(53.16, 75.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-15.64, 15.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-4.27 (5.18)	4.03 (5.65)
95% CI of LS mean	(-14.81, 6.27)	(-7.47, 15.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.30 (-7.41, 24.00)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	69.03 (4.36)	62.82 (4.76)
95% CI of LS mean	(60.12, 77.93)	(53.10, 72.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.20 (-19.58, 7.17)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	0.12 (4.43)	2.47 (4.84)
95% CI of LS mean	(-8.92, 9.15)	(-7.40, 12.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.35 (-11.15, 15.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	76.39 (19.23)	60.71 (18.90)
Absolute Change at Week 52		
n	18	13
Mean (SD)	6.02 (13.65)	3.85 (18.82)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	75.89 (4.51)	61.10 (5.30)
95% CI of LS mean	(66.66, 85.12)	(50.27, 71.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-14.79 (-29.16, -0.42)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	6.31 (3.60)	3.36 (4.27)
95% CI of LS mean	(-1.06, 13.68)	(-5.38, 12.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.95 (-14.47, 8.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	0.72 (3.48)	3.28 (3.84)
95% CI of LS mean	(-6.39, 7.83)	(-4.56, 11.13)
P-value within Treatment	0.8377	0.3993
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.57 (-8.16, 13.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6289
Hedges' G (SE)		0.16 (0.33)
Hedges' 95% CI		(-0.51, 0.84)
Hedges' P-value		0.6240

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Baseline		
n	169	169
Mean (SD)	66.55 (17.49)	70.76 (19.05)
Week 8 (MMRM)		
n	170	167
LS mean (SE)	64.57 (1.49)	68.10 (1.50)
95% CI of LS mean	(61.64, 67.51)	(65.14, 71.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.52 (-0.64, 7.68)
Absolute Change at Week 8 (MMRM)		
n	167	165
LS mean (SE)	-2.26 (1.35)	-2.30 (1.36)
95% CI of LS mean	(-4.91, 0.40)	(-4.96, 0.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-3.80, 3.72)
Week 16 (MMRM)		
n	168	168
LS mean (SE)	64.59 (1.56)	68.11 (1.57)
95% CI of LS mean	(61.52, 67.67)	(65.03, 71.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.52 (-0.84, 7.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Absolute Change at Week 16 (MMRM)		
n	165	166
LS mean (SE)	-1.98 (1.21)	-2.01 (1.20)
95% CI of LS mean	(-4.35, 0.40)	(-4.38, 0.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-3.39, 3.32)
Week 24 (MMRM)		
n	168	167
LS mean (SE)	63.75 (1.61)	68.03 (1.62)
95% CI of LS mean	(60.58, 66.92)	(64.85, 71.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.28 (-0.22, 8.78)
Absolute Change at Week 24 (MMRM)		
n	165	165
LS mean (SE)	-2.99 (1.27)	-2.48 (1.27)
95% CI of LS mean	(-5.49, -0.48)	(-4.98, 0.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.51 (-3.03, 4.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Week 52		
n	165	164
Mean (SD)	65.91 (18.35)	69.92 (19.77)
Absolute Change at Week 52		
n	162	162
Mean (SD)	-0.96 (14.91)	-0.93 (18.13)
Week 52 (MMRM)		
n	164	162
LS mean (SE)	65.75 (1.48)	69.70 (1.49)
95% CI of LS mean	(62.84, 68.66)	(66.78, 72.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.96 (-0.17, 8.08)
Absolute Change at Week 52 (MMRM)		
n	161	160
LS mean (SE)	-1.08 (1.31)	-0.89 (1.32)
95% CI of LS mean	(-3.66, 1.50)	(-3.48, 1.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.19 (-3.47, 3.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Absolute Change through Week 52 (MMRM)		
n	165	166
LS mean (SE)	-2.01 (1.03)	-1.79 (1.03)
95% CI of LS mean	(-4.05, 0.02)	(-3.83, 0.24)
P-value within Treatment	0.0523	0.0841
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-2.66, 3.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8791
Hedges' G (SE)		0.02 (0.11)
Hedges' 95% CI		(-0.20, 0.23)
Hedges' P-value		0.8789

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Baseline		
n	109	114
Mean (SD)	67.79 (18.86)	72.08 (18.88)
Week 8 (MMRM)		
n	110	115
LS mean (SE)	66.53 (1.84)	69.21 (1.81)
95% CI of LS mean	(62.89, 70.16)	(65.65, 72.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.68 (-2.42, 7.78)
Absolute Change at Week 8 (MMRM)		
n	107	114
LS mean (SE)	-1.73 (1.65)	-2.65 (1.60)
95% CI of LS mean	(-4.98, 1.52)	(-5.80, 0.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-5.46, 3.62)
Week 16 (MMRM)		
n	109	115
LS mean (SE)	66.07 (1.93)	69.50 (1.88)
95% CI of LS mean	(62.26, 69.87)	(65.78, 73.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.43 (-1.89, 8.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Absolute Change at Week 16 (MMRM)		
n	106	114
LS mean (SE)	-1.85 (1.50)	-2.36 (1.45)
95% CI of LS mean	(-4.81, 1.11)	(-5.21, 0.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-4.62, 3.62)
Week 24 (MMRM)		
n	109	115
LS mean (SE)	66.60 (1.94)	69.57 (1.89)
95% CI of LS mean	(62.78, 70.42)	(65.84, 73.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.97 (-2.38, 8.31)
Absolute Change at Week 24 (MMRM)		
n	106	114
LS mean (SE)	-1.54 (1.51)	-2.28 (1.46)
95% CI of LS mean	(-4.52, 1.44)	(-5.16, 0.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.74 (-4.89, 3.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Week 52		
n	107	111
Mean (SD)	68.77 (18.74)	69.67 (20.44)
Absolute Change at Week 52		
n	104	110
Mean (SD)	0.51 (13.65)	-2.27 (15.88)
Week 52 (MMRM)		
n	106	111
LS mean (SE)	68.63 (1.89)	69.79 (1.85)
95% CI of LS mean	(64.91, 72.35)	(66.16, 73.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-4.05, 6.38)
Absolute Change at Week 52 (MMRM)		
n	103	110
LS mean (SE)	0.40 (1.46)	-2.17 (1.42)
95% CI of LS mean	(-2.49, 3.28)	(-4.96, 0.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.57 (-6.59, 1.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Absolute Change through Week 52 (MMRM)		
n	106	114
LS mean (SE)	-1.00 (1.21)	-2.27 (1.17)
95% CI of LS mean	(-3.38, 1.38)	(-4.57, 0.03)
P-value within Treatment	0.4094	0.0531
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.27 (-4.59, 2.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4510
Hedges' G (SE)		-0.10 (0.13)
Hedges' 95% CI		(-0.37, 0.16)
Hedges' P-value		0.4503

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Baseline		
n	80	73
Mean (SD)	65.42 (16.03)	65.87 (21.39)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	62.94 (2.17)	65.62 (2.33)
95% CI of LS mean	(58.65, 67.23)	(61.02, 70.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.68 (-3.61, 8.98)
Absolute Change at Week 8 (MMRM)		
n	79	67
LS mean (SE)	-2.67 (2.06)	0.34 (2.22)
95% CI of LS mean	(-6.74, 1.39)	(-4.05, 4.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.02 (-2.97, 9.01)
Week 16 (MMRM)		
n	78	69
LS mean (SE)	62.56 (2.33)	64.93 (2.48)
95% CI of LS mean	(57.95, 67.17)	(60.03, 69.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.37 (-4.37, 9.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Absolute Change at Week 16 (MMRM)		
n	78	68
LS mean (SE)	-3.02 (1.99)	0.34 (2.13)
95% CI of LS mean	(-6.96, 0.92)	(-3.88, 4.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.36 (-2.42, 9.14)
Week 24 (MMRM)		
n	78	68
LS mean (SE)	61.07 (2.40)	64.23 (2.56)
95% CI of LS mean	(56.32, 65.81)	(59.16, 69.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.16 (-3.79, 10.11)
Absolute Change at Week 24 (MMRM)		
n	78	67
LS mean (SE)	-4.52 (2.10)	-1.29 (2.26)
95% CI of LS mean	(-8.66, -0.37)	(-5.75, 3.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-2.87, 9.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Week 52		
n	77	68
Mean (SD)	64.29 (18.23)	67.77 (19.42)
Absolute Change at Week 52		
n	77	66
Mean (SD)	-1.30 (16.39)	2.15 (21.20)
Week 52 (MMRM)		
n	76	64
LS mean (SE)	64.12 (2.12)	67.87 (2.29)
95% CI of LS mean	(59.93, 68.31)	(63.35, 72.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.75 (-2.42, 9.92)
Absolute Change at Week 52 (MMRM)		
n	76	63
LS mean (SE)	-1.53 (2.14)	2.37 (2.33)
95% CI of LS mean	(-5.77, 2.71)	(-2.25, 6.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.90 (-2.38, 10.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	-3.02 (1.71)	0.47 (1.83)
95% CI of LS mean	(-6.40, 0.35)	(-3.16, 4.10)
P-value within Treatment	0.0788	0.7977
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.49 (-1.47, 8.45)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1660
Hedges' G (SE)		0.23 (0.17)
Hedges' 95% CI		(-0.10, 0.56)
Hedges' P-value		0.1668

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Baseline		
n	83	84
Mean (SD)	67.57 (16.26)	68.75 (20.69)
Week 8 (MMRM)		
n	83	82
LS mean (SE)	65.32 (2.13)	65.80 (2.13)
95% CI of LS mean	(61.12, 69.52)	(61.59, 70.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-5.47, 6.43)
Absolute Change at Week 8 (MMRM)		
n	82	81
LS mean (SE)	-2.35 (1.80)	-3.08 (1.81)
95% CI of LS mean	(-5.91, 1.20)	(-6.65, 0.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.72 (-5.77, 4.32)
Week 16 (MMRM)		
n	83	83
LS mean (SE)	65.32 (2.26)	68.11 (2.26)
95% CI of LS mean	(60.86, 69.78)	(63.66, 72.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.80 (-3.52, 9.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Absolute Change at Week 16 (MMRM)		
n	82	82
LS mean (SE)	-2.25 (1.70)	-0.69 (1.70)
95% CI of LS mean	(-5.60, 1.10)	(-4.04, 2.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.56 (-3.18, 6.30)
Week 24 (MMRM)		
n	83	82
LS mean (SE)	63.61 (2.26)	65.91 (2.26)
95% CI of LS mean	(59.15, 68.07)	(61.44, 70.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.30 (-4.02, 8.62)
Absolute Change at Week 24 (MMRM)		
n	82	81
LS mean (SE)	-3.98 (1.80)	-2.97 (1.81)
95% CI of LS mean	(-7.53, -0.43)	(-6.53, 0.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-4.02, 6.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Week 52		
n	82	76
Mean (SD)	66.36 (17.74)	67.87 (21.29)
Absolute Change at Week 52		
n	81	75
Mean (SD)	-1.34 (14.76)	-0.33 (17.67)
Week 52 (MMRM)		
n	81	75
LS mean (SE)	66.28 (2.15)	68.45 (2.18)
95% CI of LS mean	(62.04, 70.52)	(64.14, 72.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.17 (-3.88, 8.23)
Absolute Change at Week 52 (MMRM)		
n	80	74
LS mean (SE)	-1.48 (1.82)	-0.42 (1.87)
95% CI of LS mean	(-5.08, 2.11)	(-4.11, 3.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.07 (-4.09, 6.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Absolute Change through Week 52 (MMRM)		
n	82	82
LS mean (SE)	-2.57 (1.45)	-1.36 (1.46)
95% CI of LS mean	(-5.43, 0.29)	(-4.23, 1.51)
P-value within Treatment	0.0774	0.3514
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-2.85, 5.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5560
Hedges' G (SE)		0.09 (0.16)
Hedges' 95% CI		(-0.22, 0.40)
Hedges' P-value		0.5558

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Baseline		
n	106	103
Mean (SD)	66.17 (18.82)	70.39 (19.62)
Week 8 (MMRM)		
n	106	101
LS mean (SE)	64.90 (1.89)	69.50 (1.93)
95% CI of LS mean	(61.18, 68.62)	(65.68, 73.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.60 (-0.74, 9.93)
Absolute Change at Week 8 (MMRM)		
n	104	100
LS mean (SE)	-1.85 (1.80)	-0.35 (1.84)
95% CI of LS mean	(-5.40, 1.70)	(-3.97, 3.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.50 (-3.57, 6.58)
Week 16 (MMRM)		
n	104	101
LS mean (SE)	64.13 (1.99)	67.39 (2.03)
95% CI of LS mean	(60.20, 68.06)	(63.39, 71.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.26 (-2.35, 8.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Absolute Change at Week 16 (MMRM)		
n	102	100
LS mean (SE)	-2.31 (1.69)	-2.01 (1.71)
95% CI of LS mean	(-5.64, 1.02)	(-5.38, 1.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.30 (-4.44, 5.05)
Week 24 (MMRM)		
n	104	101
LS mean (SE)	64.93 (2.05)	68.80 (2.08)
95% CI of LS mean	(60.89, 68.96)	(64.70, 72.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.88 (-1.88, 9.64)
Absolute Change at Week 24 (MMRM)		
n	102	100
LS mean (SE)	-1.73 (1.70)	-1.17 (1.72)
95% CI of LS mean	(-5.08, 1.61)	(-4.55, 2.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.57 (-4.19, 5.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Week 52		
n	102	103
Mean (SD)	67.32 (19.36)	69.74 (19.10)
Absolute Change at Week 52		
n	100	101
Mean (SD)	0.61 (14.96)	-0.83 (18.54)
Week 52 (MMRM)		
n	101	100
LS mean (SE)	67.22 (1.89)	69.46 (1.91)
95% CI of LS mean	(63.49, 70.94)	(65.69, 73.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.24 (-3.06, 7.54)
Absolute Change at Week 52 (MMRM)		
n	99	99
LS mean (SE)	0.54 (1.69)	-0.65 (1.70)
95% CI of LS mean	(-2.80, 3.88)	(-4.01, 2.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.18 (-5.92, 3.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Absolute Change through Week 52 (MMRM)		
n	102	100
LS mean (SE)	-1.17 (1.38)	-1.27 (1.40)
95% CI of LS mean	(-3.89, 1.55)	(-4.03, 1.48)
P-value within Treatment	0.3981	0.3631
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-3.98, 3.77)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9578
Hedges' G (SE)		-0.01 (0.14)
Hedges' 95% CI		(-0.28, 0.27)
Hedges' P-value		0.9578

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Baseline		
n	108	99
Mean (SD)	84.88 (26.72)	80.47 (30.49)
Week 8 (MMRM)		
n	109	98
LS mean (SE)	83.95 (2.53)	84.12 (2.67)
95% CI of LS mean	(78.96, 88.93)	(78.86, 89.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-7.09, 7.43)
Absolute Change at Week 8 (MMRM)		
n	107	96
LS mean (SE)	-1.25 (1.95)	3.80 (2.06)
95% CI of LS mean	(-5.10, 2.60)	(-0.27, 7.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.05 (-0.57, 10.66)
Week 16 (MMRM)		
n	109	98
LS mean (SE)	81.68 (2.78)	83.09 (2.93)
95% CI of LS mean	(76.20, 87.16)	(77.31, 88.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-6.57, 9.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Absolute Change at Week 16 (MMRM)		
n	107	96
LS mean (SE)	-3.63 (2.32)	2.75 (2.45)
95% CI of LS mean	(-8.21, 0.96)	(-2.09, 7.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.38 (-0.30, 13.05)
Week 24 (MMRM)		
n	109	97
LS mean (SE)	86.37 (2.54)	83.58 (2.68)
95% CI of LS mean	(81.36, 91.37)	(78.29, 88.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.78 (-10.09, 4.52)
Absolute Change at Week 24 (MMRM)		
n	107	95
LS mean (SE)	1.38 (2.29)	3.19 (2.43)
95% CI of LS mean	(-3.15, 5.90)	(-1.60, 7.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.81 (-4.78, 8.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Week 52		
n	108	94
Mean (SD)	86.73 (23.65)	81.56 (28.34)
Absolute Change at Week 52		
n	106	92
Mean (SD)	0.94 (22.75)	0.72 (21.53)
Week 52 (MMRM)		
n	108	93
LS mean (SE)	85.76 (2.52)	81.43 (2.69)
95% CI of LS mean	(80.78, 90.74)	(76.12, 86.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.34 (-11.63, 2.95)
Absolute Change at Week 52 (MMRM)		
n	106	91
LS mean (SE)	0.50 (2.11)	0.94 (2.26)
95% CI of LS mean	(-3.67, 4.66)	(-3.52, 5.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.44 (-5.67, 6.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 110	VNZ/TEZ/D-IVA N = 101
Absolute Change through Week 52 (MMRM)		
n	107	96
LS mean (SE)	-0.58 (1.87)	2.29 (1.98)
95% CI of LS mean	(-4.28, 3.11)	(-1.61, 6.20)
P-value within Treatment	0.7553	0.2484
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.88 (-2.51, 8.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2937
Hedges' G (SE)		0.15 (0.14)
Hedges' 95% CI		(-0.13, 0.42)
Hedges' P-value		0.2929

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Baseline		
n	80	86
Mean (SD)	84.58 (27.53)	84.11 (27.40)
Week 8 (MMRM)		
n	79	85
LS mean (SE)	87.12 (3.01)	82.49 (2.90)
95% CI of LS mean	(81.18, 93.06)	(76.76, 88.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.63 (-12.89, 3.63)
Absolute Change at Week 8 (MMRM)		
n	78	85
LS mean (SE)	2.48 (2.50)	-1.49 (2.39)
95% CI of LS mean	(-2.45, 7.41)	(-6.22, 3.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.98 (-10.81, 2.86)
Week 16 (MMRM)		
n	78	86
LS mean (SE)	82.75 (3.23)	82.92 (3.09)
95% CI of LS mean	(76.37, 89.12)	(76.81, 89.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-8.67, 9.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Absolute Change at Week 16 (MMRM)		
n	77	86
LS mean (SE)	-1.79 (2.72)	-1.10 (2.58)
95% CI of LS mean	(-7.15, 3.57)	(-6.19, 4.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.69 (-6.71, 8.09)
Week 24 (MMRM)		
n	78	85
LS mean (SE)	82.37 (3.51)	82.14 (3.37)
95% CI of LS mean	(75.43, 89.30)	(75.47, 88.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-9.85, 9.39)
Absolute Change at Week 24 (MMRM)		
n	77	85
LS mean (SE)	-2.25 (2.90)	-1.88 (2.77)
95% CI of LS mean	(-7.98, 3.49)	(-7.35, 3.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-7.57, 8.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Week 52		
n	74	82
Mean (SD)	85.14 (26.54)	82.93 (26.32)
Absolute Change at Week 52		
n	73	82
Mean (SD)	1.37 (28.02)	-1.22 (22.50)
Week 52 (MMRM)		
n	73	82
LS mean (SE)	84.77 (3.09)	82.14 (2.95)
95% CI of LS mean	(78.67, 90.87)	(76.32, 87.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.63 (-11.06, 5.80)
Absolute Change at Week 52 (MMRM)		
n	72	82
LS mean (SE)	0.28 (2.93)	-1.95 (2.77)
95% CI of LS mean	(-5.51, 6.06)	(-7.43, 3.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.23 (-10.20, 5.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 81	VNZ/TEZ/D-IVA N = 86
Absolute Change through Week 52 (MMRM)		
n	77	86
LS mean (SE)	-1.25 (2.47)	-1.64 (2.35)
95% CI of LS mean	(-6.13, 3.62)	(-6.29, 3.00)
P-value within Treatment	0.6125	0.4852
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-7.13, 6.35)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9090
Hedges' G (SE)		-0.02 (0.16)
Hedges' 95% CI		(-0.33, 0.29)
Hedges' P-value		0.9089

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Baseline		
n	21	20
Mean (SD)	73.02 (35.93)	71.67 (39.40)
Week 8 (MMRM)		
n	21	19
LS mean (SE)	76.06 (7.09)	75.59 (7.45)
95% CI of LS mean	(61.68, 90.43)	(60.47, 90.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-21.37, 20.43)
Absolute Change at Week 8 (MMRM)		
n	21	19
LS mean (SE)	2.59 (5.54)	5.91 (5.83)
95% CI of LS mean	(-8.64, 13.83)	(-5.91, 17.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.31 (-13.03, 19.66)
Week 16 (MMRM)		
n	20	19
LS mean (SE)	78.98 (6.51)	75.59 (6.76)
95% CI of LS mean	(65.81, 92.15)	(61.90, 89.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.39 (-22.44, 15.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 16 (MMRM)		
n	20	19
LS mean (SE)	5.93 (5.39)	5.91 (5.57)
95% CI of LS mean	(-5.01, 16.88)	(-5.41, 17.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-15.82, 15.77)
Week 24 (MMRM)		
n	20	19
LS mean (SE)	77.49 (7.39)	68.57 (7.69)
95% CI of LS mean	(62.50, 92.48)	(52.96, 84.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.92 (-30.61, 12.77)
Absolute Change at Week 24 (MMRM)		
n	20	19
LS mean (SE)	4.27 (5.70)	-1.11 (5.90)
95% CI of LS mean	(-7.28, 15.82)	(-13.08, 10.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.38 (-22.06, 11.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Week 52		
n	18	20
Mean (SD)	79.63 (28.33)	81.67 (22.88)
Absolute Change at Week 52		
n	18	20
Mean (SD)	9.26 (40.91)	10.00 (28.82)
Week 52 (MMRM)		
n	18	19
LS mean (SE)	80.15 (5.96)	80.85 (5.98)
95% CI of LS mean	(68.07, 92.23)	(68.70, 93.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.70 (-16.48, 17.89)
Absolute Change at Week 52 (MMRM)		
n	18	19
LS mean (SE)	6.82 (7.81)	11.17 (7.87)
95% CI of LS mean	(-8.99, 22.63)	(-4.79, 27.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.35 (-18.16, 26.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change through Week 52 (MMRM)		
n	20	19
LS mean (SE)	5.67 (5.51)	5.32 (5.68)
95% CI of LS mean	(-5.49, 16.84)	(-6.19, 16.84)
P-value within Treatment	0.3098	0.3548
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-16.44, 15.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9648
Hedges' G (SE)		-0.01 (0.31)
Hedges' 95% CI		(-0.65, 0.62)
Hedges' P-value		0.9646

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Baseline		
n	168	167
Mean (SD)	86.31 (25.36)	83.63 (27.35)
Week 8 (MMRM)		
n	167	164
LS mean (SE)	86.55 (2.01)	84.13 (2.03)
95% CI of LS mean	(82.60, 90.50)	(80.14, 88.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.43 (-8.04, 3.19)
Absolute Change at Week 8 (MMRM)		
n	164	162
LS mean (SE)	0.17 (1.60)	0.66 (1.61)
95% CI of LS mean	(-2.98, 3.33)	(-2.51, 3.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-3.99, 4.97)
Week 16 (MMRM)		
n	167	165
LS mean (SE)	82.66 (2.23)	83.74 (2.25)
95% CI of LS mean	(78.27, 87.05)	(79.31, 88.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.08 (-5.16, 7.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	164	163
LS mean (SE)	-3.84 (1.89)	0.25 (1.89)
95% CI of LS mean	(-7.55, -0.13)	(-3.48, 3.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.09 (-1.17, 9.35)
Week 24 (MMRM)		
n	167	163
LS mean (SE)	85.68 (2.17)	84.41 (2.19)
95% CI of LS mean	(81.41, 89.94)	(80.10, 88.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.27 (-7.33, 4.80)
Absolute Change at Week 24 (MMRM)		
n	164	161
LS mean (SE)	-0.59 (1.89)	0.92 (1.90)
95% CI of LS mean	(-4.30, 3.13)	(-2.82, 4.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.50 (-3.77, 6.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Week 52		
n	165	159
Mean (SD)	86.87 (24.33)	82.60 (27.77)
Absolute Change at Week 52		
n	162	156
Mean (SD)	0.21 (22.44)	-1.50 (20.51)
Week 52 (MMRM)		
n	163	156
LS mean (SE)	86.11 (2.08)	81.66 (2.11)
95% CI of LS mean	(82.03, 90.20)	(77.52, 85.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.45 (-10.27, 1.37)
Absolute Change at Week 52 (MMRM)		
n	160	154
LS mean (SE)	-0.29 (1.71)	-1.87 (1.73)
95% CI of LS mean	(-3.66, 3.08)	(-5.28, 1.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-6.37, 3.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 171	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	164	163
LS mean (SE)	-1.57 (1.55)	-0.23 (1.56)
95% CI of LS mean	(-4.63, 1.48)	(-3.31, 2.84)
P-value within Treatment	0.3117	0.8807
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.34 (-3.00, 5.67)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5440
Hedges' G (SE)		0.07 (0.11)
Hedges' 95% CI		(-0.15, 0.28)
Hedges' P-value		0.5439

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Baseline		
n	19	16
Mean (SD)	78.95 (33.72)	70.83 (36.26)
Week 8 (MMRM)		
n	19	16
LS mean (SE)	81.65 (7.86)	73.87 (8.60)
95% CI of LS mean	(65.58, 97.72)	(56.29, 91.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.78 (-32.08, 16.51)
Absolute Change at Week 8 (MMRM)		
n	19	16
LS mean (SE)	2.66 (4.53)	3.09 (4.95)
95% CI of LS mean	(-6.59, 11.92)	(-7.03, 13.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-13.55, 14.41)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	78.15 (8.01)	78.04 (8.76)
95% CI of LS mean	(61.75, 94.54)	(60.11, 95.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-24.87, 24.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change at Week 16 (MMRM)		
n	19	16
LS mean (SE)	-0.85 (6.26)	7.26 (6.83)
95% CI of LS mean	(-13.63, 11.93)	(-6.69, 21.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.10 (-11.00, 27.21)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	85.16 (7.83)	78.04 (8.57)
95% CI of LS mean	(69.13, 101.19)	(60.51, 95.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.13 (-31.36, 17.11)
Absolute Change at Week 24 (MMRM)		
n	19	16
LS mean (SE)	6.17 (6.07)	7.26 (6.63)
95% CI of LS mean	(-6.21, 18.55)	(-6.26, 20.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-17.44, 19.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Week 52		
n	18	14
Mean (SD)	81.48 (30.73)	73.81 (37.39)
Absolute Change at Week 52		
n	18	13
Mean (SD)	1.85 (33.28)	0.00 (13.61)
Week 52 (MMRM)		
n	18	13
LS mean (SE)	79.79 (8.55)	67.52 (9.64)
95% CI of LS mean	(62.23, 97.35)	(47.79, 87.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-12.28 (-39.09, 14.54)
Absolute Change at Week 52 (MMRM)		
n	18	13
LS mean (SE)	0.84 (6.33)	-3.60 (7.27)
95% CI of LS mean	(-12.14, 13.81)	(-18.45, 11.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.44 (-24.31, 15.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 17
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	2.05 (5.15)	3.64 (5.68)
95% CI of LS mean	(-8.46, 12.56)	(-7.94, 15.21)
P-value within Treatment	0.6929	0.5264
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.58 (-14.27, 17.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8399
Hedges' G (SE)		0.07 (0.33)
Hedges' 95% CI		(-0.61, 0.74)
Hedges' P-value		0.8374

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Baseline		
n	169	169
Mean (SD)	85.40 (26.18)	83.23 (28.20)
Week 8 (MMRM)		
n	169	167
LS mean (SE)	85.77 (1.99)	84.17 (2.01)
95% CI of LS mean	(81.84, 89.69)	(80.23, 88.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.59 (-7.16, 3.98)
Absolute Change at Week 8 (MMRM)		
n	166	165
LS mean (SE)	0.17 (1.66)	1.04 (1.67)
95% CI of LS mean	(-3.09, 3.44)	(-2.24, 4.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-3.76, 5.50)
Week 16 (MMRM)		
n	168	168
LS mean (SE)	82.69 (2.17)	83.39 (2.17)
95% CI of LS mean	(78.42, 86.95)	(79.12, 87.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.70 (-5.33, 6.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Absolute Change at Week 16 (MMRM)		
n	165	166
LS mean (SE)	-2.98 (1.84)	0.23 (1.84)
95% CI of LS mean	(-6.61, 0.64)	(-3.39, 3.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-1.91, 8.34)
Week 24 (MMRM)		
n	168	166
LS mean (SE)	84.68 (2.17)	83.24 (2.18)
95% CI of LS mean	(80.41, 88.95)	(78.95, 87.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-7.49, 4.62)
Absolute Change at Week 24 (MMRM)		
n	165	164
LS mean (SE)	-0.76 (1.90)	0.06 (1.90)
95% CI of LS mean	(-4.49, 2.97)	(-3.67, 3.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.83 (-4.45, 6.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Week 52		
n	164	164
Mean (SD)	86.59 (24.13)	83.13 (26.24)
Absolute Change at Week 52		
n	161	162
Mean (SD)	1.04 (23.99)	-0.21 (22.44)
Week 52 (MMRM)		
n	163	162
LS mean (SE)	86.06 (1.98)	82.85 (1.98)
95% CI of LS mean	(82.18, 89.95)	(78.95, 86.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.21 (-8.72, 2.30)
Absolute Change at Week 52 (MMRM)		
n	160	160
LS mean (SE)	0.46 (1.83)	-0.33 (1.83)
95% CI of LS mean	(-3.15, 4.07)	(-3.94, 3.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.79 (-5.90, 4.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 172	VNZ/TEZ/D-IVA N = 171
Absolute Change through Week 52 (MMRM)		
n	165	166
LS mean (SE)	-1.10 (1.59)	-0.01 (1.59)
95% CI of LS mean	(-4.22, 2.03)	(-3.14, 3.11)
P-value within Treatment	0.4909	0.9941
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.08 (-3.34, 5.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6301
Hedges' G (SE)		0.05 (0.11)
Hedges' 95% CI		(-0.16, 0.27)
Hedges' P-value		0.6299

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Baseline		
n	109	114
Mean (SD)	83.18 (27.45)	77.19 (32.38)
Week 8 (MMRM)		
n	109	115
LS mean (SE)	82.16 (2.82)	78.65 (2.76)
95% CI of LS mean	(76.61, 87.71)	(73.21, 84.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.52 (-11.30, 4.26)
Absolute Change at Week 8 (MMRM)		
n	106	114
LS mean (SE)	-1.32 (2.29)	1.27 (2.22)
95% CI of LS mean	(-5.83, 3.19)	(-3.10, 5.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.59 (-3.71, 8.88)
Week 16 (MMRM)		
n	109	115
LS mean (SE)	78.64 (3.05)	77.20 (2.98)
95% CI of LS mean	(72.64, 84.65)	(71.33, 83.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.45 (-9.86, 6.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Absolute Change at Week 16 (MMRM)		
n	106	114
LS mean (SE)	-5.00 (2.49)	-0.19 (2.41)
95% CI of LS mean	(-9.91, -0.10)	(-4.94, 4.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.81 (-2.03, 11.65)
Week 24 (MMRM)		
n	109	114
LS mean (SE)	80.78 (3.02)	78.45 (2.95)
95% CI of LS mean	(74.84, 86.73)	(72.62, 84.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.34 (-10.67, 6.00)
Absolute Change at Week 24 (MMRM)		
n	106	113
LS mean (SE)	-2.48 (2.39)	1.04 (2.32)
95% CI of LS mean	(-7.20, 2.23)	(-3.53, 5.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.53 (-3.05, 10.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Week 52		
n	107	111
Mean (SD)	81.93 (28.33)	78.98 (29.79)
Absolute Change at Week 52		
n	104	110
Mean (SD)	-1.92 (23.14)	0.61 (23.02)
Week 52 (MMRM)		
n	106	111
LS mean (SE)	80.78 (2.87)	77.59 (2.81)
95% CI of LS mean	(75.13, 86.43)	(72.06, 83.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.19 (-11.11, 4.73)
Absolute Change at Week 52 (MMRM)		
n	103	110
LS mean (SE)	-2.75 (2.29)	0.12 (2.21)
95% CI of LS mean	(-7.26, 1.75)	(-4.25, 4.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.87 (-3.41, 9.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 112	VNZ/TEZ/D-IVA N = 115
Absolute Change through Week 52 (MMRM)		
n	106	114
LS mean (SE)	-3.41 (2.04)	0.32 (1.97)
95% CI of LS mean	(-7.43, 0.60)	(-3.57, 4.21)
P-value within Treatment	0.0952	0.8709
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.73 (-1.87, 9.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1901
Hedges' G (SE)		0.18 (0.13)
Hedges' 95% CI		(-0.09, 0.44)
Hedges' P-value		0.1901

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Baseline		
n	80	73
Mean (SD)	87.08 (26.25)	90.41 (20.40)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	89.97 (2.27)	90.78 (2.43)
95% CI of LS mean	(85.49, 94.46)	(85.98, 95.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-5.76, 7.39)
Absolute Change at Week 8 (MMRM)		
n	79	67
LS mean (SE)	3.09 (1.88)	0.82 (2.02)
95% CI of LS mean	(-0.62, 6.79)	(-3.19, 4.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.27 (-7.73, 3.19)
Week 16 (MMRM)		
n	78	69
LS mean (SE)	87.33 (2.42)	92.24 (2.57)
95% CI of LS mean	(82.55, 92.11)	(87.16, 97.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.92 (-2.07, 11.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Absolute Change at Week 16 (MMRM)		
n	78	68
LS mean (SE)	0.55 (2.45)	2.28 (2.62)
95% CI of LS mean	(-4.29, 5.39)	(-2.91, 7.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-5.37, 8.83)
Week 24 (MMRM)		
n	78	68
LS mean (SE)	90.31 (2.52)	89.79 (2.69)
95% CI of LS mean	(85.32, 95.30)	(84.46, 95.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-7.82, 6.78)
Absolute Change at Week 24 (MMRM)		
n	78	67
LS mean (SE)	3.53 (2.73)	-0.19 (2.94)
95% CI of LS mean	(-1.87, 8.93)	(-6.00, 5.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.72 (-11.66, 4.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Week 52		
n	76	68
Mean (SD)	92.11 (17.10)	88.24 (21.37)
Absolute Change at Week 52		
n	76	66
Mean (SD)	5.26 (26.70)	-1.52 (19.77)
Week 52 (MMRM)		
n	75	64
LS mean (SE)	91.94 (2.20)	87.89 (2.37)
95% CI of LS mean	(87.59, 96.29)	(83.20, 92.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.05 (-10.46, 2.35)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	5.29 (2.68)	-1.84 (2.90)
95% CI of LS mean	(-0.01, 10.58)	(-7.58, 3.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.13 (-14.94, 0.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 75
Absolute Change through Week 52 (MMRM)		
n	78	68
LS mean (SE)	3.12 (2.22)	0.08 (2.38)
95% CI of LS mean	(-1.26, 7.51)	(-4.63, 4.79)
P-value within Treatment	0.1613	0.9729
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.04 (-9.48, 3.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3519
Hedges' G (SE)		-0.15 (0.17)
Hedges' 95% CI		(-0.48, 0.17)
Hedges' P-value		0.3522

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Baseline		
n	83	84
Mean (SD)	86.35 (26.05)	82.94 (27.62)
Week 8 (MMRM)		
n	83	82
LS mean (SE)	87.36 (3.08)	82.05 (3.09)
95% CI of LS mean	(81.28, 93.44)	(75.96, 88.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.32 (-13.93, 3.30)
Absolute Change at Week 8 (MMRM)		
n	82	81
LS mean (SE)	1.19 (2.12)	-0.81 (2.12)
95% CI of LS mean	(-2.99, 5.37)	(-5.00, 3.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.00 (-7.93, 3.92)
Week 16 (MMRM)		
n	83	83
LS mean (SE)	83.35 (3.10)	85.73 (3.10)
95% CI of LS mean	(77.22, 89.48)	(79.60, 91.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-6.30, 11.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Absolute Change at Week 16 (MMRM)		
n	82	82
LS mean (SE)	-2.87 (2.67)	2.87 (2.67)
95% CI of LS mean	(-8.15, 2.41)	(-2.41, 8.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.74 (-1.73, 13.22)
Week 24 (MMRM)		
n	83	81
LS mean (SE)	85.76 (3.32)	83.01 (3.34)
95% CI of LS mean	(79.19, 92.32)	(76.42, 89.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.75 (-12.06, 6.57)
Absolute Change at Week 24 (MMRM)		
n	82	80
LS mean (SE)	-0.43 (2.63)	0.11 (2.65)
95% CI of LS mean	(-5.62, 4.76)	(-5.12, 5.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.54 (-6.83, 7.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Week 52		
n	82	76
Mean (SD)	86.99 (25.53)	83.33 (27.49)
Absolute Change at Week 52		
n	81	75
Mean (SD)	0.82 (21.07)	-0.44 (20.86)
Week 52 (MMRM)		
n	81	75
LS mean (SE)	86.92 (2.99)	81.72 (3.04)
95% CI of LS mean	(81.01, 92.84)	(75.73, 87.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.20 (-13.63, 3.23)
Absolute Change at Week 52 (MMRM)		
n	80	74
LS mean (SE)	0.80 (2.37)	-1.25 (2.42)
95% CI of LS mean	(-3.88, 5.48)	(-6.04, 3.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.05 (-8.74, 4.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 84	VNZ/TEZ/D-IVA N = 85
Absolute Change through Week 52 (MMRM)		
n	82	82
LS mean (SE)	-0.84 (2.17)	0.58 (2.18)
95% CI of LS mean	(-5.13, 3.46)	(-3.73, 4.89)
P-value within Treatment	0.7011	0.7920
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-4.67, 7.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6475
Hedges' G (SE)		0.07 (0.16)
Hedges' 95% CI		(-0.24, 0.38)
Hedges' P-value		0.6473

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Baseline		
n	106	103
Mean (SD)	83.65 (27.70)	81.88 (30.17)
Week 8 (MMRM)		
n	105	101
LS mean (SE)	83.94 (2.48)	84.10 (2.54)
95% CI of LS mean	(79.04, 88.84)	(79.09, 89.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-6.85, 7.17)
Absolute Change at Week 8 (MMRM)		
n	103	100
LS mean (SE)	-0.06 (2.22)	2.72 (2.26)
95% CI of LS mean	(-4.44, 4.32)	(-1.73, 7.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.78 (-3.47, 9.03)
Week 16 (MMRM)		
n	104	101
LS mean (SE)	81.53 (2.84)	80.45 (2.90)
95% CI of LS mean	(75.92, 87.13)	(74.73, 86.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.08 (-9.09, 6.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Absolute Change at Week 16 (MMRM)		
n	102	100
LS mean (SE)	-2.52 (2.40)	-0.96 (2.43)
95% CI of LS mean	(-7.26, 2.22)	(-5.76, 3.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.56 (-5.19, 8.30)
Week 24 (MMRM)		
n	104	101
LS mean (SE)	84.13 (2.67)	82.41 (2.72)
95% CI of LS mean	(78.85, 89.40)	(77.04, 87.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.71 (-9.24, 5.82)
Absolute Change at Week 24 (MMRM)		
n	102	100
LS mean (SE)	0.41 (2.50)	1.04 (2.53)
95% CI of LS mean	(-4.52, 5.34)	(-3.95, 6.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-6.38, 7.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Week 52		
n	101	103
Mean (SD)	85.48 (24.23)	81.88 (27.13)
Absolute Change at Week 52		
n	99	101
Mean (SD)	1.35 (27.73)	0.00 (22.61)
Week 52 (MMRM)		
n	100	100
LS mean (SE)	84.45 (2.56)	81.38 (2.59)
95% CI of LS mean	(79.39, 89.51)	(76.27, 86.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.07 (-10.27, 4.12)
Absolute Change at Week 52 (MMRM)		
n	98	99
LS mean (SE)	0.41 (2.52)	0.03 (2.53)
95% CI of LS mean	(-4.57, 5.39)	(-4.97, 5.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-7.44, 6.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 108	VNZ/TEZ/D-IVA N = 105
Absolute Change through Week 52 (MMRM)		
n	102	100
LS mean (SE)	-0.57 (2.12)	0.04 (2.14)
95% CI of LS mean	(-4.74, 3.61)	(-4.19, 4.26)
P-value within Treatment	0.7895	0.9864
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (-5.34, 6.54)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8418
Hedges' G (SE)		0.03 (0.14)
Hedges' 95% CI		(-0.25, 0.30)
Hedges' P-value		0.8417

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Baseline		
n	172	166
Mean (SD)	76.36 (22.14)	78.45 (22.84)
Week 8 (MMRM)		
n	172	162
LS mean (SE)	77.77 (1.67)	79.42 (1.72)
95% CI of LS mean	(74.49, 81.06)	(76.04, 82.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.65 (-3.07, 6.36)
Absolute Change at Week 8 (MMRM)		
n	168	160
LS mean (SE)	1.15 (0.99)	1.16 (1.01)
95% CI of LS mean	(-0.79, 3.09)	(-0.83, 3.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-2.76, 2.79)
Week 16 (MMRM)		
n	171	163
LS mean (SE)	76.94 (1.65)	79.65 (1.69)
95% CI of LS mean	(73.70, 80.18)	(76.33, 82.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.72 (-1.93, 7.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	167	160
LS mean (SE)	0.13 (1.07)	1.65 (1.09)
95% CI of LS mean	(-1.97, 2.24)	(-0.50, 3.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.52 (-1.49, 4.52)
Week 24 (MMRM)		
n	171	162
LS mean (SE)	75.83 (1.72)	79.66 (1.76)
95% CI of LS mean	(72.45, 79.21)	(76.19, 83.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.83 (-1.02, 8.67)
Absolute Change at Week 24 (MMRM)		
n	167	159
LS mean (SE)	-1.00 (1.21)	1.78 (1.24)
95% CI of LS mean	(-3.39, 1.39)	(-0.67, 4.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.78 (-0.64, 6.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Week 52		
n	169	158
Mean (SD)	78.50 (21.18)	80.45 (20.74)
Absolute Change at Week 52		
n	165	154
Mean (SD)	1.82 (14.64)	1.73 (14.27)
Week 52 (MMRM)		
n	167	154
LS mean (SE)	78.53 (1.60)	79.89 (1.65)
95% CI of LS mean	(75.38, 81.68)	(76.64, 83.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.36 (-3.17, 5.88)
Absolute Change at Week 52 (MMRM)		
n	163	151
LS mean (SE)	1.69 (1.14)	1.79 (1.18)
95% CI of LS mean	(-0.55, 3.93)	(-0.53, 4.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-3.13, 3.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	167	160
LS mean (SE)	0.28 (0.93)	1.74 (0.96)
95% CI of LS mean	(-1.56, 2.11)	(-0.14, 3.62)
P-value within Treatment	0.7673	0.0698
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.46 (-1.17, 4.09)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2741
Hedges' G (SE)		0.12 (0.11)
Hedges' 95% CI		(-0.10, 0.34)
Hedges' P-value		0.2744

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Baseline		
n	25	26
Mean (SD)	78.22 (20.15)	73.93 (24.13)
Week 8 (MMRM)		
n	25	26
LS mean (SE)	83.88 (3.71)	75.33 (3.64)
95% CI of LS mean	(76.41, 91.35)	(68.00, 82.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.55 (-19.06, 1.96)
Absolute Change at Week 8 (MMRM)		
n	25	26
LS mean (SE)	4.22 (2.91)	2.78 (2.85)
95% CI of LS mean	(-1.64, 10.07)	(-2.96, 8.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-9.66, 6.79)
Week 16 (MMRM)		
n	25	26
LS mean (SE)	85.66 (3.73)	81.74 (3.66)
95% CI of LS mean	(78.15, 93.16)	(74.38, 89.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.92 (-14.48, 6.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	25	26
LS mean (SE)	6.00 (2.46)	9.19 (2.42)
95% CI of LS mean	(1.04, 10.95)	(4.33, 14.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.20 (-3.77, 10.17)
Week 24 (MMRM)		
n	25	26
LS mean (SE)	82.99 (4.16)	76.18 (4.08)
95% CI of LS mean	(74.63, 91.35)	(67.99, 84.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.81 (-18.56, 4.94)
Absolute Change at Week 24 (MMRM)		
n	25	26
LS mean (SE)	3.33 (2.85)	3.64 (2.80)
95% CI of LS mean	(-2.41, 9.07)	(-1.99, 9.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-7.76, 8.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Week 52		
n	24	26
Mean (SD)	81.02 (17.18)	79.06 (20.45)
Absolute Change at Week 52		
n	24	26
Mean (SD)	1.85 (14.53)	5.13 (13.42)
Week 52 (MMRM)		
n	24	26
LS mean (SE)	80.90 (3.68)	78.32 (3.57)
95% CI of LS mean	(73.50, 88.29)	(71.13, 85.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.58 (-12.94, 7.78)
Absolute Change at Week 52 (MMRM)		
n	24	26
LS mean (SE)	1.28 (2.77)	5.77 (2.67)
95% CI of LS mean	(-4.29, 6.85)	(0.40, 11.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.49 (-3.27, 12.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	25	26
LS mean (SE)	3.53 (2.12)	6.20 (2.07)
95% CI of LS mean	(-0.73, 7.80)	(2.03, 10.37)
P-value within Treatment	0.1019	0.0044
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.67 (-3.33, 8.66)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3754
Hedges' G (SE)		0.25 (0.28)
Hedges' 95% CI		(-0.31, 0.80)
Hedges' P-value		0.3744

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Baseline		
n	172	165
Mean (SD)	81.94 (18.73)	85.45 (15.40)
Week 8 (MMRM)		
n	171	162
LS mean (SE)	80.98 (1.38)	86.43 (1.42)
95% CI of LS mean	(78.27, 83.70)	(83.65, 89.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.45 (1.56, 9.35)
Absolute Change at Week 8 (MMRM)		
n	167	159
LS mean (SE)	-1.26 (1.16)	1.62 (1.19)
95% CI of LS mean	(-3.54, 1.02)	(-0.72, 3.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.88 (-0.38, 6.15)
Week 16 (MMRM)		
n	171	163
LS mean (SE)	80.42 (1.47)	83.67 (1.50)
95% CI of LS mean	(77.54, 83.31)	(80.71, 86.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.25 (-0.89, 7.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	167	159
LS mean (SE)	-1.82 (1.17)	-1.43 (1.21)
95% CI of LS mean	(-4.14, 0.49)	(-3.80, 0.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.40 (-2.91, 3.71)
Week 24 (MMRM)		
n	171	160
LS mean (SE)	81.58 (1.31)	85.61 (1.35)
95% CI of LS mean	(79.00, 84.15)	(82.96, 88.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.03 (0.34, 7.72)
Absolute Change at Week 24 (MMRM)		
n	167	157
LS mean (SE)	-0.56 (1.09)	0.58 (1.12)
95% CI of LS mean	(-2.70, 1.57)	(-1.62, 2.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-1.93, 4.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Week 52		
n	168	158
Mean (SD)	82.01 (18.39)	82.28 (17.65)
Absolute Change at Week 52		
n	164	153
Mean (SD)	0.03 (16.40)	-2.61 (12.79)
Week 52 (MMRM)		
n	166	154
LS mean (SE)	82.23 (1.37)	82.26 (1.41)
95% CI of LS mean	(79.54, 84.93)	(79.48, 85.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.03 (-3.84, 3.90)
Absolute Change at Week 52 (MMRM)		
n	162	150
LS mean (SE)	0.12 (1.15)	-2.54 (1.19)
95% CI of LS mean	(-2.14, 2.38)	(-4.88, -0.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.66 (-5.91, 0.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	167	159
LS mean (SE)	-0.76 (0.96)	-1.13 (0.98)
95% CI of LS mean	(-2.64, 1.13)	(-3.07, 0.81)
P-value within Treatment	0.4306	0.2517
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-3.08, 2.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7852
Hedges' G (SE)		-0.03 (0.11)
Hedges' 95% CI		(-0.25, 0.19)
Hedges' P-value		0.7852

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Baseline		
n	25	26
Mean (SD)	87.56 (14.46)	82.48 (17.55)
Week 8 (MMRM)		
n	25	26
LS mean (SE)	86.92 (3.11)	85.66 (3.05)
95% CI of LS mean	(80.66, 93.17)	(79.53, 91.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.26 (-10.05, 7.54)
Absolute Change at Week 8 (MMRM)		
n	25	26
LS mean (SE)	-0.84 (3.04)	3.37 (2.98)
95% CI of LS mean	(-6.96, 5.28)	(-2.62, 9.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.21 (-4.38, 12.80)
Week 16 (MMRM)		
n	25	26
LS mean (SE)	88.25 (3.49)	83.52 (3.43)
95% CI of LS mean	(81.22, 95.28)	(76.63, 90.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.73 (-14.61, 5.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	25	26
LS mean (SE)	0.49 (3.26)	1.23 (3.20)
95% CI of LS mean	(-6.07, 7.06)	(-5.20, 7.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.74 (-8.47, 9.95)
Week 24 (MMRM)		
n	25	26
LS mean (SE)	86.92 (2.83)	87.80 (2.77)
95% CI of LS mean	(81.22, 92.61)	(82.21, 93.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-7.13, 8.89)
Absolute Change at Week 24 (MMRM)		
n	25	26
LS mean (SE)	-0.84 (2.59)	5.51 (2.53)
95% CI of LS mean	(-6.04, 4.36)	(0.41, 10.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.35 (-0.97, 13.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Week 52		
n	24	26
Mean (SD)	87.04 (16.92)	82.91 (18.12)
Absolute Change at Week 52		
n	24	26
Mean (SD)	-0.46 (16.86)	0.43 (11.54)
Week 52 (MMRM)		
n	24	26
LS mean (SE)	86.88 (3.44)	83.09 (3.33)
95% CI of LS mean	(79.97, 93.79)	(76.39, 89.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.79 (-13.45, 5.87)
Absolute Change at Week 52 (MMRM)		
n	24	26
LS mean (SE)	-0.85 (2.84)	0.81 (2.75)
95% CI of LS mean	(-6.57, 4.86)	(-4.72, 6.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.66 (-6.31, 9.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	25	26
LS mean (SE)	-0.40 (2.29)	2.52 (2.24)
95% CI of LS mean	(-5.00, 4.20)	(-1.98, 7.02)
P-value within Treatment	0.8619	0.2663
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.92 (-3.55, 9.39)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3690
Hedges' G (SE)		0.25 (0.28)
Hedges' 95% CI		(-0.30, 0.81)
Hedges' P-value		0.3681

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Baseline		
n	172	166
Mean (SD)	93.35 (14.25)	91.23 (15.42)
Week 8 (MMRM)		
n	172	162
LS mean (SE)	92.19 (1.23)	90.71 (1.27)
95% CI of LS mean	(89.76, 94.61)	(88.22, 93.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.48 (-4.95, 2.00)
Absolute Change at Week 8 (MMRM)		
n	168	160
LS mean (SE)	-1.58 (0.89)	0.01 (0.91)
95% CI of LS mean	(-3.34, 0.17)	(-1.79, 1.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.60 (-0.92, 4.11)
Week 16 (MMRM)		
n	171	163
LS mean (SE)	91.71 (1.16)	90.09 (1.19)
95% CI of LS mean	(89.43, 93.98)	(87.75, 92.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.62 (-4.88, 1.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	167	160
LS mean (SE)	-2.18 (0.93)	-0.70 (0.95)
95% CI of LS mean	(-4.00, -0.35)	(-2.57, 1.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.47 (-1.14, 4.09)
Week 24 (MMRM)		
n	171	162
LS mean (SE)	92.73 (1.21)	90.35 (1.24)
95% CI of LS mean	(90.36, 95.11)	(87.92, 92.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.38 (-5.78, 1.02)
Absolute Change at Week 24 (MMRM)		
n	167	159
LS mean (SE)	-1.10 (0.87)	-0.43 (0.89)
95% CI of LS mean	(-2.81, 0.60)	(-2.18, 1.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.67 (-1.77, 3.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Week 52		
n	169	158
Mean (SD)	93.82 (12.76)	91.28 (17.57)
Absolute Change at Week 52		
n	165	154
Mean (SD)	-0.07 (9.70)	0.22 (12.15)
Week 52 (MMRM)		
n	167	154
LS mean (SE)	93.47 (1.17)	90.92 (1.21)
95% CI of LS mean	(91.18, 95.77)	(88.55, 93.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.55 (-5.86, 0.75)
Absolute Change at Week 52 (MMRM)		
n	163	151
LS mean (SE)	-0.36 (0.85)	0.30 (0.88)
95% CI of LS mean	(-2.03, 1.30)	(-1.42, 2.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.67 (-1.73, 3.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	167	160
LS mean (SE)	-1.21 (0.69)	-0.28 (0.71)
95% CI of LS mean	(-2.57, 0.14)	(-1.66, 1.11)
P-value within Treatment	0.0784	0.6946
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.94 (-1.00, 2.88)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3421
Hedges' G (SE)		0.11 (0.11)
Hedges' 95% CI		(-0.11, 0.32)
Hedges' P-value		0.3423

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Baseline		
n	25	26
Mean (SD)	89.33 (15.21)	90.17 (22.52)
Week 8 (MMRM)		
n	25	26
LS mean (SE)	93.72 (3.27)	89.37 (3.21)
95% CI of LS mean	(87.13, 100.30)	(82.92, 95.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.34 (-13.61, 4.92)
Absolute Change at Week 8 (MMRM)		
n	25	26
LS mean (SE)	3.06 (1.50)	0.47 (1.47)
95% CI of LS mean	(0.05, 6.08)	(-2.49, 3.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.59 (-6.84, 1.66)
Week 16 (MMRM)		
n	25	26
LS mean (SE)	92.83 (3.11)	92.79 (3.05)
95% CI of LS mean	(86.57, 99.09)	(86.66, 98.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-8.84, 8.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	25	26
LS mean (SE)	2.18 (1.91)	3.89 (1.87)
95% CI of LS mean	(-1.67, 6.02)	(0.12, 7.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.72 (-3.69, 7.12)
Week 24 (MMRM)		
n	25	26
LS mean (SE)	95.05 (3.74)	88.95 (3.67)
95% CI of LS mean	(87.52, 102.58)	(81.56, 96.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.10 (-16.69, 4.48)
Absolute Change at Week 24 (MMRM)		
n	25	26
LS mean (SE)	4.40 (2.36)	0.04 (2.31)
95% CI of LS mean	(-0.35, 9.14)	(-4.61, 4.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.35 (-11.01, 2.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Week 52		
n	24	26
Mean (SD)	93.06 (10.26)	90.60 (22.60)
Absolute Change at Week 52		
n	24	26
Mean (SD)	4.17 (13.43)	0.43 (11.96)
Week 52 (MMRM)		
n	24	26
LS mean (SE)	93.58 (3.34)	89.80 (3.25)
95% CI of LS mean	(86.87, 100.29)	(83.26, 96.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.78 (-13.19, 5.64)
Absolute Change at Week 52 (MMRM)		
n	24	26
LS mean (SE)	2.84 (2.62)	0.90 (2.54)
95% CI of LS mean	(-2.44, 8.12)	(-4.22, 6.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.94 (-9.31, 5.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	25	26
LS mean (SE)	3.14 (1.95)	1.61 (1.91)
95% CI of LS mean	(-0.80, 7.08)	(-2.24, 5.46)
P-value within Treatment	0.1154	0.4037
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.53 (-7.05, 4.00)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5805
Hedges' G (SE)		-0.15 (0.28)
Hedges' 95% CI		(-0.71, 0.40)
Hedges' P-value		0.5797

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Baseline		
n	172	166
Mean (SD)	80.59 (18.66)	82.71 (18.10)
Week 8 (MMRM)		
n	172	162
LS mean (SE)	81.13 (1.31)	83.50 (1.35)
95% CI of LS mean	(78.55, 83.70)	(80.86, 86.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-1.31, 6.07)
Absolute Change at Week 8 (MMRM)		
n	168	160
LS mean (SE)	0.00 (0.89)	1.39 (0.91)
95% CI of LS mean	(-1.75, 1.74)	(-0.40, 3.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.40 (-1.10, 3.90)
Week 16 (MMRM)		
n	171	163
LS mean (SE)	81.48 (1.36)	82.95 (1.40)
95% CI of LS mean	(78.79, 84.16)	(80.20, 85.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.47 (-2.37, 5.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	167	160
LS mean (SE)	0.23 (0.97)	0.93 (0.99)
95% CI of LS mean	(-1.67, 2.14)	(-1.02, 2.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.69 (-2.03, 3.42)
Week 24 (MMRM)		
n	171	162
LS mean (SE)	81.34 (1.32)	82.54 (1.36)
95% CI of LS mean	(78.74, 83.94)	(79.87, 85.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.20 (-2.53, 4.93)
Absolute Change at Week 24 (MMRM)		
n	167	159
LS mean (SE)	0.33 (1.04)	0.34 (1.06)
95% CI of LS mean	(-1.70, 2.37)	(-1.74, 2.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-2.91, 2.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Week 52		
n	169	158
Mean (SD)	80.89 (18.99)	82.97 (16.29)
Absolute Change at Week 52		
n	165	154
Mean (SD)	0.14 (12.87)	0.88 (13.12)
Week 52 (MMRM)		
n	167	154
LS mean (SE)	81.05 (1.35)	83.19 (1.39)
95% CI of LS mean	(78.39, 83.71)	(80.45, 85.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.14 (-1.68, 5.96)
Absolute Change at Week 52 (MMRM)		
n	163	151
LS mean (SE)	-0.03 (1.01)	0.94 (1.04)
95% CI of LS mean	(-2.01, 1.95)	(-1.11, 2.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-1.88, 3.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	167	160
LS mean (SE)	0.18 (0.86)	0.74 (0.88)
95% CI of LS mean	(-1.52, 1.88)	(-1.00, 2.48)
P-value within Treatment	0.8365	0.4055
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.56 (-1.87, 2.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6517
Hedges' G (SE)		0.05 (0.11)
Hedges' 95% CI		(-0.17, 0.27)
Hedges' P-value		0.6517

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Baseline		
n	25	26
Mean (SD)	82.13 (15.84)	79.26 (12.48)
Week 8 (MMRM)		
n	25	26
LS mean (SE)	84.18 (2.95)	79.18 (2.90)
95% CI of LS mean	(78.24, 90.13)	(73.36, 85.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.00 (-13.36, 3.36)
Absolute Change at Week 8 (MMRM)		
n	25	26
LS mean (SE)	1.75 (1.63)	0.20 (1.60)
95% CI of LS mean	(-1.52, 5.03)	(-3.01, 3.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.55 (-6.16, 3.05)
Week 16 (MMRM)		
n	25	26
LS mean (SE)	85.62 (2.94)	78.80 (2.89)
95% CI of LS mean	(79.69, 91.54)	(72.99, 84.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.82 (-15.15, 1.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	25	26
LS mean (SE)	3.19 (2.33)	-0.18 (2.29)
95% CI of LS mean	(-1.50, 7.88)	(-4.78, 4.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.37 (-9.95, 3.21)
Week 24 (MMRM)		
n	25	26
LS mean (SE)	84.02 (3.28)	81.78 (3.21)
95% CI of LS mean	(77.42, 90.61)	(75.32, 88.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.23 (-11.50, 7.03)
Absolute Change at Week 24 (MMRM)		
n	25	26
LS mean (SE)	1.59 (2.56)	2.80 (2.51)
95% CI of LS mean	(-3.56, 6.73)	(-2.24, 7.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-6.01, 8.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Week 52		
n	24	26
Mean (SD)	83.72 (15.68)	82.50 (14.63)
Absolute Change at Week 52		
n	24	26
Mean (SD)	1.77 (12.41)	3.24 (14.45)
Week 52 (MMRM)		
n	24	26
LS mean (SE)	82.61 (3.28)	82.07 (3.19)
95% CI of LS mean	(75.99, 89.24)	(75.62, 88.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.54 (-9.82, 8.73)
Absolute Change at Week 52 (MMRM)		
n	24	26
LS mean (SE)	0.12 (3.01)	3.09 (2.92)
95% CI of LS mean	(-5.99, 6.22)	(-2.84, 9.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.97 (-5.55, 11.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	25	26
LS mean (SE)	1.63 (2.30)	1.90 (2.25)
95% CI of LS mean	(-3.01, 6.28)	(-2.64, 6.45)
P-value within Treatment	0.4828	0.4035
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-6.24, 6.79)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9335
Hedges' G (SE)		0.02 (0.28)
Hedges' 95% CI		(-0.53, 0.58)
Hedges' P-value		0.9333

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Baseline		
n	172	166
Mean (SD)	81.95 (19.03)	82.68 (20.36)
Week 8 (MMRM)		
n	172	162
LS mean (SE)	79.46 (1.60)	81.80 (1.65)
95% CI of LS mean	(76.31, 82.61)	(78.56, 85.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.35 (-2.17, 6.86)
Absolute Change at Week 8 (MMRM)		
n	168	160
LS mean (SE)	-2.76 (1.20)	-0.41 (1.23)
95% CI of LS mean	(-5.12, -0.40)	(-2.83, 2.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.35 (-1.03, 5.73)
Week 16 (MMRM)		
n	171	163
LS mean (SE)	79.37 (1.56)	82.23 (1.60)
95% CI of LS mean	(76.30, 82.45)	(79.07, 85.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.85 (-1.56, 7.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	167	160
LS mean (SE)	-2.80 (1.18)	-0.17 (1.21)
95% CI of LS mean	(-5.12, -0.48)	(-2.55, 2.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-0.70, 5.95)
Week 24 (MMRM)		
n	171	162
LS mean (SE)	81.40 (1.53)	82.55 (1.57)
95% CI of LS mean	(78.39, 84.40)	(79.46, 85.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.15 (-3.16, 5.46)
Absolute Change at Week 24 (MMRM)		
n	167	159
LS mean (SE)	-0.83 (1.06)	0.20 (1.09)
95% CI of LS mean	(-2.92, 1.26)	(-1.94, 2.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.03 (-1.96, 4.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Week 52		
n	169	158
Mean (SD)	82.76 (18.90)	83.54 (19.79)
Absolute Change at Week 52		
n	165	154
Mean (SD)	0.45 (12.76)	1.44 (12.36)
Week 52 (MMRM)		
n	167	154
LS mean (SE)	82.70 (1.44)	83.83 (1.49)
95% CI of LS mean	(79.87, 85.53)	(80.91, 86.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.13 (-2.94, 5.21)
Absolute Change at Week 52 (MMRM)		
n	163	151
LS mean (SE)	0.55 (0.98)	1.54 (1.01)
95% CI of LS mean	(-1.37, 2.48)	(-0.45, 3.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.99 (-1.78, 3.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	167	160
LS mean (SE)	-1.03 (0.83)	0.52 (0.85)
95% CI of LS mean	(-2.66, 0.61)	(-1.16, 2.20)
P-value within Treatment	0.2190	0.5400
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-0.80, 3.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1949
Hedges' G (SE)		0.14 (0.11)
Hedges' 95% CI		(-0.07, 0.36)
Hedges' P-value		0.1954

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Baseline		
n	25	26
Mean (SD)	85.96 (14.97)	86.23 (15.51)
Week 8 (MMRM)		
n	25	26
LS mean (SE)	88.50 (2.69)	89.16 (2.64)
95% CI of LS mean	(83.09, 93.91)	(83.85, 94.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.66 (-6.95, 8.27)
Absolute Change at Week 8 (MMRM)		
n	25	26
LS mean (SE)	2.24 (1.89)	3.22 (1.85)
95% CI of LS mean	(-1.56, 6.04)	(-0.50, 6.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.98 (-4.36, 6.32)
Week 16 (MMRM)		
n	25	26
LS mean (SE)	89.66 (2.46)	90.44 (2.41)
95% CI of LS mean	(84.71, 94.62)	(85.58, 95.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.77 (-6.20, 7.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	25	26
LS mean (SE)	3.41 (2.29)	4.50 (2.25)
95% CI of LS mean	(-1.20, 8.01)	(-0.02, 9.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-5.38, 7.56)
Week 24 (MMRM)		
n	25	26
LS mean (SE)	90.33 (3.31)	89.81 (3.25)
95% CI of LS mean	(83.67, 96.99)	(83.28, 96.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-9.88, 8.83)
Absolute Change at Week 24 (MMRM)		
n	25	26
LS mean (SE)	4.07 (2.29)	3.87 (2.25)
95% CI of LS mean	(-0.53, 8.68)	(-0.65, 8.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-6.68, 6.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Week 52		
n	24	26
Mean (SD)	90.97 (14.31)	91.51 (10.51)
Absolute Change at Week 52		
n	24	26
Mean (SD)	5.42 (10.58)	5.28 (10.10)
Week 52 (MMRM)		
n	24	26
LS mean (SE)	90.48 (2.55)	91.51 (2.48)
95% CI of LS mean	(85.35, 95.61)	(86.50, 96.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.03 (-6.17, 8.23)
Absolute Change at Week 52 (MMRM)		
n	24	26
LS mean (SE)	4.29 (2.12)	5.57 (2.07)
95% CI of LS mean	(0.01, 8.58)	(1.40, 9.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.28 (-4.72, 7.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	25	26
LS mean (SE)	3.92 (1.94)	4.65 (1.90)
95% CI of LS mean	(0.02, 7.82)	(0.82, 8.47)
P-value within Treatment	0.0487	0.0183
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.72 (-4.76, 6.21)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7922
Hedges' G (SE)		0.07 (0.28)
Hedges' 95% CI		(-0.48, 0.63)
Hedges' P-value		0.7912

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Baseline		
n	172	166
Mean (SD)	74.51 (17.14)	75.81 (18.38)
Week 8 (MMRM)		
n	172	162
LS mean (SE)	74.77 (1.30)	76.40 (1.33)
95% CI of LS mean	(72.22, 77.32)	(73.78, 79.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-2.03, 5.29)
Absolute Change at Week 8 (MMRM)		
n	168	160
LS mean (SE)	0.12 (1.06)	1.11 (1.09)
95% CI of LS mean	(-1.97, 2.22)	(-1.03, 3.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.99 (-2.01, 3.99)
Week 16 (MMRM)		
n	171	163
LS mean (SE)	73.74 (1.41)	74.11 (1.45)
95% CI of LS mean	(70.97, 76.52)	(71.26, 76.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-3.61, 4.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	167	160
LS mean (SE)	-1.11 (1.09)	-1.14 (1.12)
95% CI of LS mean	(-3.27, 1.04)	(-3.34, 1.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-3.10, 3.06)
Week 24 (MMRM)		
n	171	162
LS mean (SE)	76.24 (1.32)	76.73 (1.36)
95% CI of LS mean	(73.64, 78.84)	(74.06, 79.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-3.24, 4.22)
Absolute Change at Week 24 (MMRM)		
n	167	159
LS mean (SE)	1.45 (1.00)	1.47 (1.02)
95% CI of LS mean	(-0.51, 3.42)	(-0.54, 3.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-2.79, 2.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Week 52		
n	169	158
Mean (SD)	77.39 (16.64)	77.11 (17.41)
Absolute Change at Week 52		
n	165	154
Mean (SD)	2.49 (12.88)	1.72 (13.27)
Week 52 (MMRM)		
n	167	154
LS mean (SE)	77.45 (1.29)	77.25 (1.33)
95% CI of LS mean	(74.91, 79.99)	(74.63, 79.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-3.85, 3.45)
Absolute Change at Week 52 (MMRM)		
n	163	151
LS mean (SE)	2.63 (1.01)	1.86 (1.05)
95% CI of LS mean	(0.64, 4.62)	(-0.20, 3.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.77 (-3.64, 2.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	167	160
LS mean (SE)	0.99 (0.87)	0.73 (0.89)
95% CI of LS mean	(-0.71, 2.69)	(-1.01, 2.48)
P-value within Treatment	0.2538	0.4109
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-2.70, 2.18)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8345
Hedges' G (SE)		-0.02 (0.11)
Hedges' 95% CI		(-0.24, 0.19)
Hedges' P-value		0.8345

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Baseline		
n	25	26
Mean (SD)	72.67 (17.71)	70.54 (17.97)
Week 8 (MMRM)		
n	25	26
LS mean (SE)	81.03 (3.35)	71.24 (3.29)
95% CI of LS mean	(74.28, 87.78)	(64.62, 77.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.79 (-19.28, -0.30)
Absolute Change at Week 8 (MMRM)		
n	25	26
LS mean (SE)	8.21 (2.36)	0.84 (2.31)
95% CI of LS mean	(3.46, 12.96)	(-3.82, 5.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.37 (-14.06, -0.69)
Week 16 (MMRM)		
n	25	26
LS mean (SE)	82.36 (3.45)	75.94 (3.38)
95% CI of LS mean	(75.42, 89.30)	(69.14, 82.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.42 (-16.18, 3.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	25	26
LS mean (SE)	9.54 (3.24)	5.54 (3.17)
95% CI of LS mean	(3.03, 16.06)	(-0.85, 11.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.01 (-13.16, 5.14)
Week 24 (MMRM)		
n	25	26
LS mean (SE)	78.58 (3.34)	76.03 (3.27)
95% CI of LS mean	(71.87, 85.29)	(69.45, 82.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.55 (-11.99, 6.89)
Absolute Change at Week 24 (MMRM)		
n	25	26
LS mean (SE)	5.77 (2.88)	5.63 (2.82)
95% CI of LS mean	(-0.02, 11.55)	(-0.04, 11.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-8.27, 7.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Week 52		
n	24	26
Mean (SD)	79.96 (12.28)	79.11 (18.20)
Absolute Change at Week 52		
n	24	26
Mean (SD)	7.74 (16.38)	8.57 (17.89)
Week 52 (MMRM)		
n	24	26
LS mean (SE)	80.28 (3.19)	78.65 (3.10)
95% CI of LS mean	(73.86, 86.70)	(72.41, 84.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.63 (-10.62, 7.36)
Absolute Change at Week 52 (MMRM)		
n	24	26
LS mean (SE)	7.38 (3.53)	8.25 (3.44)
95% CI of LS mean	(0.27, 14.49)	(1.33, 15.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-9.07, 10.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	25	26
LS mean (SE)	7.56 (2.89)	6.47 (2.83)
95% CI of LS mean	(1.74, 13.38)	(0.77, 12.17)
P-value within Treatment	0.0120	0.0269
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.09 (-9.26, 7.08)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7894
Hedges' G (SE)		-0.07 (0.28)
Hedges' 95% CI		(-0.63, 0.48)
Hedges' P-value		0.7886

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Baseline		
n	172	166
Mean (SD)	70.22 (19.48)	73.69 (18.16)
Week 8 (MMRM)		
n	171	162
LS mean (SE)	70.72 (1.47)	73.70 (1.51)
95% CI of LS mean	(67.83, 73.61)	(70.74, 76.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.98 (-1.16, 7.12)
Absolute Change at Week 8 (MMRM)		
n	167	160
LS mean (SE)	0.60 (0.97)	0.42 (0.99)
95% CI of LS mean	(-1.30, 2.50)	(-1.53, 2.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-2.90, 2.54)
Week 16 (MMRM)		
n	171	163
LS mean (SE)	70.54 (1.54)	74.06 (1.58)
95% CI of LS mean	(67.51, 73.57)	(70.94, 77.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.51 (-0.83, 7.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	167	160
LS mean (SE)	0.21 (1.03)	1.15 (1.06)
95% CI of LS mean	(-1.82, 2.24)	(-0.92, 3.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.94 (-1.96, 3.85)
Week 24 (MMRM)		
n	171	162
LS mean (SE)	72.30 (1.50)	73.74 (1.54)
95% CI of LS mean	(69.36, 75.24)	(70.72, 76.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.44 (-2.77, 5.66)
Absolute Change at Week 24 (MMRM)		
n	167	159
LS mean (SE)	2.01 (1.02)	0.47 (1.05)
95% CI of LS mean	(0.00, 4.02)	(-1.59, 2.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.54 (-4.42, 1.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Week 52		
n	169	158
Mean (SD)	73.04 (20.16)	76.93 (18.79)
Absolute Change at Week 52		
n	165	154
Mean (SD)	2.69 (15.67)	3.61 (13.01)
Week 52 (MMRM)		
n	167	154
LS mean (SE)	72.89 (1.48)	76.72 (1.53)
95% CI of LS mean	(69.98, 75.79)	(73.72, 79.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.84 (-0.34, 8.02)
Absolute Change at Week 52 (MMRM)		
n	163	151
LS mean (SE)	2.55 (1.14)	3.38 (1.17)
95% CI of LS mean	(0.31, 4.79)	(1.07, 5.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.83 (-2.38, 4.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	167	160
LS mean (SE)	1.59 (0.89)	1.67 (0.91)
95% CI of LS mean	(-0.16, 3.34)	(-0.13, 3.46)
P-value within Treatment	0.0748	0.0688
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-2.43, 2.59)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9527
Hedges' G (SE)		0.01 (0.11)
Hedges' 95% CI		(-0.21, 0.22)
Hedges' P-value		0.9527

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Baseline		
n	25	26
Mean (SD)	71.56 (24.23)	63.25 (26.62)
Week 8 (MMRM)		
n	25	26
LS mean (SE)	72.45 (4.26)	68.80 (4.18)
95% CI of LS mean	(63.85, 81.04)	(60.38, 77.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.64 (-15.73, 8.44)
Absolute Change at Week 8 (MMRM)		
n	25	26
LS mean (SE)	0.49 (4.18)	5.94 (4.10)
95% CI of LS mean	(-7.93, 8.91)	(-2.31, 14.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.46 (-6.39, 17.30)
Week 16 (MMRM)		
n	25	26
LS mean (SE)	71.11 (4.34)	65.38 (4.25)
95% CI of LS mean	(62.38, 79.85)	(56.82, 73.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.73 (-18.01, 6.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 16 (MMRM)		
n	25	26
LS mean (SE)	-0.85 (4.64)	2.52 (4.54)
95% CI of LS mean	(-10.18, 8.49)	(-6.63, 11.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.37 (-9.75, 16.49)
Week 24 (MMRM)		
n	25	26
LS mean (SE)	73.33 (4.60)	67.95 (4.51)
95% CI of LS mean	(64.09, 82.58)	(58.88, 77.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.39 (-18.38, 7.61)
Absolute Change at Week 24 (MMRM)		
n	25	26
LS mean (SE)	1.38 (4.21)	5.09 (4.13)
95% CI of LS mean	(-7.11, 9.86)	(-3.23, 13.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.71 (-8.22, 15.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Week 52		
n	24	26
Mean (SD)	78.24 (17.79)	72.65 (19.93)
Absolute Change at Week 52		
n	24	26
Mean (SD)	6.48 (18.22)	9.40 (25.28)
Week 52 (MMRM)		
n	24	26
LS mean (SE)	77.93 (3.81)	72.22 (3.71)
95% CI of LS mean	(70.26, 85.60)	(64.76, 79.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.71 (-16.46, 5.05)
Absolute Change at Week 52 (MMRM)		
n	24	26
LS mean (SE)	5.83 (4.59)	9.36 (4.46)
95% CI of LS mean	(-3.40, 15.06)	(0.37, 18.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.53 (-9.40, 16.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 26
Absolute Change through Week 52 (MMRM)		
n	25	26
LS mean (SE)	2.12 (4.04)	5.66 (3.95)
95% CI of LS mean	(-6.01, 10.25)	(-2.31, 13.62)
P-value within Treatment	0.6021	0.1595
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.54 (-7.90, 14.98)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5365
Hedges' G (SE)		0.17 (0.28)
Hedges' 95% CI		(-0.38, 0.73)
Hedges' P-value		0.5351

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Baseline		
n	165	164
Mean (SD)	71.31 (19.48)	74.59 (19.33)
Week 8 (MMRM)		
n	165	160
LS mean (SE)	69.76 (1.49)	72.68 (1.51)
95% CI of LS mean	(66.82, 72.70)	(69.70, 75.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.92 (-1.27, 7.10)
Absolute Change at Week 8 (MMRM)		
n	162	158
LS mean (SE)	-1.93 (1.09)	-1.65 (1.10)
95% CI of LS mean	(-4.07, 0.20)	(-3.81, 0.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-2.75, 3.32)
Week 16 (MMRM)		
n	163	161
LS mean (SE)	71.18 (1.53)	72.64 (1.54)
95% CI of LS mean	(68.18, 74.18)	(69.61, 75.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.46 (-2.81, 5.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Absolute Change at Week 16 (MMRM)		
n	160	159
LS mean (SE)	-0.85 (1.12)	-1.62 (1.12)
95% CI of LS mean	(-3.05, 1.35)	(-3.83, 0.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.78 (-3.89, 2.34)
Week 24 (MMRM)		
n	163	160
LS mean (SE)	70.43 (1.54)	74.18 (1.55)
95% CI of LS mean	(67.40, 73.45)	(71.13, 77.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.75 (-0.55, 8.05)
Absolute Change at Week 24 (MMRM)		
n	160	158
LS mean (SE)	-1.48 (1.06)	-0.33 (1.07)
95% CI of LS mean	(-3.57, 0.62)	(-2.44, 1.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.15 (-1.83, 4.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Week 52		
n	161	156
Mean (SD)	72.08 (20.34)	74.72 (20.02)
Absolute Change at Week 52		
n	158	153
Mean (SD)	0.39 (12.23)	0.07 (14.67)
Week 52 (MMRM)		
n	159	152
LS mean (SE)	72.66 (1.53)	74.95 (1.55)
95% CI of LS mean	(69.65, 75.68)	(71.89, 78.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.29 (-2.00, 6.58)
Absolute Change at Week 52 (MMRM)		
n	156	150
LS mean (SE)	0.71 (1.08)	0.34 (1.10)
95% CI of LS mean	(-1.42, 2.83)	(-1.82, 2.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-3.39, 2.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Absolute Change through Week 52 (MMRM)		
n	160	159
LS mean (SE)	-0.54 (0.85)	-0.54 (0.85)
95% CI of LS mean	(-2.20, 1.13)	(-2.22, 1.14)
P-value within Treatment	0.5250	0.5289
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-2.36, 2.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9992
Hedges' G (SE)		0.00 (0.11)
Hedges' 95% CI		(-0.22, 0.22)
Hedges' P-value		0.9992

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Baseline		
n	24	23
Mean (SD)	69.91 (17.79)	69.08 (20.64)
Week 8 (MMRM)		
n	24	23
LS mean (SE)	75.42 (3.75)	74.45 (3.83)
95% CI of LS mean	(67.86, 82.98)	(66.72, 82.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-11.93, 9.99)
Absolute Change at Week 8 (MMRM)		
n	24	23
LS mean (SE)	4.81 (3.01)	6.10 (3.08)
95% CI of LS mean	(-1.27, 10.88)	(-0.11, 12.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.29 (-7.51, 10.09)
Week 16 (MMRM)		
n	24	23
LS mean (SE)	73.56 (4.40)	73.48 (4.50)
95% CI of LS mean	(64.69, 82.44)	(64.41, 82.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-12.90, 12.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 16 (MMRM)		
n	24	23
LS mean (SE)	2.95 (3.20)	5.13 (3.27)
95% CI of LS mean	(-3.50, 9.40)	(-1.46, 11.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.18 (-7.15, 11.51)
Week 24 (MMRM)		
n	24	23
LS mean (SE)	70.32 (4.81)	72.51 (4.92)
95% CI of LS mean	(60.61, 80.04)	(62.59, 82.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-11.81, 16.19)
Absolute Change at Week 24 (MMRM)		
n	24	23
LS mean (SE)	-0.29 (3.74)	4.16 (3.82)
95% CI of LS mean	(-7.84, 7.26)	(-3.55, 11.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.45 (-6.43, 15.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Week 52		
n	23	23
Mean (SD)	76.81 (17.05)	76.81 (20.63)
Absolute Change at Week 52		
n	23	23
Mean (SD)	6.76 (15.98)	7.73 (15.87)
Week 52 (MMRM)		
n	23	23
LS mean (SE)	75.51 (4.08)	76.38 (4.13)
95% CI of LS mean	(67.26, 83.75)	(68.01, 84.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-11.01, 12.75)
Absolute Change at Week 52 (MMRM)		
n	23	23
LS mean (SE)	5.26 (3.50)	8.03 (3.53)
95% CI of LS mean	(-1.81, 12.33)	(0.89, 15.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.77 (-7.37, 12.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Absolute Change through Week 52 (MMRM)		
n	24	23
LS mean (SE)	2.64 (3.01)	5.77 (3.07)
95% CI of LS mean	(-3.43, 8.72)	(-0.42, 11.97)
P-value within Treatment	0.3847	0.0670
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.13 (-5.66, 11.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4758
Hedges' G (SE)		0.21 (0.29)
Hedges' 95% CI		(-0.37, 0.79)
Hedges' P-value		0.4709

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Baseline		
n	165	163
Mean (SD)	87.93 (16.68)	87.68 (15.50)
Week 8 (MMRM)		
n	164	160
LS mean (SE)	86.67 (1.19)	87.33 (1.21)
95% CI of LS mean	(84.33, 89.02)	(84.95, 89.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-2.69, 3.99)
Absolute Change at Week 8 (MMRM)		
n	161	157
LS mean (SE)	-1.36 (1.00)	-0.18 (1.01)
95% CI of LS mean	(-3.33, 0.61)	(-2.17, 1.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.18 (-1.62, 3.99)
Week 16 (MMRM)		
n	163	161
LS mean (SE)	85.34 (1.27)	88.35 (1.28)
95% CI of LS mean	(82.84, 87.85)	(85.82, 90.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.00 (-0.55, 6.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Absolute Change at Week 16 (MMRM)		
n	160	158
LS mean (SE)	-2.52 (1.13)	1.32 (1.14)
95% CI of LS mean	(-4.75, -0.29)	(-0.92, 3.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.85 (0.68, 7.01)
Week 24 (MMRM)		
n	163	159
LS mean (SE)	86.62 (1.22)	87.63 (1.24)
95% CI of LS mean	(84.21, 89.02)	(85.20, 90.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.02 (-2.41, 4.44)
Absolute Change at Week 24 (MMRM)		
n	160	156
LS mean (SE)	-1.48 (1.05)	0.35 (1.07)
95% CI of LS mean	(-3.55, 0.60)	(-1.74, 2.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.83 (-1.12, 4.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Week 52		
n	160	156
Mean (SD)	88.44 (15.01)	88.30 (15.26)
Absolute Change at Week 52		
n	157	152
Mean (SD)	0.32 (11.32)	1.10 (14.15)
Week 52 (MMRM)		
n	158	152
LS mean (SE)	88.36 (1.19)	88.29 (1.20)
95% CI of LS mean	(86.02, 90.69)	(85.92, 90.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-3.39, 3.26)
Absolute Change at Week 52 (MMRM)		
n	155	149
LS mean (SE)	0.35 (1.02)	0.94 (1.03)
95% CI of LS mean	(-1.65, 2.35)	(-1.09, 2.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-2.26, 3.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Absolute Change through Week 52 (MMRM)		
n	160	158
LS mean (SE)	-1.22 (0.87)	0.87 (0.88)
95% CI of LS mean	(-2.94, 0.50)	(-0.87, 2.61)
P-value within Treatment	0.1655	0.3243
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.09 (-0.36, 4.53)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0941
Hedges' G (SE)		0.19 (0.11)
Hedges' 95% CI		(-0.03, 0.41)
Hedges' P-value		0.0948

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Baseline		
n	24	23
Mean (SD)	85.76 (18.79)	85.14 (17.76)
Week 8 (MMRM)		
n	24	23
LS mean (SE)	90.40 (2.52)	90.09 (2.58)
95% CI of LS mean	(85.32, 95.48)	(84.89, 95.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-7.67, 7.05)
Absolute Change at Week 8 (MMRM)		
n	24	23
LS mean (SE)	3.49 (2.59)	6.14 (2.65)
95% CI of LS mean	(-1.73, 8.72)	(0.79, 11.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.65 (-4.94, 10.23)
Week 16 (MMRM)		
n	24	23
LS mean (SE)	90.40 (2.43)	91.54 (2.49)
95% CI of LS mean	(85.49, 95.31)	(86.53, 96.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-5.97, 8.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 16 (MMRM)		
n	24	23
LS mean (SE)	3.49 (2.91)	7.59 (2.97)
95% CI of LS mean	(-2.37, 9.35)	(1.60, 13.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.09 (-4.38, 12.57)
Week 24 (MMRM)		
n	24	23
LS mean (SE)	89.36 (2.38)	91.54 (2.44)
95% CI of LS mean	(84.55, 94.16)	(86.63, 96.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.18 (-4.79, 9.15)
Absolute Change at Week 24 (MMRM)		
n	24	23
LS mean (SE)	2.45 (3.18)	7.59 (3.25)
95% CI of LS mean	(-3.97, 8.87)	(1.03, 14.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.14 (-4.13, 14.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Week 52		
n	23	23
Mean (SD)	91.30 (12.93)	91.67 (10.66)
Absolute Change at Week 52		
n	23	23
Mean (SD)	6.16 (17.08)	6.52 (17.22)
Week 52 (MMRM)		
n	23	23
LS mean (SE)	91.31 (2.42)	91.18 (2.46)
95% CI of LS mean	(86.42, 96.20)	(86.22, 96.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-7.19, 6.93)
Absolute Change at Week 52 (MMRM)		
n	23	23
LS mean (SE)	4.16 (3.76)	7.22 (3.82)
95% CI of LS mean	(-3.42, 11.73)	(-0.49, 14.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.07 (-7.82, 13.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Absolute Change through Week 52 (MMRM)		
n	24	23
LS mean (SE)	3.37 (3.11)	7.47 (3.17)
95% CI of LS mean	(-2.90, 9.64)	(1.06, 13.87)
P-value within Treatment	0.2848	0.0234
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.10 (-4.95, 13.15)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3661
Hedges' G (SE)		0.26 (0.29)
Hedges' 95% CI		(-0.32, 0.85)
Hedges' P-value		0.3631

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Baseline		
n	165	164
Mean (SD)	65.94 (17.76)	69.16 (20.81)
Week 8 (MMRM)		
n	165	160
LS mean (SE)	64.42 (1.53)	67.33 (1.55)
95% CI of LS mean	(61.42, 67.42)	(64.29, 70.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.91 (-1.37, 7.18)
Absolute Change at Week 8 (MMRM)		
n	162	158
LS mean (SE)	-1.91 (1.40)	-1.55 (1.42)
95% CI of LS mean	(-4.66, 0.84)	(-4.34, 1.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-3.56, 4.27)
Week 16 (MMRM)		
n	163	161
LS mean (SE)	63.31 (1.61)	67.60 (1.63)
95% CI of LS mean	(60.14, 66.49)	(64.40, 70.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.29 (-0.22, 8.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Absolute Change at Week 16 (MMRM)		
n	160	159
LS mean (SE)	-2.78 (1.32)	-0.99 (1.32)
95% CI of LS mean	(-5.37, -0.18)	(-3.59, 1.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.79 (-1.89, 5.46)
Week 24 (MMRM)		
n	163	160
LS mean (SE)	63.21 (1.62)	67.36 (1.64)
95% CI of LS mean	(60.02, 66.40)	(64.14, 70.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.15 (-0.39, 8.68)
Absolute Change at Week 24 (MMRM)		
n	160	158
LS mean (SE)	-3.04 (1.34)	-1.63 (1.35)
95% CI of LS mean	(-5.67, -0.41)	(-4.28, 1.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.40 (-2.33, 5.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Week 52		
n	161	156
Mean (SD)	66.25 (18.68)	68.38 (20.23)
Absolute Change at Week 52		
n	158	153
Mean (SD)	-0.09 (14.76)	-0.65 (18.52)
Week 52 (MMRM)		
n	159	152
LS mean (SE)	66.21 (1.52)	68.44 (1.55)
95% CI of LS mean	(63.22, 69.21)	(65.40, 71.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.23 (-2.04, 6.50)
Absolute Change at Week 52 (MMRM)		
n	156	150
LS mean (SE)	-0.12 (1.34)	-0.60 (1.36)
95% CI of LS mean	(-2.76, 2.52)	(-3.28, 2.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-4.24, 3.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Absolute Change through Week 52 (MMRM)		
n	160	159
LS mean (SE)	-1.98 (1.08)	-1.08 (1.09)
95% CI of LS mean	(-4.11, 0.15)	(-3.22, 1.07)
P-value within Treatment	0.0688	0.3252
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.90 (-2.12, 3.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5575
Hedges' G (SE)		0.07 (0.11)
Hedges' 95% CI		(-0.15, 0.29)
Hedges' P-value		0.5576

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Baseline		
n	24	23
Mean (SD)	72.57 (16.57)	73.19 (13.52)
Week 8 (MMRM)		
n	24	23
LS mean (SE)	70.15 (3.62)	70.64 (3.70)
95% CI of LS mean	(62.85, 77.46)	(63.17, 78.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-10.11, 11.08)
Absolute Change at Week 8 (MMRM)		
n	24	23
LS mean (SE)	-3.07 (3.14)	-1.87 (3.20)
95% CI of LS mean	(-9.39, 3.25)	(-8.33, 4.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.19 (-7.94, 10.33)
Week 16 (MMRM)		
n	24	23
LS mean (SE)	74.32 (3.63)	68.10 (3.71)
95% CI of LS mean	(67.01, 81.64)	(60.62, 75.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.22 (-16.83, 4.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 16 (MMRM)		
n	24	23
LS mean (SE)	1.10 (2.86)	-4.41 (2.92)
95% CI of LS mean	(-4.66, 6.86)	(-10.29, 1.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.51 (-13.85, 2.83)
Week 24 (MMRM)		
n	24	23
LS mean (SE)	72.59 (4.04)	68.10 (4.13)
95% CI of LS mean	(64.44, 80.73)	(59.77, 76.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.49 (-16.27, 7.30)
Absolute Change at Week 24 (MMRM)		
n	24	23
LS mean (SE)	-0.64 (3.18)	-4.41 (3.25)
95% CI of LS mean	(-7.05, 5.78)	(-10.96, 2.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.77 (-13.04, 5.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Week 52		
n	23	23
Mean (SD)	71.38 (17.91)	72.83 (18.50)
Absolute Change at Week 52		
n	23	23
Mean (SD)	-1.45 (15.82)	-0.36 (15.59)
Week 52 (MMRM)		
n	23	23
LS mean (SE)	71.37 (3.88)	72.09 (3.93)
95% CI of LS mean	(63.54, 79.20)	(64.15, 80.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.71 (-10.57, 12.00)
Absolute Change at Week 52 (MMRM)		
n	23	23
LS mean (SE)	-1.81 (3.25)	-0.42 (3.28)
95% CI of LS mean	(-8.36, 4.75)	(-7.04, 6.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.38 (-8.03, 10.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Absolute Change through Week 52 (MMRM)		
n	24	23
LS mean (SE)	-0.45 (2.61)	-3.08 (2.66)
95% CI of LS mean	(-5.71, 4.82)	(-8.45, 2.29)
P-value within Treatment	0.8646	0.2537
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.63 (-10.28, 5.01)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4909
Hedges' G (SE)		-0.20 (0.29)
Hedges' 95% CI		(-0.78, 0.38)
Hedges' P-value		0.4849

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Baseline		
n	165	164
Mean (SD)	86.06 (26.56)	82.93 (28.72)
Week 8 (MMRM)		
n	164	160
LS mean (SE)	85.72 (2.09)	82.90 (2.11)
95% CI of LS mean	(81.61, 89.82)	(78.74, 87.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.82 (-8.66, 3.03)
Absolute Change at Week 8 (MMRM)		
n	161	158
LS mean (SE)	-0.40 (1.63)	0.20 (1.65)
95% CI of LS mean	(-3.62, 2.81)	(-3.04, 3.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (-3.96, 5.16)
Week 16 (MMRM)		
n	163	161
LS mean (SE)	83.56 (2.19)	83.53 (2.21)
95% CI of LS mean	(79.25, 87.87)	(79.18, 87.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-6.15, 6.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Absolute Change at Week 16 (MMRM)		
n	160	159
LS mean (SE)	-2.62 (1.91)	0.83 (1.92)
95% CI of LS mean	(-6.38, 1.14)	(-2.95, 4.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.45 (-1.88, 8.79)
Week 24 (MMRM)		
n	163	159
LS mean (SE)	85.60 (2.23)	83.19 (2.26)
95% CI of LS mean	(81.20, 89.99)	(78.75, 87.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.41 (-8.66, 3.84)
Absolute Change at Week 24 (MMRM)		
n	160	157
LS mean (SE)	-0.33 (1.91)	0.47 (1.93)
95% CI of LS mean	(-4.09, 3.43)	(-3.32, 4.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.80 (-4.54, 6.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Week 52		
n	160	156
Mean (SD)	87.29 (23.61)	83.33 (26.91)
Absolute Change at Week 52		
n	157	153
Mean (SD)	1.06 (24.00)	0.00 (21.29)
Week 52 (MMRM)		
n	158	152
LS mean (SE)	86.76 (2.02)	82.37 (2.05)
95% CI of LS mean	(82.79, 90.74)	(78.33, 86.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.40 (-10.06, 1.27)
Absolute Change at Week 52 (MMRM)		
n	155	150
LS mean (SE)	0.70 (1.81)	-0.40 (1.84)
95% CI of LS mean	(-2.87, 4.26)	(-4.01, 3.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.10 (-6.17, 3.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 168	VNZ/TEZ/D-IVA N = 167
Absolute Change through Week 52 (MMRM)		
n	160	159
LS mean (SE)	-0.75 (1.59)	0.30 (1.61)
95% CI of LS mean	(-3.89, 2.38)	(-2.86, 3.46)
P-value within Treatment	0.6369	0.8522
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.05 (-3.40, 5.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6422
Hedges' G (SE)		0.05 (0.11)
Hedges' 95% CI		(-0.17, 0.27)
Hedges' P-value		0.6422

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Baseline		
n	24	23
Mean (SD)	76.39 (28.62)	78.26 (31.15)
Week 8 (MMRM)		
n	24	23
LS mean (SE)	85.05 (5.42)	83.72 (5.54)
95% CI of LS mean	(74.11, 95.99)	(72.53, 94.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.34 (-17.21, 14.53)
Absolute Change at Week 8 (MMRM)		
n	24	23
LS mean (SE)	6.44 (4.88)	7.78 (4.99)
95% CI of LS mean	(-3.41, 16.28)	(-2.29, 17.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.34 (-12.91, 15.60)
Week 16 (MMRM)		
n	24	23
LS mean (SE)	75.33 (6.68)	76.47 (6.83)
95% CI of LS mean	(61.86, 88.80)	(62.71, 90.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-18.30, 20.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 16 (MMRM)		
n	24	23
LS mean (SE)	-3.29 (5.03)	0.53 (5.14)
95% CI of LS mean	(-13.43, 6.86)	(-9.84, 10.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.82 (-10.85, 18.49)
Week 24 (MMRM)		
n	24	23
LS mean (SE)	80.88 (6.09)	77.92 (6.23)
95% CI of LS mean	(68.60, 93.17)	(65.36, 90.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.97 (-20.73, 14.80)
Absolute Change at Week 24 (MMRM)		
n	24	23
LS mean (SE)	2.27 (5.50)	1.98 (5.63)
95% CI of LS mean	(-8.83, 13.36)	(-9.36, 13.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-16.31, 15.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Week 52		
n	23	23
Mean (SD)	78.26 (31.15)	76.81 (29.19)
Absolute Change at Week 52		
n	23	23
Mean (SD)	1.45 (30.94)	-1.45 (25.58)
Week 52 (MMRM)		
n	23	23
LS mean (SE)	78.43 (6.27)	75.02 (6.35)
95% CI of LS mean	(65.80, 91.06)	(62.22, 87.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.41 (-21.58, 14.76)
Absolute Change at Week 52 (MMRM)		
n	23	23
LS mean (SE)	-0.29 (5.98)	-0.92 (6.04)
95% CI of LS mean	(-12.34, 11.75)	(-13.10, 11.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.62 (-17.90, 16.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.3.2.3
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 23
Absolute Change through Week 52 (MMRM)		
n	24	23
LS mean (SE)	-0.44 (4.80)	0.53 (4.90)
95% CI of LS mean	(-10.11, 9.24)	(-9.34, 10.40)
P-value within Treatment	0.9278	0.9141
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-13.03, 14.97)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8898
Hedges' G (SE)		0.04 (0.29)
Hedges' 95% CI		(-0.54, 0.62)
Hedges' P-value		0.8883

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	-
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6
Subgroup criteria are not met for this subgroup factor.		

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.9.4.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6364
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.4824
Region (North America vs. Rest of the World) [1]	0.8582

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.12.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6968
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.2381
Region (North America vs. Rest of the World) [1]	0.1158

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.12.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.2214
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.7160
Region (North America vs. Rest of the World) [1]	0.7554

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.12.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0939
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.7154
Region (North America vs. Rest of the World) [1]	0.1247

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.12.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Effectiveness

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.1338

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.12.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Side Effects

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.1376

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.12.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Convenience

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.3521

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.12.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Global Satisfaction

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no)	0.7889

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$ and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Baseline		
n	9	5
Mean (SD)	80.86 (12.14)	74.44 (42.05)
Week 52		
n	8	5
Mean (SD)	82.64 (10.04)	86.67 (11.52)
Absolute Change at Week 52		
n	8	5
Mean (SD)	0.69 (8.63)	12.22 (44.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Absolute Change at Week 52 (MMRM)		
n	8	5
LS mean (SE)	1.73 (10.26)	10.56 (13.03)
95% CI of LS mean	(-21.49, 24.95)	(-18.92, 40.04)
P-value within Treatment	0.8696	0.4387
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.82 (-28.99, 46.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6103
Hedges' G (SE)		0.28 (0.53)
Hedges' 95% CI		(-0.89, 1.46)
Hedges' P-value		0.6069

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	19
Mean (SD)	80.56 (15.78)	79.82 (24.51)
Week 52		
n	20	18
Mean (SD)	83.06 (18.86)	83.64 (16.66)
Absolute Change at Week 52		
n	20	17
Mean (SD)	2.78 (23.05)	5.88 (25.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	17
LS mean (SE)	3.05 (5.58)	5.56 (6.06)
95% CI of LS mean	(-8.31, 14.41)	(-6.77, 17.89)
P-value within Treatment	0.5884	0.3655
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.51 (-14.34, 19.36)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7637
Hedges' G (SE)		0.10 (0.32)
Hedges' 95% CI		(-0.56, 0.75)
Hedges' P-value		0.7626

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 27	VNZ/TEZ/D-IVA N = 25

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Baseline		
n	19	11
Mean (SD)	79.24 (16.44)	73.74 (37.28)
Week 52		
n	18	10
Mean (SD)	82.72 (18.07)	85.56 (14.39)
Absolute Change at Week 52		
n	18	10
Mean (SD)	2.78 (22.08)	14.44 (40.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	18	10
LS mean (SE)	3.33 (7.23)	13.45 (9.73)
95% CI of LS mean	(-11.59, 18.25)	(-6.63, 33.53)
P-value within Treatment	0.6491	0.1796
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.12 (-15.02, 35.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4144
Hedges' G (SE)		0.32 (0.39)
Hedges' 95% CI		(-0.47, 1.11)
Hedges' P-value		0.4139

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	14
Mean (SD)	82.87 (11.47)	84.13 (17.28)
Week 52		
n	10	14
Mean (SD)	83.33 (14.58)	84.52 (16.76)
Absolute Change at Week 52		
n	10	13
Mean (SD)	1.11 (16.10)	1.28 (15.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	10	12
LS mean (SE)	3.09 (5.37)	-0.26 (4.86)
95% CI of LS mean	(-8.19, 14.37)	(-10.48, 9.96)
P-value within Treatment	0.5721	0.9580
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.35 (-19.18, 12.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6621
Hedges' G (SE)		-0.19 (0.41)
Hedges' 95% CI		(-1.05, 0.67)
Hedges' P-value		0.6494

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Baseline		
n	15	10
Mean (SD)	80.74 (15.69)	73.89 (28.93)
Week 52		
n	14	10
Mean (SD)	83.33 (12.52)	78.89 (18.11)
Absolute Change at Week 52		
n	14	10
Mean (SD)	1.59 (13.15)	5.00 (31.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 52 (MMRM)		
n	14	10
LS mean (SE)	0.67 (6.51)	6.28 (7.83)
95% CI of LS mean	(-12.90, 14.24)	(-10.05, 22.61)
P-value within Treatment	0.9185	0.4319
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.61 (-16.63, 27.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6048
Hedges' G (SE)		0.22 (0.40)
Hedges' 95% CI		(-0.61, 1.05)
Hedges' P-value		0.5874

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Baseline		
n	16	15
Mean (SD)	80.56 (14.05)	83.33 (27.22)
Week 52		
n	14	14
Mean (SD)	82.54 (20.42)	89.29 (12.22)
Absolute Change at Week 52		
n	14	13
Mean (SD)	2.78 (25.39)	8.55 (28.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Absolute Change at Week 52 (MMRM)		
n	14	12
LS mean (SE)	2.58 (7.65)	9.49 (8.27)
95% CI of LS mean	(-13.28, 18.45)	(-7.67, 26.64)
P-value within Treatment	0.7389	0.2638
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.90 (-16.61, 30.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5487
Hedges' G (SE)		0.23 (0.38)
Hedges' 95% CI		(-0.56, 1.02)
Hedges' P-value		0.5472

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Baseline		
n	9	5
Mean (SD)	93.06 (18.60)	100.00 (0.00)
Week 52		
n	8	5
Mean (SD)	96.09 (8.80)	100.00 (0.00)
Absolute Change at Week 52		
n	8	5
Mean (SD)	3.91 (11.05)	0.00 (0.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Absolute Change at Week 52 (MMRM)		
n	8	5
LS mean (SE)	3.96 (2.74)	-0.08 (3.48)
95% CI of LS mean	(-2.24, 10.15)	(-7.95, 7.78)
P-value within Treatment	0.1822	0.9813
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.04 (-14.13, 6.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3884
Hedges' G (SE)		-0.48 (0.54)
Hedges' 95% CI		(-1.67, 0.70)
Hedges' P-value		0.3875

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	18
Mean (SD)	97.44 (10.68)	98.26 (4.70)
Week 52		
n	20	18
Mean (SD)	97.19 (8.72)	93.75 (15.01)
Absolute Change at Week 52		
n	20	16
Mean (SD)	-2.50 (8.93)	-3.52 (12.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	16
LS mean (SE)	-2.69 (2.35)	-3.28 (2.63)
95% CI of LS mean	(-7.48, 2.10)	(-8.64, 2.08)
P-value within Treatment	0.2617	0.2213
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.60 (-7.83, 6.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8676
Hedges' G (SE)		-0.06 (0.33)
Hedges' 95% CI		(-0.72, 0.61)
Hedges' P-value		0.8668

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 27	VNZ/TEZ/D-IVA N = 25

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Baseline		
n	19	11
Mean (SD)	97.04 (12.90)	100.00 (0.00)
Week 52		
n	18	10
Mean (SD)	97.22 (8.08)	96.25 (11.86)
Absolute Change at Week 52		
n	18	10
Mean (SD)	0.35 (9.70)	-3.75 (11.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	18	10
LS mean (SE)	0.57 (2.47)	-4.15 (3.32)
95% CI of LS mean	(-4.53, 5.66)	(-11.00, 2.71)
P-value within Treatment	0.8201	0.2239
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.71 (-13.29, 3.87)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2681
Hedges' G (SE)		-0.44 (0.39)
Hedges' 95% CI		(-1.23, 0.36)
Hedges' P-value		0.2699

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	13
Mean (SD)	94.79 (14.31)	97.60 (5.44)
Week 52		
n	10	14
Mean (SD)	96.25 (9.86)	94.64 (14.47)
Absolute Change at Week 52		
n	10	12
Mean (SD)	-2.50 (10.29)	-1.56 (9.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	10	11
LS mean (SE)	-3.50 (3.47)	-0.79 (3.29)
95% CI of LS mean	(-10.82, 3.81)	(-7.73, 6.15)
P-value within Treatment	0.3263	0.8126
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.71 (-7.84, 13.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5949
Hedges' G (SE)		0.24 (0.42)
Hedges' 95% CI		(-0.64, 1.12)
Hedges' P-value		0.5784

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Baseline		
n	15	9
Mean (SD)	96.25 (14.52)	97.92 (6.25)
Week 52		
n	14	10
Mean (SD)	95.98 (10.29)	91.25 (18.68)
Absolute Change at Week 52		
n	14	9
Mean (SD)	0.00 (12.26)	-7.64 (15.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 52 (MMRM)		
n	14	9
LS mean (SE)	0.61 (3.55)	-8.58 (4.56)
95% CI of LS mean	(-6.83, 8.04)	(-18.13, 0.97)
P-value within Treatment	0.8666	0.0754
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.19 (-22.03, 3.66)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1510
Hedges' G (SE)		-0.66 (0.42)
Hedges' 95% CI		(-1.54, 0.22)
Hedges' P-value		0.1346

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Baseline		
n	16	15
Mean (SD)	96.09 (12.47)	99.17 (2.20)
Week 52		
n	14	14
Mean (SD)	97.77 (6.76)	98.21 (6.68)
Absolute Change at Week 52		
n	14	13
Mean (SD)	-1.34 (7.01)	0.96 (2.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Absolute Change at Week 52 (MMRM)		
n	14	12
LS mean (SE)	-1.13 (1.46)	0.79 (1.57)
95% CI of LS mean	(-4.15, 1.89)	(-2.47, 4.06)
P-value within Treatment	0.4472	0.6191
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.92 (-2.55, 6.39)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3830
Hedges' G (SE)		0.34 (0.38)
Hedges' 95% CI		(-0.45, 1.13)
Hedges' P-value		0.3829

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Baseline		
n	9	5
Mean (SD)	74.69 (15.49)	83.33 (10.39)
Week 52		
n	8	5
Mean (SD)	87.50 (18.96)	84.44 (10.69)
Absolute Change at Week 52		
n	8	5
Mean (SD)	11.81 (17.68)	1.11 (16.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Absolute Change at Week 52 (MMRM)		
n	8	5
LS mean (SE)	11.34 (5.51)	1.86 (6.99)
95% CI of LS mean	(-1.12, 23.80)	(-13.96, 17.67)
P-value within Treatment	0.0696	0.7967
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.49 (-29.77, 10.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3178
Hedges' G (SE)		-0.57 (0.54)
Hedges' 95% CI		(-1.76, 0.63)
Hedges' P-value		0.3188

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	19
Mean (SD)	80.30 (14.52)	82.16 (16.73)
Week 52		
n	20	18
Mean (SD)	80.28 (23.12)	85.80 (13.64)
Absolute Change at Week 52		
n	20	17
Mean (SD)	0.28 (17.70)	4.25 (15.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	17
LS mean (SE)	0.04 (3.71)	4.53 (4.03)
95% CI of LS mean	(-7.51, 7.59)	(-3.67, 12.73)
P-value within Treatment	0.9914	0.2694
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.49 (-6.72, 15.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4210
Hedges' G (SE)		0.26 (0.32)
Hedges' 95% CI		(-0.39, 0.92)
Hedges' P-value		0.4205

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 27	VNZ/TEZ/D-IVA N = 25

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Baseline		
n	19	11
Mean (SD)	78.95 (13.30)	82.83 (13.71)
Week 52		
n	18	10
Mean (SD)	82.10 (23.92)	86.67 (9.87)
Absolute Change at Week 52		
n	18	10
Mean (SD)	2.47 (20.54)	5.00 (12.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	18	10
LS mean (SE)	2.94 (4.30)	4.15 (5.79)
95% CI of LS mean	(-5.94, 11.82)	(-7.80, 16.10)
P-value within Treatment	0.5007	0.4802
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-13.75, 16.17)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8687
Hedges' G (SE)		0.06 (0.38)
Hedges' 95% CI		(-0.72, 0.85)
Hedges' P-value		0.8679

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	14
Mean (SD)	78.24 (17.48)	83.33 (17.30)
Week 52		
n	10	14
Mean (SD)	82.78 (18.97)	85.71 (15.05)
Absolute Change at Week 52		
n	10	13
Mean (SD)	5.56 (13.61)	2.14 (17.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	10	12
LS mean (SE)	6.09 (5.56)	1.87 (5.04)
95% CI of LS mean	(-5.59, 17.77)	(-8.71, 12.45)
P-value within Treatment	0.2877	0.7150
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.22 (-20.62, 12.17)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5951
Hedges' G (SE)		-0.23 (0.41)
Hedges' 95% CI		(-1.09, 0.63)
Hedges' P-value		0.5808

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Baseline		
n	15	10
Mean (SD)	78.15 (16.33)	82.78 (15.81)
Week 52		
n	14	10
Mean (SD)	83.73 (19.91)	85.00 (14.12)
Absolute Change at Week 52		
n	14	10
Mean (SD)	4.76 (15.69)	2.22 (14.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 52 (MMRM)		
n	14	10
LS mean (SE)	3.90 (3.95)	3.43 (4.76)
95% CI of LS mean	(-4.35, 12.15)	(-6.50, 13.35)
P-value within Treatment	0.3359	0.4793
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-13.99, 13.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9430
Hedges' G (SE)		-0.03 (0.40)
Hedges' 95% CI		(-0.86, 0.80)
Hedges' P-value		0.9400

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Baseline		
n	16	15
Mean (SD)	79.17 (13.68)	83.33 (15.85)
Week 52		
n	14	14
Mean (SD)	80.95 (24.43)	86.90 (12.44)
Absolute Change at Week 52		
n	14	13
Mean (SD)	2.38 (20.87)	4.27 (16.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Absolute Change at Week 52 (MMRM)		
n	14	12
LS mean (SE)	2.49 (5.39)	4.50 (5.83)
95% CI of LS mean	(-8.69, 13.67)	(-7.58, 16.59)
P-value within Treatment	0.6487	0.4478
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.01 (-14.55, 18.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8032
Hedges' G (SE)		0.10 (0.38)
Hedges' 95% CI		(-0.69, 0.88)
Hedges' P-value		0.8019

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Baseline		
n	9	5
Mean (SD)	76.19 (7.14)	92.86 (7.14)
Week 52		
n	8	5
Mean (SD)	88.39 (11.41)	85.71 (11.29)
Absolute Change at Week 52		
n	8	5
Mean (SD)	11.61 (10.06)	-7.14 (13.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 9	VNZ/TEZ/D-IVA N = 5
Absolute Change at Week 52 (MMRM)		
n	8	5
LS mean (SE)	10.62 (3.14)	-5.56 (3.99)
95% CI of LS mean	(3.51, 17.73)	(-14.59, 3.47)
P-value within Treatment	0.0082	0.1969
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-16.18 (-27.77, -4.60)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0115
Hedges' G (SE)		-1.69 (0.63)
Hedges' 95% CI		(-3.07, -0.31)
Hedges' P-value		0.0205

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	19
Mean (SD)	84.09 (18.03)	84.21 (16.07)
Week 52		
n	20	18
Mean (SD)	86.79 (17.54)	86.51 (15.86)
Absolute Change at Week 52		
n	20	17
Mean (SD)	2.86 (14.17)	3.78 (18.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	17
LS mean (SE)	3.37 (3.67)	3.18 (3.99)
95% CI of LS mean	(-4.10, 10.84)	(-4.93, 11.29)
P-value within Treatment	0.3654	0.4307
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-11.27, 10.89)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9724
Hedges' G (SE)		-0.01 (0.32)
Hedges' 95% CI		(-0.67, 0.64)
Hedges' P-value		0.9722

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening <18 years

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 26

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 4	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 27	VNZ/TEZ/D-IVA N = 25

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Baseline		
n	19	11
Mean (SD)	80.45 (18.11)	88.31 (14.02)
Week 52		
n	18	10
Mean (SD)	88.10 (14.49)	88.57 (13.13)
Absolute Change at Week 52		
n	18	10
Mean (SD)	7.14 (11.75)	0.71 (20.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Male

	ELX/TEZ/IVA N = 19	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	18	10
LS mean (SE)	6.93 (3.57)	1.09 (4.81)
95% CI of LS mean	(-0.44, 14.31)	(-8.83, 11.01)
P-value within Treatment	0.0641	0.8222
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.84 (-18.26, 6.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3415
Hedges' G (SE)		-0.37 (0.39)
Hedges' 95% CI		(-1.17, 0.42)
Hedges' P-value		0.3420

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	14
Mean (SD)	83.93 (12.23)	85.20 (15.96)
Week 52		
n	10	14
Mean (SD)	85.71 (18.75)	85.71 (16.09)
Absolute Change at Week 52		
n	10	13
Mean (SD)	2.14 (16.51)	1.65 (16.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Female

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	10	12
LS mean (SE)	3.17 (5.65)	0.93 (5.12)
95% CI of LS mean	(-8.70, 15.05)	(-9.83, 11.69)
P-value within Treatment	0.5817	0.8581
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.24 (-18.91, 14.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7807
Hedges' G (SE)		-0.12 (0.41)
Hedges' 95% CI		(-0.98, 0.74)
Hedges' P-value		0.7719

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Baseline		
n	15	10
Mean (SD)	76.67 (16.08)	83.57 (15.81)
Week 52		
n	14	10
Mean (SD)	84.69 (16.54)	82.14 (16.92)
Absolute Change at Week 52		
n	14	10
Mean (SD)	7.65 (8.62)	-1.43 (18.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = North America

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 52 (MMRM)		
n	14	10
LS mean (SE)	7.37 (3.82)	-1.03 (4.60)
95% CI of LS mean	(-0.61, 15.34)	(-10.62, 8.57)
P-value within Treatment	0.0683	0.8258
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.39 (-21.46, 4.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1955
Hedges' G (SE)		-0.56 (0.41)
Hedges' 95% CI		(-1.41, 0.28)
Hedges' P-value		0.1817

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Baseline		
n	16	15
Mean (SD)	86.61 (14.73)	88.57 (14.49)
Week 52		
n	14	14
Mean (SD)	89.80 (15.27)	90.31 (12.41)
Absolute Change at Week 52		
n	14	13
Mean (SD)	3.06 (17.21)	3.30 (17.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = Rest of World

	ELX/TEZ/IVA N = 16	VNZ/TEZ/D-IVA N = 16
Absolute Change at Week 52 (MMRM)		
n	14	12
LS mean (SE)	2.00 (4.36)	4.81 (4.71)
95% CI of LS mean	(-7.04, 11.04)	(-4.96, 14.58)
P-value within Treatment	0.6509	0.3182
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.81 (-10.58, 16.20)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6674
Hedges' G (SE)		0.17 (0.38)
Hedges' 95% CI		(-0.62, 0.95)
Hedges' P-value		0.6657

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Effectiveness
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 20
Baseline		
n	25	20
Mean (SD)	81.11 (14.61)	78.06 (29.92)
Week 52		
n	22	18
Mean (SD)	78.54 (16.11)	82.72 (15.70)
Absolute Change at Week 52		
n	22	18
Mean (SD)	-2.78 (18.45)	6.79 (32.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Effectiveness
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	22	17
LS mean (SE)	-3.90 (5.73)	8.64 (6.56)
95% CI of LS mean	(-15.53, 7.73)	(-4.68, 21.96)
P-value within Treatment	0.5004	0.1963
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.54 (-5.60, 30.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1692
Hedges' G (SE)		0.46 (0.32)
Hedges' 95% CI		(-0.19, 1.11)
Hedges' P-value		0.1632

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Effectiveness
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	5
Mean (SD)	78.70 (15.88)	85.56 (17.39)
Week 52		
n	6	6
Mean (SD)	99.07 (2.27)	91.67 (13.94)
Absolute Change at Week 52		
n	6	5
Mean (SD)	20.37 (13.91)	7.78 (14.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Effectiveness
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52 (MMRM)		
n	6	5
LS mean (SE)	20.26 (7.31)	7.91 (8.16)
95% CI of LS mean	(2.98, 37.55)	(-11.39, 27.21)
P-value within Treatment	0.0276	0.3648
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-12.35 (-40.83, 16.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3392
Hedges' G (SE)		-0.63 (0.57)
Hedges' 95% CI		(-1.91, 0.66)
Hedges' P-value		0.3006

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Side Effects
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 20
Baseline		
n	25	19
Mean (SD)	95.50 (14.72)	99.01 (4.30)
Week 52		
n	22	18
Mean (SD)	97.16 (8.35)	95.14 (14.31)
Absolute Change at Week 52		
n	22	17
Mean (SD)	0.00 (9.64)	-4.04 (11.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Side Effects
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	22	16
LS mean (SE)	0.29 (2.23)	-4.70 (2.64)
95% CI of LS mean	(-4.24, 4.83)	(-10.07, 0.67)
P-value within Treatment	0.8957	0.0840
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.00 (-12.23, 2.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1696
Hedges' G (SE)		-0.47 (0.33)
Hedges' 95% CI		(-1.13, 0.20)
Hedges' P-value		0.1620

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Side Effects
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	5
Mean (SD)	98.96 (2.55)	97.50 (3.42)
Week 52		
n	6	6
Mean (SD)	95.83 (10.21)	95.83 (10.21)
Absolute Change at Week 52		
n	6	5
Mean (SD)	-3.13 (11.00)	2.50 (3.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Side Effects
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52 (MMRM)		
n	6	5
LS mean (SE)	-1.84 (4.18)	0.96 (4.67)
95% CI of LS mean	(-11.73, 8.05)	(-10.08, 12.00)
P-value within Treatment	0.6727	0.8427
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.80 (-13.49, 19.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6962
Hedges' G (SE)		0.25 (0.56)
Hedges' 95% CI		(-1.01, 1.51)
Hedges' P-value		0.6660

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Convenience
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 20
Baseline		
n	25	20
Mean (SD)	79.33 (14.66)	85.28 (14.22)
Week 52		
n	22	18
Mean (SD)	83.59 (19.43)	86.42 (13.09)
Absolute Change at Week 52		
n	22	18
Mean (SD)	4.04 (16.28)	1.54 (13.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Convenience
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	22	17
LS mean (SE)	4.03 (3.30)	1.64 (3.78)
95% CI of LS mean	(-2.67, 10.74)	(-6.04, 9.32)
P-value within Treatment	0.2299	0.6669
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.39 (-12.85, 8.06)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6451
Hedges' G (SE)		-0.15 (0.32)
Hedges' 95% CI		(-0.79, 0.49)
Hedges' P-value		0.6366

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Convenience
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	5
Mean (SD)	75.93 (16.36)	74.44 (19.08)
Week 52		
n	6	6
Mean (SD)	77.78 (31.23)	85.19 (13.46)
Absolute Change at Week 52		
n	6	5
Mean (SD)	1.85 (25.74)	10.00 (19.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Convenience
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52 (MMRM)		
n	6	5
LS mean (SE)	0.98 (11.86)	11.05 (13.24)
95% CI of LS mean	(-27.07, 29.02)	(-20.26, 42.37)
P-value within Treatment	0.9367	0.4316
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.08 (-36.14, 56.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6220
Hedges' G (SE)		0.31 (0.56)
Hedges' 95% CI		(-0.95, 1.58)
Hedges' P-value		0.5867

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Global Satisfaction
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 20
Baseline		
n	25	20
Mean (SD)	82.29 (15.72)	86.07 (14.92)
Week 52		
n	22	18
Mean (SD)	85.39 (17.00)	85.71 (14.90)
Absolute Change at Week 52		
n	22	18
Mean (SD)	2.92 (13.35)	0.00 (18.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Global Satisfaction
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	22	17
LS mean (SE)	3.75 (3.30)	-1.07 (3.78)
95% CI of LS mean	(-2.96, 10.45)	(-8.75, 6.61)
P-value within Treatment	0.2643	0.7794
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.82 (-15.27, 5.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3564
Hedges' G (SE)		-0.30 (0.32)
Hedges' 95% CI		(-0.95, 0.34)
Hedges' P-value		0.3462

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Global Satisfaction
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	5
Mean (SD)	79.76 (18.30)	88.57 (16.44)
Week 52		
n	6	6
Mean (SD)	94.05 (8.35)	90.48 (14.75)
Absolute Change at Week 52		
n	6	5
Mean (SD)	14.29 (11.07)	5.71 (17.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.2.2.12.1.2.1
Study VX20-121-102: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Domain: Global Satisfaction
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52 (MMRM)		
n	6	5
LS mean (SE)	10.48 (6.47)	10.28 (7.23)
95% CI of LS mean	(-4.83, 25.78)	(-6.81, 27.38)
P-value within Treatment	0.1496	0.1978
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-25.42, 25.03)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9860
Hedges' G (SE)		-0.01 (0.55)
Hedges' 95% CI		(-1.26, 1.24)
Hedges' P-value		0.9844

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- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) devided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any TEAEs	191 (94.55)	183 (93.37)
Relative Risk (RR) (95% CI)		0.9874 (0.9394, 1.0379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6195
Odds Ratio (OR) (95% CI)		0.8107 (0.3542, 1.8558)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6195
Risk Difference (RD) (95% CI)		-0.0119 (-0.0587, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6193
Infections and infestations	143 (70.79)	129 (65.82)
Relative Risk (RR) (95% CI)		0.9297 (0.8129, 1.0633)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2874
Odds Ratio (OR) (95% CI)		0.7944 (0.5203, 1.2129)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2864
Risk Difference (RD) (95% CI)		-0.0498 (-0.1411, 0.0416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2856

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
COVID-19	54 (26.73)	49 (25.00)
Relative Risk (RR) (95% CI)		0.9352 (0.6703, 1.3048)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6933
Odds Ratio (OR) (95% CI)		0.9136 (0.5831, 1.4314)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6932
Risk Difference (RD) (95% CI)		-0.0173 (-0.1033, 0.0687)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6930
Nasopharyngitis	35 (17.33)	45 (22.96)
Relative Risk (RR) (95% CI)		1.3251 (0.8921, 1.9681)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1632
Odds Ratio (OR) (95% CI)		1.4219 (0.8681, 2.3293)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1621

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0563 (-0.0224, 0.1350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1606

- MedDRA version 26.1.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Influenza	10 (4.95)	19 (9.69)
Relative Risk (RR) (95% CI)		1.9582 (0.9342, 4.1045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0751
Odds Ratio (OR) (95% CI)		2.0610 (0.9331, 4.5526)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0737
Risk Difference (RD) (95% CI)		0.0474 (-0.0037, 0.0985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0688
Upper respiratory tract infection	27 (13.37)	17 (8.67)
Relative Risk (RR) (95% CI)		0.6489 (0.3655, 1.1522)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1398
Odds Ratio (OR) (95% CI)		0.6156 (0.3241, 1.1693)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1383

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0469 (-0.1082, 0.0143)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1333

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Viral upper respiratory tract infection	18 (8.91)	17 (8.67)
Relative Risk (RR) (95% CI)		0.9734 (0.5168, 1.8332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9334
Odds Ratio (OR) (95% CI)		0.9708 (0.4850, 1.9434)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9334
Risk Difference (RD) (95% CI)		-0.0024 (-0.0580, 0.0533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9334
Sinusitis	10 (4.95)	10 (5.10)
Relative Risk (RR) (95% CI)		1.0306 (0.4386, 2.4214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9448
Odds Ratio (OR) (95% CI)		1.0323 (0.4199, 2.5375)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9448

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0015 (-0.0414, 0.0445)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9449

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Respiratory tract infection	12 (5.94)	8 (4.08)
Relative Risk (RR) (95% CI)		0.6871 (0.2871, 1.6445)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3993
Odds Ratio (OR) (95% CI)		0.6738 (0.2693, 1.6857)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3987
Risk Difference (RD) (95% CI)		-0.0186 (-0.0614, 0.0242)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3944
Rhinitis	6 (2.97)	8 (4.08)
Relative Risk (RR) (95% CI)		1.3741 (0.4857, 3.8882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5492
Odds Ratio (OR) (95% CI)		1.3901 (0.4734, 4.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5490

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0111 (-0.0252, 0.0474)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5481

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Oral candidiasis	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524
Respiratory, thoracic and mediastinal disorders	98 (48.51)	94 (47.96)
Relative Risk (RR) (95% CI)		0.9885 (0.8065, 1.2118)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9117
Odds Ratio (OR) (95% CI)		0.9780 (0.6600, 1.4492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9117
Risk Difference (RD) (95% CI)		-0.0056 (-0.1037, 0.0926)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9117

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Cough	41 (20.30)	45 (22.96)
Relative Risk (RR) (95% CI)		1.1312 (0.7776, 1.6454)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5192
Odds Ratio (OR) (95% CI)		1.1702 (0.7257, 1.8872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5191
Risk Difference (RD) (95% CI)		0.0266 (-0.0543, 0.1075)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5189
Oropharyngeal pain	23 (11.39)	24 (12.24)
Relative Risk (RR) (95% CI)		1.0754 (0.6285, 1.8401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7907
Odds Ratio (OR) (95% CI)		1.0859 (0.5906, 1.9966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7907

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0086 (-0.0549, 0.0720)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7908

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nasal congestion	24 (11.88)	19 (9.69)
Relative Risk (RR) (95% CI)		0.8159 (0.4619, 1.4411)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4833
Odds Ratio (OR) (95% CI)		0.7961 (0.4211, 1.5051)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4829
Risk Difference (RD) (95% CI)		-0.0219 (-0.0828, 0.0390)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4813
Rhinorrhoea	14 (6.93)	19 (9.69)
Relative Risk (RR) (95% CI)		1.3987 (0.7216, 2.7110)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3204
Odds Ratio (OR) (95% CI)		1.4415 (0.7015, 2.9621)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3197

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0276 (-0.0266, 0.0819)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3181

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Sputum increased	21 (10.40)	18 (9.18)
Relative Risk (RR) (95% CI)		0.8834 (0.4857, 1.6066)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6845
Odds Ratio (OR) (95% CI)		0.8716 (0.4493, 1.6909)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6844
Risk Difference (RD) (95% CI)		-0.0121 (-0.0705, 0.0462)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6839
Sinus congestion	5 (2.48)	14 (7.14)
Relative Risk (RR) (95% CI)		2.8857 (1.0594, 7.8601)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0382
Odds Ratio (OR) (95% CI)		3.0308 (1.0704, 8.5817)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0368

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0467 (0.0047, 0.0886)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0292

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Haemoptysis	11 (5.45)	13 (6.63)
Relative Risk (RR) (95% CI)		1.2180 (0.5592, 2.6531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6196
Odds Ratio (OR) (95% CI)		1.2335 (0.5389, 2.8235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6195
Risk Difference (RD) (95% CI)		0.0119 (-0.0350, 0.0587)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6193
Productive cough	5 (2.48)	12 (6.12)
Relative Risk (RR) (95% CI)		2.4735 (0.8878, 6.8910)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0832
Odds Ratio (OR) (95% CI)		2.5696 (0.8881, 7.4349)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0817

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Study VX20-121-102: Summary of TEAEs by SOC and PT
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Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0365 (-0.0033, 0.0763)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0726

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Respiration abnormal	5 (2.48)	8 (4.08)
Relative Risk (RR) (95% CI)		1.6490 (0.5489, 4.9535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3728
Odds Ratio (OR) (95% CI)		1.6766 (0.5389, 5.2166)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3722
Risk Difference (RD) (95% CI)		0.0161 (-0.0190, 0.0511)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3686
Dyspnoea	7 (3.47)	7 (3.57)
Relative Risk (RR) (95% CI)		1.0306 (0.3683, 2.8841)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9542
Odds Ratio (OR) (95% CI)		1.0317 (0.3551, 2.9977)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9542

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0011 (-0.0351, 0.0373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9542

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Sputum discoloured	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524
Investigations	72 (35.64)	72 (36.73)
Relative Risk (RR) (95% CI)		1.0306 (0.7939, 1.3379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8208
Odds Ratio (OR) (95% CI)		1.0484 (0.6965, 1.5781)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8208
Risk Difference (RD) (95% CI)		0.0109 (-0.0835, 0.1053)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8208

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Blood creatine phosphokinase increased	24 (11.88)	18 (9.18)
Relative Risk (RR) (95% CI)		0.7730 (0.4334, 1.3787)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3831
Odds Ratio (OR) (95% CI)		0.7500 (0.3933, 1.4302)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3824
Risk Difference (RD) (95% CI)		-0.0270 (-0.0872, 0.0332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3799
Alanine aminotransferase increased	11 (5.45)	13 (6.63)
Relative Risk (RR) (95% CI)		1.2180 (0.5592, 2.6531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6196
Odds Ratio (OR) (95% CI)		1.2335 (0.5389, 2.8235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6195

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0119 (-0.0350, 0.0587)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6193

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Aspartate aminotransferase increased	9 (4.46)	12 (6.12)
Relative Risk (RR) (95% CI)		1.3741 (0.5923, 3.1882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4592
Odds Ratio (OR) (95% CI)		1.3986 (0.5757, 3.3973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4588
Risk Difference (RD) (95% CI)		0.0167 (-0.0273, 0.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4578
Weight decreased	1 (0.50)	9 (4.59)
Relative Risk (RR) (95% CI)		9.2755 (1.1862, 72.5295)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0338
Odds Ratio (OR) (95% CI)		9.6738 (1.2139, 77.0904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0321

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0410 (0.0101, 0.0718)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0093

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
SARS-CoV-2 test positive	3 (1.49)	8 (4.08)
Relative Risk (RR) (95% CI)		2.7483 (0.7399, 10.2088)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1311
Odds Ratio (OR) (95% CI)		2.8227 (0.7378, 10.7993)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1296
Risk Difference (RD) (95% CI)		0.0260 (-0.0064, 0.0583)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1155
Bacterial test positive	6 (2.97)	7 (3.57)
Relative Risk (RR) (95% CI)		1.2024 (0.4114, 3.5144)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7363
Odds Ratio (OR) (95% CI)		1.2099 (0.3993, 3.6660)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7362

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0060 (-0.0290, 0.0410)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7362

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Blood bilirubin increased	7 (3.47)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5889 (0.1751, 1.9802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3921
Odds Ratio (OR) (95% CI)		0.5804 (0.1672, 2.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3915
Risk Difference (RD) (95% CI)		-0.0142 (-0.0463, 0.0178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3839
Gastrointestinal disorders	68 (33.66)	64 (32.65)
Relative Risk (RR) (95% CI)		0.9700 (0.7338, 1.2823)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8306
Odds Ratio (OR) (95% CI)		0.9554 (0.6294, 1.4505)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8305
Risk Difference (RD) (95% CI)		-0.0101 (-0.1026, 0.0824)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8305

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Diarrhoea	15 (7.43)	21 (10.71)
Relative Risk (RR) (95% CI)		1.4429 (0.7663, 2.7167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2561
Odds Ratio (OR) (95% CI)		1.4960 (0.7474, 2.9943)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2552
Risk Difference (RD) (95% CI)		0.0329 (-0.0235, 0.0893)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2532
Abdominal pain upper	6 (2.97)	12 (6.12)
Relative Risk (RR) (95% CI)		2.0612 (0.7892, 5.3837)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1398
Odds Ratio (OR) (95% CI)		2.1304 (0.7834, 5.7936)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1384

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0315 (-0.0094, 0.0724)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1311

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Abdominal pain	14 (6.93)	10 (5.10)
Relative Risk (RR) (95% CI)		0.7362 (0.3350, 1.6177)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4457
Odds Ratio (OR) (95% CI)		0.7220 (0.3128, 1.6664)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4452
Risk Difference (RD) (95% CI)		-0.0183 (-0.0649, 0.0284)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4422
Constipation	10 (4.95)	7 (3.57)
Relative Risk (RR) (95% CI)		0.7214 (0.2802, 1.8574)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4986
Odds Ratio (OR) (95% CI)		0.7111 (0.2651, 1.9072)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4982

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0138 (-0.0534, 0.0258)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4951

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nausea	17 (8.42)	7 (3.57)
Relative Risk (RR) (95% CI)		0.4244 (0.1799, 1.0008)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0502
Odds Ratio (OR) (95% CI)		0.4031 (0.1633, 0.9946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0486
Risk Difference (RD) (95% CI)		-0.0484 (-0.0947, -0.0022)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0402
Flatulence	7 (3.47)	6 (3.06)
Relative Risk (RR) (95% CI)		0.8834 (0.3022, 2.5820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8207
Odds Ratio (OR) (95% CI)		0.8797 (0.2903, 2.6655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8207

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0040 (-0.0389, 0.0309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8204

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Abdominal distension	10 (4.95)	5 (2.55)
Relative Risk (RR) (95% CI)		0.5153 (0.1794, 1.4805)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2182
Odds Ratio (OR) (95% CI)		0.5026 (0.1686, 1.4980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2170
Risk Difference (RD) (95% CI)		-0.0240 (-0.0612, 0.0132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2059
Vomiting	8 (3.96)	3 (1.53)
Relative Risk (RR) (95% CI)		0.3865 (0.1040, 1.4356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1556
Odds Ratio (OR) (95% CI)		0.3769 (0.0985, 1.4421)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1541

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Study VX20-121-102: Summary of TEAEs by SOC and PT
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Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0243 (-0.0562, 0.0076)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1357

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Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
General disorders and administration site conditions	47 (23.27)	56 (28.57)
Relative Risk (RR) (95% CI)		1.2280 (0.8791, 1.7153)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2285
Odds Ratio (OR) (95% CI)		1.3191 (0.8411, 2.0690)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2277
Risk Difference (RD) (95% CI)		0.0530 (-0.0330, 0.1390)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2267
Pyrexia	21 (10.40)	24 (12.24)
Relative Risk (RR) (95% CI)		1.1778 (0.6784, 2.0450)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		1.2027 (0.6458, 2.2395)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0185 (-0.0438, 0.0808)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5606

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Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Fatigue	16 (7.92)	18 (9.18)
Relative Risk (RR) (95% CI)		1.1594 (0.6089, 2.2079)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6526
Odds Ratio (OR) (95% CI)		1.1756 (0.5814, 2.3770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6525
Risk Difference (RD) (95% CI)		0.0126 (-0.0423, 0.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6525
Pain	6 (2.97)	8 (4.08)
Relative Risk (RR) (95% CI)		1.3741 (0.4857, 3.8882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5492
Odds Ratio (OR) (95% CI)		1.3901 (0.4734, 4.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5490

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0111 (-0.0252, 0.0474)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5481

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Musculoskeletal and connective tissue disorders	48 (23.76)	41 (20.92)
Relative Risk (RR) (95% CI)		0.8803 (0.6095, 1.2714)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4967
Odds Ratio (OR) (95% CI)		0.8487 (0.5290, 1.3615)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4962
Risk Difference (RD) (95% CI)		-0.0284 (-0.1102, 0.0533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4955
Arthralgia	11 (5.45)	10 (5.10)
Relative Risk (RR) (95% CI)		0.9369 (0.4071, 2.1562)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8782
Odds Ratio (OR) (95% CI)		0.9335 (0.3873, 2.2503)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8782
Risk Difference (RD) (95% CI)		-0.0034 (-0.0473, 0.0405)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8781

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Back pain	16 (7.92)	9 (4.59)
Relative Risk (RR) (95% CI)		0.5797 (0.2624, 1.2807)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1776
Odds Ratio (OR) (95% CI)		0.5595 (0.2412, 1.2979)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1762
Risk Difference (RD) (95% CI)		-0.0333 (-0.0807, 0.0141)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1686
Myalgia	3 (1.49)	7 (3.57)
Relative Risk (RR) (95% CI)		2.4048 (0.6308, 9.1669)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1987
Odds Ratio (OR) (95% CI)		2.4568 (0.6261, 9.6401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1975

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0209 (-0.0100, 0.0517)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1854

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nervous system disorders	34 (16.83)	39 (19.90)
Relative Risk (RR) (95% CI)		1.1822 (0.7800, 1.7916)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4302
Odds Ratio (OR) (95% CI)		1.2274 (0.7380, 2.0414)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4298
Risk Difference (RD) (95% CI)		0.0307 (-0.0454, 0.1067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4295
Headache	22 (10.89)	25 (12.76)
Relative Risk (RR) (95% CI)		1.1712 (0.6837, 2.0061)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5651
Odds Ratio (OR) (95% CI)		1.1962 (0.6500, 2.2014)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5649
Risk Difference (RD) (95% CI)		0.0186 (-0.0448, 0.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5648

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Injury, poisoning and procedural complications	36 (17.82)	36 (18.37)
Relative Risk (RR) (95% CI)		1.0306 (0.6785, 1.5656)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8876
Odds Ratio (OR) (95% CI)		1.0375 (0.6227, 1.7285)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8876
Risk Difference (RD) (95% CI)		0.0055 (-0.0702, 0.0811)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8876
Skin and subcutaneous tissue disorders	35 (17.33)	30 (15.31)
Relative Risk (RR) (95% CI)		0.8834 (0.5654, 1.3803)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5861
Odds Ratio (OR) (95% CI)		0.8623 (0.5061, 1.4692)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5858
Risk Difference (RD) (95% CI)		-0.0202 (-0.0928, 0.0524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5852

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Rash	9 (4.46)	12 (6.12)
Relative Risk (RR) (95% CI)		1.3741 (0.5923, 3.1882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4592
Odds Ratio (OR) (95% CI)		1.3986 (0.5757, 3.3973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4588
Risk Difference (RD) (95% CI)		0.0167 (-0.0273, 0.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4578
Acne	8 (3.96)	5 (2.55)
Relative Risk (RR) (95% CI)		0.6441 (0.2144, 1.9350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4332
Odds Ratio (OR) (95% CI)		0.6348 (0.2040, 1.9752)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4327

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0141 (-0.0489, 0.0207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4272

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Metabolism and nutrition disorders	18 (8.91)	20 (10.20)
Relative Risk (RR) (95% CI)		1.1451 (0.6249, 2.0985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6610
Odds Ratio (OR) (95% CI)		1.1616 (0.5947, 2.2689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6610
Risk Difference (RD) (95% CI)		0.0129 (-0.0449, 0.0707)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6609
Hypoglycaemia	7 (3.47)	5 (2.55)
Relative Risk (RR) (95% CI)		0.7362 (0.2376, 2.2804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5954
Odds Ratio (OR) (95% CI)		0.7292 (0.2275, 2.3376)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5952
Risk Difference (RD) (95% CI)		-0.0091 (-0.0427, 0.0244)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5929

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Psychiatric disorders	34 (16.83)	19 (9.69)
Relative Risk (RR) (95% CI)		0.5759 (0.3404, 0.9744)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0397
Odds Ratio (OR) (95% CI)		0.5304 (0.2912, 0.9663)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0383
Risk Difference (RD) (95% CI)		-0.0714 (-0.1375, -0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0345
Depression	7 (3.47)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5889 (0.1751, 1.9802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3921
Odds Ratio (OR) (95% CI)		0.5804 (0.1672, 2.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3915
Risk Difference (RD) (95% CI)		-0.0142 (-0.0463, 0.0178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3839

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
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Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Insomnia	8 (3.96)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5153 (0.1577, 1.6838)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2724
Odds Ratio (OR) (95% CI)		0.5052 (0.1496, 1.7056)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2714
Risk Difference (RD) (95% CI)		-0.0192 (-0.0526, 0.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2599
Immune system disorders	2 (0.99)	8 (4.08)
Relative Risk (RR) (95% CI)		4.1224 (0.8865, 19.1715)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0709
Odds Ratio (OR) (95% CI)		4.2553 (0.8922, 20.2954)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0692
Risk Difference (RD) (95% CI)		0.0309 (0.0000, 0.0618)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0498

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Study VX20-121-102: Summary of TEAEs by SOC and PT
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Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Eye disorders	9 (4.46)	7 (3.57)
Relative Risk (RR) (95% CI)		0.8016 (0.3045, 2.1103)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6543
Odds Ratio (OR) (95% CI)		0.7942 (0.2899, 2.1761)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6542
Risk Difference (RD) (95% CI)		-0.0088 (-0.0474, 0.0297)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6529
Reproductive system and breast disorders	15 (7.43)	7 (3.57)
Relative Risk (RR) (95% CI)		0.4810 (0.2004, 1.1542)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1012
Odds Ratio (OR) (95% CI)		0.4617 (0.1841, 1.1582)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0996
Risk Difference (RD) (95% CI)		-0.0385 (-0.0831, 0.0060)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0897

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Table 1.3.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Ear and labyrinth disorders	10 (4.95)	5 (2.55)
Relative Risk (RR) (95% CI)		0.5153 (0.1794, 1.4805)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2182
Odds Ratio (OR) (95% CI)		0.5026 (0.1686, 1.4980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2170
Risk Difference (RD) (95% CI)		-0.0240 (-0.0612, 0.0132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2059
Renal and urinary disorders	16 (7.92)	5 (2.55)
Relative Risk (RR) (95% CI)		0.3221 (0.1203, 0.8622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0241
Odds Ratio (OR) (95% CI)		0.3043 (0.1093, 0.8476)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0228
Risk Difference (RD) (95% CI)		-0.0537 (-0.0970, -0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0151

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any TEAEs	191 (94.55)	183 (93.37)
Relative Risk (RR) (95% CI)		0.9874 (0.9394, 1.0379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6195
Odds Ratio (OR) (95% CI)		0.8107 (0.3542, 1.8558)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6195
Risk Difference (RD) (95% CI)		-0.0119 (-0.0587, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6193
Grade 1/Mild	75 (37.13)	77 (39.29)
Relative Risk (RR) (95% CI)		1.0581 (0.8241, 1.3586)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6579
Odds Ratio (OR) (95% CI)		1.0957 (0.7311, 1.6420)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6579

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0216 (-0.0739, 0.1170)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6579

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	102 (50.50)	88 (44.90)
Relative Risk (RR) (95% CI)		0.8892 (0.7232, 1.0932)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2651
Odds Ratio (OR) (95% CI)		0.7988 (0.5387, 1.1847)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2640
Risk Difference (RD) (95% CI)		-0.0560 (-0.1540, 0.0420)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2629
Grade 3/Severe	14 (6.93)	18 (9.18)
Relative Risk (RR) (95% CI)		1.3251 (0.6779, 2.5901)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4104
Odds Ratio (OR) (95% CI)		1.3579 (0.6558, 2.8119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4100

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0225 (-0.0310, 0.0760)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4091

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Infections and infestations	143 (70.79)	129 (65.82)
Relative Risk (RR) (95% CI)		0.9297 (0.8129, 1.0633)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2874
Odds Ratio (OR) (95% CI)		0.7944 (0.5203, 1.2129)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2864
Risk Difference (RD) (95% CI)		-0.0498 (-0.1411, 0.0416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2856
Grade 1/Mild	83 (41.09)	69 (35.20)
Relative Risk (RR) (95% CI)		0.8568 (0.6661, 1.1020)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2287
Odds Ratio (OR) (95% CI)		0.7790 (0.5193, 1.1686)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2274

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0589 (-0.1541, 0.0364)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2259

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	57 (28.22)	53 (27.04)
Relative Risk (RR) (95% CI)		0.9583 (0.6971, 1.3173)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7930
Odds Ratio (OR) (95% CI)		0.9428 (0.6075, 1.4633)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7929
Risk Difference (RD) (95% CI)		-0.0118 (-0.0996, 0.0761)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7929
Grade 3/Severe	3 (1.49)	7 (3.57)
Relative Risk (RR) (95% CI)		2.4048 (0.6308, 9.1669)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1987
Odds Ratio (OR) (95% CI)		2.4568 (0.6261, 9.6401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1975

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0209 (-0.0100, 0.0517)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1854

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
COVID-19	54 (26.73)	49 (25.00)
Relative Risk (RR) (95% CI)		0.9352 (0.6703, 1.3048)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6933
Odds Ratio (OR) (95% CI)		0.9136 (0.5831, 1.4314)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6932
Risk Difference (RD) (95% CI)		-0.0173 (-0.1033, 0.0687)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6930
Grade 1/Mild	37 (18.32)	34 (17.35)
Relative Risk (RR) (95% CI)		0.9470 (0.6209, 1.4444)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8006
Odds Ratio (OR) (95% CI)		0.9359 (0.5600, 1.5643)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8005

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0097 (-0.0849, 0.0655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8004

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	17 (8.42)	15 (7.65)
Relative Risk (RR) (95% CI)		0.9094 (0.4672, 1.7699)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7798
Odds Ratio (OR) (95% CI)		0.9019 (0.4373, 1.8601)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7797
Risk Difference (RD) (95% CI)		-0.0076 (-0.0610, 0.0458)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7795
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nasopharyngitis	35 (17.33)	45 (22.96)
Relative Risk (RR) (95% CI)		1.3251 (0.8921, 1.9681)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1632
Odds Ratio (OR) (95% CI)		1.4219 (0.8681, 2.3293)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1621
Risk Difference (RD) (95% CI)		0.0563 (-0.0224, 0.1350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1606
Grade 1/Mild	28 (13.86)	29 (14.80)
Relative Risk (RR) (95% CI)		1.0674 (0.6601, 1.7262)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7902
Odds Ratio (OR) (95% CI)		1.0791 (0.6158, 1.8911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7902

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0093 (-0.0595, 0.0782)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7902

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	7 (3.47)	16 (8.16)
Relative Risk (RR) (95% CI)		2.3557 (0.9907, 5.6013)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0525
Odds Ratio (OR) (95% CI)		2.4762 (0.9957, 6.1578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0511
Risk Difference (RD) (95% CI)		0.0470 (0.0011, 0.0929)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0448
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Influenza	10 (4.95)	19 (9.69)
Relative Risk (RR) (95% CI)		1.9582 (0.9342, 4.1045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0751
Odds Ratio (OR) (95% CI)		2.0610 (0.9331, 4.5526)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0737
Risk Difference (RD) (95% CI)		0.0474 (-0.0037, 0.0985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0688
Grade 1/Mild	7 (3.47)	6 (3.06)
Relative Risk (RR) (95% CI)		0.8834 (0.3022, 2.5820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8207
Odds Ratio (OR) (95% CI)		0.8797 (0.2903, 2.6655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8207

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0040 (-0.0389, 0.0309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8204

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	11 (5.61)
Relative Risk (RR) (95% CI)		5.6684 (1.2727, 25.2460)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0228
Odds Ratio (OR) (95% CI)		5.9459 (1.3007, 27.1820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0215
Risk Difference (RD) (95% CI)		0.0462 (0.0112, 0.0812)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0096
Grade 3/Severe	1 (0.50)	2 (1.02)
Relative Risk (RR) (95% CI)		2.0612 (0.1884, 22.5492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5535
Odds Ratio (OR) (95% CI)		2.0722 (0.1864, 23.0379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5533

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0053 (-0.0118, 0.0223)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5465

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Upper respiratory tract infection	27 (13.37)	17 (8.67)
Relative Risk (RR) (95% CI)		0.6489 (0.3655, 1.1522)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1398
Odds Ratio (OR) (95% CI)		0.6156 (0.3241, 1.1693)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1383
Risk Difference (RD) (95% CI)		-0.0469 (-0.1082, 0.0143)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1333
Grade 1/Mild	18 (8.91)	15 (7.65)
Relative Risk (RR) (95% CI)		0.8588 (0.4455, 1.6558)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6496
Odds Ratio (OR) (95% CI)		0.8471 (0.4143, 1.7322)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6494

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0126 (-0.0667, 0.0415)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6487

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	9 (4.46)	2 (1.02)
Relative Risk (RR) (95% CI)		0.2290 (0.0501, 1.0467)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0573
Odds Ratio (OR) (95% CI)		0.2211 (0.0472, 1.0365)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0556
Risk Difference (RD) (95% CI)		-0.0344 (-0.0661, -0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0339
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Viral upper respiratory tract infection	18 (8.91)	17 (8.67)
Relative Risk (RR) (95% CI)		0.9734 (0.5168, 1.8332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9334
Odds Ratio (OR) (95% CI)		0.9708 (0.4850, 1.9434)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9334
Risk Difference (RD) (95% CI)		-0.0024 (-0.0580, 0.0533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9334
Grade 1/Mild	16 (7.92)	13 (6.63)
Relative Risk (RR) (95% CI)		0.8374 (0.4138, 1.6946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6217
Odds Ratio (OR) (95% CI)		0.8258 (0.3863, 1.7654)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6215

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0129 (-0.0639, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6206

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	4 (2.04)
Relative Risk (RR) (95% CI)		2.0612 (0.3819, 11.1258)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4004
Odds Ratio (OR) (95% CI)		2.0833 (0.3772, 11.5059)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3999
Risk Difference (RD) (95% CI)		0.0105 (-0.0135, 0.0346)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3918
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Sinusitis	10 (4.95)	10 (5.10)
Relative Risk (RR) (95% CI)		1.0306 (0.4386, 2.4214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9448
Odds Ratio (OR) (95% CI)		1.0323 (0.4199, 2.5375)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9448
Risk Difference (RD) (95% CI)		0.0015 (-0.0414, 0.0445)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9449
Grade 1/Mild	5 (2.48)	6 (3.06)
Relative Risk (RR) (95% CI)		1.2367 (0.3837, 3.9865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7220
Odds Ratio (OR) (95% CI)		1.2442 (0.3735, 4.1451)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7219

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0059 (-0.0264, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7218

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	4 (2.04)
Relative Risk (RR) (95% CI)		0.8245 (0.2247, 3.0253)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7711
Odds Ratio (OR) (95% CI)		0.8208 (0.2172, 3.1027)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7710
Risk Difference (RD) (95% CI)		-0.0043 (-0.0335, 0.0248)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7704
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
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- [1] Relative risk from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Respiratory tract infection	12 (5.94)	8 (4.08)
Relative Risk (RR) (95% CI)		0.6871 (0.2871, 1.6445)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3993
Odds Ratio (OR) (95% CI)		0.6738 (0.2693, 1.6857)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3987
Risk Difference (RD) (95% CI)		-0.0186 (-0.0614, 0.0242)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3944
Grade 1/Mild	7 (3.47)	5 (2.55)
Relative Risk (RR) (95% CI)		0.7362 (0.2376, 2.2804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5954
Odds Ratio (OR) (95% CI)		0.7292 (0.2275, 2.3376)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5952

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0091 (-0.0427, 0.0244)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5929

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	3 (1.53)
Relative Risk (RR) (95% CI)		0.6184 (0.1498, 2.5526)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5064
Odds Ratio (OR) (95% CI)		0.6124 (0.1444, 2.5980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5060
Risk Difference (RD) (95% CI)		-0.0094 (-0.0369, 0.0180)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5003
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Rhinitis	6 (2.97)	8 (4.08)
Relative Risk (RR) (95% CI)		1.3741 (0.4857, 3.8882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5492
Odds Ratio (OR) (95% CI)		1.3901 (0.4734, 4.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5490
Risk Difference (RD) (95% CI)		0.0111 (-0.0252, 0.0474)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5481
Grade 1/Mild	4 (1.98)	8 (4.08)
Relative Risk (RR) (95% CI)		2.0612 (0.6308, 6.7351)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2312
Odds Ratio (OR) (95% CI)		2.1064 (0.6239, 7.1113)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2301

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0210 (-0.0127, 0.0547)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2218

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0099 (-0.0236, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Oral candidiasis	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524
Grade 1/Mild	6 (2.97)	3 (1.53)
Relative Risk (RR) (95% CI)		0.5153 (0.1307, 2.0318)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3435
Odds Ratio (OR) (95% CI)		0.5078 (0.1252, 2.0593)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3428

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0144 (-0.0434, 0.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3313

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Respiratory, thoracic and mediastinal disorders	98 (48.51)	94 (47.96)
Relative Risk (RR) (95% CI)		0.9885 (0.8065, 1.2118)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9117
Odds Ratio (OR) (95% CI)		0.9780 (0.6600, 1.4492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9117
Risk Difference (RD) (95% CI)		-0.0056 (-0.1037, 0.0926)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9117
Grade 1/Mild	73 (36.14)	67 (34.18)
Relative Risk (RR) (95% CI)		0.9459 (0.7242, 1.2355)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6832
Odds Ratio (OR) (95% CI)		0.9178 (0.6081, 1.3854)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6831

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0195 (-0.1133, 0.0743)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6829

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	24 (11.88)	22 (11.22)
Relative Risk (RR) (95% CI)		0.9447 (0.5483, 1.6278)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8377
Odds Ratio (OR) (95% CI)		0.9377 (0.5069, 1.7346)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8377
Risk Difference (RD) (95% CI)		-0.0066 (-0.0694, 0.0562)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8376
Grade 3/Severe	1 (0.50)	5 (2.55)
Relative Risk (RR) (95% CI)		5.1531 (0.6075, 43.7115)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1328
Odds Ratio (OR) (95% CI)		5.2618 (0.6092, 45.4502)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1312

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0206 (-0.0035, 0.0447)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0945

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Cough	41 (20.30)	45 (22.96)
Relative Risk (RR) (95% CI)		1.1312 (0.7776, 1.6454)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5192
Odds Ratio (OR) (95% CI)		1.1702 (0.7257, 1.8872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5191
Risk Difference (RD) (95% CI)		0.0266 (-0.0543, 0.1075)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5189
Grade 1/Mild	33 (16.34)	37 (18.88)
Relative Risk (RR) (95% CI)		1.1555 (0.7546, 1.7696)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5061
Odds Ratio (OR) (95% CI)		1.1917 (0.7108, 1.9982)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5059

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0254 (-0.0494, 0.1002)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5058

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	8 (3.96)	8 (4.08)
Relative Risk (RR) (95% CI)		1.0306 (0.3946, 2.6919)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9509
Odds Ratio (OR) (95% CI)		1.0319 (0.3795, 2.8059)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9509
Risk Difference (RD) (95% CI)		0.0012 (-0.0374, 0.0398)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9509
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Oropharyngeal pain	23 (11.39)	24 (12.24)
Relative Risk (RR) (95% CI)		1.0754 (0.6285, 1.8401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7907
Odds Ratio (OR) (95% CI)		1.0859 (0.5906, 1.9966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7907
Risk Difference (RD) (95% CI)		0.0086 (-0.0549, 0.0720)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7908
Grade 1/Mild	19 (9.41)	19 (9.69)
Relative Risk (RR) (95% CI)		1.0306 (0.5629, 1.8869)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9222
Odds Ratio (OR) (95% CI)		1.0339 (0.5298, 2.0177)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9222

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0029 (-0.0549, 0.0606)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9222

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	4 (1.98)	5 (2.55)
Relative Risk (RR) (95% CI)		1.2883 (0.3511, 4.7271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7025
Odds Ratio (OR) (95% CI)		1.2958 (0.3428, 4.8982)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7025
Risk Difference (RD) (95% CI)		0.0057 (-0.0236, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7022
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nasal congestion	24 (11.88)	19 (9.69)
Relative Risk (RR) (95% CI)		0.8159 (0.4619, 1.4411)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4833
Odds Ratio (OR) (95% CI)		0.7961 (0.4211, 1.5051)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4829
Risk Difference (RD) (95% CI)		-0.0219 (-0.0828, 0.0390)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4813
Grade 1/Mild	20 (9.90)	16 (8.16)
Relative Risk (RR) (95% CI)		0.8245 (0.4403, 1.5439)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5465
Odds Ratio (OR) (95% CI)		0.8089 (0.4062, 1.6110)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5462

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0174 (-0.0736, 0.0389)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5450

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	4 (1.98)	2 (1.02)
Relative Risk (RR) (95% CI)		0.5153 (0.0955, 2.7814)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4409
Odds Ratio (OR) (95% CI)		0.5103 (0.0924, 2.8183)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4404
Risk Difference (RD) (95% CI)		-0.0096 (-0.0334, 0.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4296
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Rhinorrhoea	14 (6.93)	19 (9.69)
Relative Risk (RR) (95% CI)		1.3987 (0.7216, 2.7110)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3204
Odds Ratio (OR) (95% CI)		1.4415 (0.7015, 2.9621)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3197
Risk Difference (RD) (95% CI)		0.0276 (-0.0266, 0.0819)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3181
Grade 1/Mild	13 (6.44)	14 (7.14)
Relative Risk (RR) (95% CI)		1.1099 (0.5355, 2.3005)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7792
Odds Ratio (OR) (95% CI)		1.1183 (0.5117, 2.4442)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7792

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0071 (-0.0424, 0.0565)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7792

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	5 (2.55)
Relative Risk (RR) (95% CI)		5.1531 (0.6075, 43.7115)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1328
Odds Ratio (OR) (95% CI)		5.2618 (0.6092, 45.4502)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1312
Risk Difference (RD) (95% CI)		0.0206 (-0.0035, 0.0447)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0945
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [2] Odds ratio from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Sputum increased	21 (10.40)	18 (9.18)
Relative Risk (RR) (95% CI)		0.8834 (0.4857, 1.6066)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6845
Odds Ratio (OR) (95% CI)		0.8716 (0.4493, 1.6909)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6844
Risk Difference (RD) (95% CI)		-0.0121 (-0.0705, 0.0462)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6839
Grade 1/Mild	16 (7.92)	13 (6.63)
Relative Risk (RR) (95% CI)		0.8374 (0.4138, 1.6946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6217
Odds Ratio (OR) (95% CI)		0.8258 (0.3863, 1.7654)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6215

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0129 (-0.0639, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6206

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	5 (2.55)
Relative Risk (RR) (95% CI)		1.0306 (0.3031, 3.5046)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9615
Odds Ratio (OR) (95% CI)		1.0314 (0.2939, 3.6197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9615
Risk Difference (RD) (95% CI)		0.0008 (-0.0300, 0.0315)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9615
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Sinus congestion	5 (2.48)	14 (7.14)
Relative Risk (RR) (95% CI)		2.8857 (1.0594, 7.8601)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0382
Odds Ratio (OR) (95% CI)		3.0308 (1.0704, 8.5817)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0368
Risk Difference (RD) (95% CI)		0.0467 (0.0047, 0.0886)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0292
Grade 1/Mild	4 (1.98)	11 (5.61)
Relative Risk (RR) (95% CI)		2.8342 (0.9179, 8.7506)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0701
Odds Ratio (OR) (95% CI)		2.9432 (0.9210, 9.4056)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0686

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0363 (-0.0012, 0.0738)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0578

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	3 (1.53)
Relative Risk (RR) (95% CI)		3.0918 (0.3244, 29.4705)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3265
Odds Ratio (OR) (95% CI)		3.1244 (0.3222, 30.2956)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3257
Risk Difference (RD) (95% CI)		0.0104 (-0.0094, 0.0301)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3035
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Haemoptysis	11 (5.45)	13 (6.63)
Relative Risk (RR) (95% CI)		1.2180 (0.5592, 2.6531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6196
Odds Ratio (OR) (95% CI)		1.2335 (0.5389, 2.8235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6195
Risk Difference (RD) (95% CI)		0.0119 (-0.0350, 0.0587)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6193
Grade 1/Mild	7 (3.47)	7 (3.57)
Relative Risk (RR) (95% CI)		1.0306 (0.3683, 2.8841)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9542
Odds Ratio (OR) (95% CI)		1.0317 (0.3551, 2.9977)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9542

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0011 (-0.0351, 0.0373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9542

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	4 (1.98)	4 (2.04)
Relative Risk (RR) (95% CI)		1.0306 (0.2614, 4.0635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9656
Odds Ratio (OR) (95% CI)		1.0313 (0.2543, 4.1821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9656
Risk Difference (RD) (95% CI)		0.0006 (-0.0270, 0.0282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9656
Grade 3/Severe	0	2 (1.02)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0102 (-0.0039, 0.0243)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Productive cough	5 (2.48)	12 (6.12)
Relative Risk (RR) (95% CI)		2.4735 (0.8878, 6.8910)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0832
Odds Ratio (OR) (95% CI)		2.5696 (0.8881, 7.4349)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0817
Risk Difference (RD) (95% CI)		0.0365 (-0.0033, 0.0763)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0726
Grade 1/Mild	2 (0.99)	8 (4.08)
Relative Risk (RR) (95% CI)		4.1224 (0.8865, 19.1715)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0709
Odds Ratio (OR) (95% CI)		4.2553 (0.8922, 20.2954)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0692

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0309 (0.0000, 0.0618)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0498

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	4 (2.04)
Relative Risk (RR) (95% CI)		1.3741 (0.3116, 6.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6746
Odds Ratio (OR) (95% CI)		1.3819 (0.3053, 6.2558)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6746
Risk Difference (RD) (95% CI)		0.0056 (-0.0203, 0.0314)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6740
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Respiration abnormal	5 (2.48)	8 (4.08)
Relative Risk (RR) (95% CI)		1.6490 (0.5489, 4.9535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3728
Odds Ratio (OR) (95% CI)		1.6766 (0.5389, 5.2166)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3722
Risk Difference (RD) (95% CI)		0.0161 (-0.0190, 0.0511)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3686
Grade 1/Mild	4 (1.98)	5 (2.55)
Relative Risk (RR) (95% CI)		1.2883 (0.3511, 4.7271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7025
Odds Ratio (OR) (95% CI)		1.2958 (0.3428, 4.8982)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7025

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0057 (-0.0236, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7022

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	3 (1.53)
Relative Risk (RR) (95% CI)		3.0918 (0.3244, 29.4705)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3265
Odds Ratio (OR) (95% CI)		3.1244 (0.3222, 30.2956)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3257
Risk Difference (RD) (95% CI)		0.0104 (-0.0094, 0.0301)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3035
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Dyspnoea	7 (3.47)	7 (3.57)
Relative Risk (RR) (95% CI)		1.0306 (0.3683, 2.8841)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9542
Odds Ratio (OR) (95% CI)		1.0317 (0.3551, 2.9977)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9542
Risk Difference (RD) (95% CI)		0.0011 (-0.0351, 0.0373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9542
Grade 1/Mild	7 (3.47)	2 (1.02)
Relative Risk (RR) (95% CI)		0.2945 (0.0619, 1.4001)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1243
Odds Ratio (OR) (95% CI)		0.2872 (0.0589, 1.3998)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1226

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0244 (-0.0533, 0.0044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0971

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	0	5 (2.55)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0255 (0.0034, 0.0476)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0235
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Sputum discoloured	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524
Grade 1/Mild	4 (1.98)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0198 (-0.0390, -0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0434

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	4 (2.04)
Relative Risk (RR) (95% CI)		2.0612 (0.3819, 11.1258)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4004
Odds Ratio (OR) (95% CI)		2.0833 (0.3772, 11.5059)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3999
Risk Difference (RD) (95% CI)		0.0105 (-0.0135, 0.0346)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3918
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Investigations	72 (35.64)	72 (36.73)
Relative Risk (RR) (95% CI)		1.0306 (0.7939, 1.3379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8208
Odds Ratio (OR) (95% CI)		1.0484 (0.6965, 1.5781)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8208
Risk Difference (RD) (95% CI)		0.0109 (-0.0835, 0.1053)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8208
Grade 1/Mild	41 (20.30)	47 (23.98)
Relative Risk (RR) (95% CI)		1.1814 (0.8162, 1.7102)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3770
Odds Ratio (OR) (95% CI)		1.2387 (0.7708, 1.9906)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3766

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- [2] Odds ratio from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0368 (-0.0447, 0.1184)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3761

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	28 (13.86)	23 (11.73)
Relative Risk (RR) (95% CI)		0.8466 (0.5056, 1.4174)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5265
Odds Ratio (OR) (95% CI)		0.8262 (0.4578, 1.4909)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5261
Risk Difference (RD) (95% CI)		-0.0213 (-0.0868, 0.0443)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5250
Grade 3/Severe	3 (1.49)	2 (1.02)
Relative Risk (RR) (95% CI)		0.6871 (0.1161, 4.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6791
Odds Ratio (OR) (95% CI)		0.6838 (0.1130, 4.1374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6790

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0046 (-0.0265, 0.0172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6764

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Blood creatine phosphokinase increased	24 (11.88)	18 (9.18)
Relative Risk (RR) (95% CI)		0.7730 (0.4334, 1.3787)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3831
Odds Ratio (OR) (95% CI)		0.7500 (0.3933, 1.4302)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3824
Risk Difference (RD) (95% CI)		-0.0270 (-0.0872, 0.0332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3799
Grade 1/Mild	18 (8.91)	14 (7.14)
Relative Risk (RR) (95% CI)		0.8016 (0.4101, 1.5668)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5178
Odds Ratio (OR) (95% CI)		0.7863 (0.3797, 1.6282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5174

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0177 (-0.0710, 0.0356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5158

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	4 (2.04)
Relative Risk (RR) (95% CI)		0.8245 (0.2247, 3.0253)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7711
Odds Ratio (OR) (95% CI)		0.8208 (0.2172, 3.1027)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7710
Risk Difference (RD) (95% CI)		-0.0043 (-0.0335, 0.0248)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7704
Grade 3/Severe	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Alanine aminotransferase increased	11 (5.45)	13 (6.63)
Relative Risk (RR) (95% CI)		1.2180 (0.5592, 2.6531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6196
Odds Ratio (OR) (95% CI)		1.2335 (0.5389, 2.8235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6195
Risk Difference (RD) (95% CI)		0.0119 (-0.0350, 0.0587)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6193
Grade 1/Mild	7 (3.47)	7 (3.57)
Relative Risk (RR) (95% CI)		1.0306 (0.3683, 2.8841)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9542
Odds Ratio (OR) (95% CI)		1.0317 (0.3551, 2.9977)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9542

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0011 (-0.0351, 0.0373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9542

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	6 (3.06)
Relative Risk (RR) (95% CI)		2.0612 (0.5228, 8.1271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3014
Odds Ratio (OR) (95% CI)		2.0947 (0.5165, 8.4953)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3006
Risk Difference (RD) (95% CI)		0.0158 (-0.0136, 0.0451)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2921
Grade 3/Severe	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Aspartate aminotransferase increased	9 (4.46)	12 (6.12)
Relative Risk (RR) (95% CI)		1.3741 (0.5923, 3.1882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4592
Odds Ratio (OR) (95% CI)		1.3986 (0.5757, 3.3973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4588
Risk Difference (RD) (95% CI)		0.0167 (-0.0273, 0.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4578
Grade 1/Mild	7 (3.47)	6 (3.06)
Relative Risk (RR) (95% CI)		0.8834 (0.3022, 2.5820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8207
Odds Ratio (OR) (95% CI)		0.8797 (0.2903, 2.6655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8207

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0040 (-0.0389, 0.0309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8204

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	6 (3.06)
Relative Risk (RR) (95% CI)		6.1837 (0.7513, 50.8955)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0903
Odds Ratio (OR) (95% CI)		6.3474 (0.7571, 53.2135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0885
Risk Difference (RD) (95% CI)		0.0257 (-0.0003, 0.0516)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0529
Grade 3/Severe	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Weight decreased	1 (0.50)	9 (4.59)
Relative Risk (RR) (95% CI)		9.2755 (1.1862, 72.5295)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0338
Odds Ratio (OR) (95% CI)		9.6738 (1.2139, 77.0904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0321
Risk Difference (RD) (95% CI)		0.0410 (0.0101, 0.0718)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0093
Grade 1/Mild	1 (0.50)	7 (3.57)
Relative Risk (RR) (95% CI)		7.2143 (0.8958, 58.0972)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0634
Odds Ratio (OR) (95% CI)		7.4444 (0.9074, 61.0777)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0616

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0308 (0.0030, 0.0585)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0296

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	0	2 (1.02)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0102 (-0.0039, 0.0243)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
SARS-CoV-2 test positive	3 (1.49)	8 (4.08)
Relative Risk (RR) (95% CI)		2.7483 (0.7399, 10.2088)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1311
Odds Ratio (OR) (95% CI)		2.8227 (0.7378, 10.7993)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1296
Risk Difference (RD) (95% CI)		0.0260 (-0.0064, 0.0583)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1155
Grade 1/Mild	1 (0.50)	5 (2.55)
Relative Risk (RR) (95% CI)		5.1531 (0.6075, 43.7115)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1328
Odds Ratio (OR) (95% CI)		5.2618 (0.6092, 45.4502)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1312

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0206 (-0.0035, 0.0447)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0945

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	3 (1.53)
Relative Risk (RR) (95% CI)		1.5459 (0.2611, 9.1521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6312
Odds Ratio (OR) (95% CI)		1.5544 (0.2569, 9.4045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6310
Risk Difference (RD) (95% CI)		0.0054 (-0.0165, 0.0274)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6294
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Bacterial test positive	6 (2.97)	7 (3.57)
Relative Risk (RR) (95% CI)		1.2024 (0.4114, 3.5144)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7363
Odds Ratio (OR) (95% CI)		1.2099 (0.3993, 3.6660)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7362
Risk Difference (RD) (95% CI)		0.0060 (-0.0290, 0.0410)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7362
Grade 1/Mild	4 (1.98)	5 (2.55)
Relative Risk (RR) (95% CI)		1.2883 (0.3511, 4.7271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7025
Odds Ratio (OR) (95% CI)		1.2958 (0.3428, 4.8982)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7025

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0057 (-0.0236, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7022

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	2 (1.02)
Relative Risk (RR) (95% CI)		1.0306 (0.1466, 7.2445)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9758
Odds Ratio (OR) (95% CI)		1.0309 (0.1438, 7.3916)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9758
Risk Difference (RD) (95% CI)		0.0003 (-0.0193, 0.0199)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9758
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Blood bilirubin increased	7 (3.47)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5889 (0.1751, 1.9802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3921
Odds Ratio (OR) (95% CI)		0.5804 (0.1672, 2.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3915
Risk Difference (RD) (95% CI)		-0.0142 (-0.0463, 0.0178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3839
Grade 1/Mild	4 (1.98)	3 (1.53)
Relative Risk (RR) (95% CI)		0.7730 (0.1753, 3.4092)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7338
Odds Ratio (OR) (95% CI)		0.7694 (0.1700, 3.4831)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7337

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0045 (-0.0303, 0.0213)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7325

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	1 (0.51)
Relative Risk (RR) (95% CI)		0.3435 (0.0360, 3.2745)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3530
Odds Ratio (OR) (95% CI)		0.3402 (0.0351, 3.2985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3522
Risk Difference (RD) (95% CI)		-0.0097 (-0.0292, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3255
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Gastrointestinal disorders	68 (33.66)	64 (32.65)
Relative Risk (RR) (95% CI)		0.9700 (0.7338, 1.2823)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8306
Odds Ratio (OR) (95% CI)		0.9554 (0.6294, 1.4505)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8305
Risk Difference (RD) (95% CI)		-0.0101 (-0.1026, 0.0824)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8305
Grade 1/Mild	50 (24.75)	45 (22.96)
Relative Risk (RR) (95% CI)		0.9276 (0.6526, 1.3183)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6750
Odds Ratio (OR) (95% CI)		0.9060 (0.5711, 1.4371)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6749

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0179 (-0.1017, 0.0658)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6746

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	18 (8.91)	17 (8.67)
Relative Risk (RR) (95% CI)		0.9734 (0.5168, 1.8332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9334
Odds Ratio (OR) (95% CI)		0.9708 (0.4850, 1.9434)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9334
Risk Difference (RD) (95% CI)		-0.0024 (-0.0580, 0.0533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9334
Grade 3/Severe	0	2 (1.02)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0102 (-0.0039, 0.0243)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Diarrhoea	15 (7.43)	21 (10.71)
Relative Risk (RR) (95% CI)		1.4429 (0.7663, 2.7167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2561
Odds Ratio (OR) (95% CI)		1.4960 (0.7474, 2.9943)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2552
Risk Difference (RD) (95% CI)		0.0329 (-0.0235, 0.0893)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2532
Grade 1/Mild	15 (7.43)	18 (9.18)
Relative Risk (RR) (95% CI)		1.2367 (0.6415, 2.3843)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5258
Odds Ratio (OR) (95% CI)		1.2607 (0.6165, 2.5778)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5256

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0176 (-0.0367, 0.0718)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5253

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	0	3 (1.53)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0153 (-0.0019, 0.0325)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0809
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Abdominal pain upper	6 (2.97)	12 (6.12)
Relative Risk (RR) (95% CI)		2.0612 (0.7892, 5.3837)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1398
Odds Ratio (OR) (95% CI)		2.1304 (0.7834, 5.7936)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1384
Risk Difference (RD) (95% CI)		0.0315 (-0.0094, 0.0724)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1311
Grade 1/Mild	5 (2.48)	6 (3.06)
Relative Risk (RR) (95% CI)		1.2367 (0.3837, 3.9865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7220
Odds Ratio (OR) (95% CI)		1.2442 (0.3735, 4.1451)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7219

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0059 (-0.0264, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7218

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	5 (2.55)
Relative Risk (RR) (95% CI)		5.1531 (0.6075, 43.7115)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1328
Odds Ratio (OR) (95% CI)		5.2618 (0.6092, 45.4502)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1312
Risk Difference (RD) (95% CI)		0.0206 (-0.0035, 0.0447)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0945
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Abdominal pain	14 (6.93)	10 (5.10)
Relative Risk (RR) (95% CI)		0.7362 (0.3350, 1.6177)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4457
Odds Ratio (OR) (95% CI)		0.7220 (0.3128, 1.6664)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4452
Risk Difference (RD) (95% CI)		-0.0183 (-0.0649, 0.0284)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4422
Grade 1/Mild	10 (4.95)	5 (2.55)
Relative Risk (RR) (95% CI)		0.5153 (0.1794, 1.4805)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2182
Odds Ratio (OR) (95% CI)		0.5026 (0.1686, 1.4980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2170

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0240 (-0.0612, 0.0132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2059

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	4 (1.98)	4 (2.04)
Relative Risk (RR) (95% CI)		1.0306 (0.2614, 4.0635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9656
Odds Ratio (OR) (95% CI)		1.0313 (0.2543, 4.1821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9656
Risk Difference (RD) (95% CI)		0.0006 (-0.0270, 0.0282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9656
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
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- [1] Relative risk from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Constipation	10 (4.95)	7 (3.57)
Relative Risk (RR) (95% CI)		0.7214 (0.2802, 1.8574)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4986
Odds Ratio (OR) (95% CI)		0.7111 (0.2651, 1.9072)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4982
Risk Difference (RD) (95% CI)		-0.0138 (-0.0534, 0.0258)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4951
Grade 1/Mild	5 (2.48)	6 (3.06)
Relative Risk (RR) (95% CI)		1.2367 (0.3837, 3.9865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7220
Odds Ratio (OR) (95% CI)		1.2442 (0.3735, 4.1451)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7219

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0059 (-0.0264, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7218

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0248 (-0.0462, -0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0236
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nausea	17 (8.42)	7 (3.57)
Relative Risk (RR) (95% CI)		0.4244 (0.1799, 1.0008)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0502
Odds Ratio (OR) (95% CI)		0.4031 (0.1633, 0.9946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0486
Risk Difference (RD) (95% CI)		-0.0484 (-0.0947, -0.0022)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0402
Grade 1/Mild	14 (6.93)	7 (3.57)
Relative Risk (RR) (95% CI)		0.5153 (0.2125, 1.2495)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1424
Odds Ratio (OR) (95% CI)		0.4974 (0.1963, 1.2599)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1408

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0336 (-0.0772, 0.0100)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1311

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0149 (-0.0315, 0.0018)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0810
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Flatulence	7 (3.47)	6 (3.06)
Relative Risk (RR) (95% CI)		0.8834 (0.3022, 2.5820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8207
Odds Ratio (OR) (95% CI)		0.8797 (0.2903, 2.6655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8207
Risk Difference (RD) (95% CI)		-0.0040 (-0.0389, 0.0309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8204
Grade 1/Mild	7 (3.47)	6 (3.06)
Relative Risk (RR) (95% CI)		0.8834 (0.3022, 2.5820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8207
Odds Ratio (OR) (95% CI)		0.8797 (0.2903, 2.6655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8207

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- [1] Relative risk from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0040 (-0.0389, 0.0309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8204

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Abdominal distension	10 (4.95)	5 (2.55)
Relative Risk (RR) (95% CI)		0.5153 (0.1794, 1.4805)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2182
Odds Ratio (OR) (95% CI)		0.5026 (0.1686, 1.4980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2170
Risk Difference (RD) (95% CI)		-0.0240 (-0.0612, 0.0132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2059
Grade 1/Mild	8 (3.96)	5 (2.55)
Relative Risk (RR) (95% CI)		0.6441 (0.2144, 1.9350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4332
Odds Ratio (OR) (95% CI)		0.6348 (0.2040, 1.9752)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4327

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0141 (-0.0489, 0.0207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4272

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0099 (-0.0236, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Vomiting	8 (3.96)	3 (1.53)
Relative Risk (RR) (95% CI)		0.3865 (0.1040, 1.4356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1556
Odds Ratio (OR) (95% CI)		0.3769 (0.0985, 1.4421)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1541
Risk Difference (RD) (95% CI)		-0.0243 (-0.0562, 0.0076)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1357
Grade 1/Mild	7 (3.47)	2 (1.02)
Relative Risk (RR) (95% CI)		0.2945 (0.0619, 1.4001)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1243
Odds Ratio (OR) (95% CI)		0.2872 (0.0589, 1.3998)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1226

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0244 (-0.0533, 0.0044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0971

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	1 (0.51)
Relative Risk (RR) (95% CI)		1.0306 (0.0649, 16.3624)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9829
Odds Ratio (OR) (95% CI)		1.0308 (0.0640, 16.5951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9829
Risk Difference (RD) (95% CI)		0.0002 (-0.0137, 0.0140)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9829
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
General disorders and administration site conditions	47 (23.27)	56 (28.57)
Relative Risk (RR) (95% CI)		1.2280 (0.8791, 1.7153)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2285
Odds Ratio (OR) (95% CI)		1.3191 (0.8411, 2.0690)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2277
Risk Difference (RD) (95% CI)		0.0530 (-0.0330, 0.1390)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2267
Grade 1/Mild	37 (18.32)	43 (21.94)
Relative Risk (RR) (95% CI)		1.1977 (0.8084, 1.7746)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3683
Odds Ratio (OR) (95% CI)		1.2533 (0.7667, 2.0488)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3679

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0362 (-0.0425, 0.1150)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3674

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	10 (4.95)	12 (6.12)
Relative Risk (RR) (95% CI)		1.2367 (0.5469, 2.7964)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6098
Odds Ratio (OR) (95% CI)		1.2522 (0.5282, 2.9686)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6096
Risk Difference (RD) (95% CI)		0.0117 (-0.0332, 0.0567)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6094
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Pyrexia	21 (10.40)	24 (12.24)
Relative Risk (RR) (95% CI)		1.1778 (0.6784, 2.0450)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		1.2027 (0.6458, 2.2395)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0185 (-0.0438, 0.0808)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5606
Grade 1/Mild	17 (8.42)	19 (9.69)
Relative Risk (RR) (95% CI)		1.1519 (0.6171, 2.1501)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6571
Odds Ratio (OR) (95% CI)		1.1682 (0.5883, 2.3197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6570

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0128 (-0.0436, 0.0692)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6570

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	4 (1.98)	5 (2.55)
Relative Risk (RR) (95% CI)		1.2883 (0.3511, 4.7271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7025
Odds Ratio (OR) (95% CI)		1.2958 (0.3428, 4.8982)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7025
Risk Difference (RD) (95% CI)		0.0057 (-0.0236, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7022
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Fatigue	16 (7.92)	18 (9.18)
Relative Risk (RR) (95% CI)		1.1594 (0.6089, 2.2079)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6526
Odds Ratio (OR) (95% CI)		1.1756 (0.5814, 2.3770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6525
Risk Difference (RD) (95% CI)		0.0126 (-0.0423, 0.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6525
Grade 1/Mild	11 (5.45)	12 (6.12)
Relative Risk (RR) (95% CI)		1.1243 (0.5081, 2.4877)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7725
Odds Ratio (OR) (95% CI)		1.1324 (0.4875, 2.6305)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7724

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0068 (-0.0391, 0.0527)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7725

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	5 (2.55)
Relative Risk (RR) (95% CI)		1.0306 (0.3031, 3.5046)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9615
Odds Ratio (OR) (95% CI)		1.0314 (0.2939, 3.6197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9615
Risk Difference (RD) (95% CI)		0.0008 (-0.0300, 0.0315)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9615
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Pain	6 (2.97)	8 (4.08)
Relative Risk (RR) (95% CI)		1.3741 (0.4857, 3.8882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5492
Odds Ratio (OR) (95% CI)		1.3901 (0.4734, 4.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5490
Risk Difference (RD) (95% CI)		0.0111 (-0.0252, 0.0474)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5481
Grade 1/Mild	4 (1.98)	3 (1.53)
Relative Risk (RR) (95% CI)		0.7730 (0.1753, 3.4092)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7338
Odds Ratio (OR) (95% CI)		0.7694 (0.1700, 3.4831)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7337

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0045 (-0.0303, 0.0213)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7325

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	5 (2.55)
Relative Risk (RR) (95% CI)		2.5765 (0.5058, 13.1241)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2545
Odds Ratio (OR) (95% CI)		2.6178 (0.5019, 13.6550)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2535
Risk Difference (RD) (95% CI)		0.0156 (-0.0103, 0.0416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2385
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Musculoskeletal and connective tissue disorders	48 (23.76)	41 (20.92)
Relative Risk (RR) (95% CI)		0.8803 (0.6095, 1.2714)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4967
Odds Ratio (OR) (95% CI)		0.8487 (0.5290, 1.3615)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4962
Risk Difference (RD) (95% CI)		-0.0284 (-0.1102, 0.0533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4955
Grade 1/Mild	27 (13.37)	29 (14.80)
Relative Risk (RR) (95% CI)		1.1070 (0.6809, 1.7996)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6819
Odds Ratio (OR) (95% CI)		1.1255 (0.6394, 1.9811)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6819

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0143 (-0.0541, 0.0827)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6819

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	21 (10.40)	11 (5.61)
Relative Risk (RR) (95% CI)		0.5398 (0.2674, 1.0899)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0854
Odds Ratio (OR) (95% CI)		0.5125 (0.2402, 1.0933)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0838
Risk Difference (RD) (95% CI)		-0.0478 (-0.1008, 0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0769
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Arthralgia	11 (5.45)	10 (5.10)
Relative Risk (RR) (95% CI)		0.9369 (0.4071, 2.1562)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8782
Odds Ratio (OR) (95% CI)		0.9335 (0.3873, 2.2503)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8782
Risk Difference (RD) (95% CI)		-0.0034 (-0.0473, 0.0405)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8781
Grade 1/Mild	5 (2.48)	6 (3.06)
Relative Risk (RR) (95% CI)		1.2367 (0.3837, 3.9865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7220
Odds Ratio (OR) (95% CI)		1.2442 (0.3735, 4.1451)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7219

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0059 (-0.0264, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7218

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Back pain	16 (7.92)	9 (4.59)
Relative Risk (RR) (95% CI)		0.5797 (0.2624, 1.2807)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1776
Odds Ratio (OR) (95% CI)		0.5595 (0.2412, 1.2979)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1762
Risk Difference (RD) (95% CI)		-0.0333 (-0.0807, 0.0141)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1686
Grade 1/Mild	9 (4.46)	8 (4.08)
Relative Risk (RR) (95% CI)		0.9161 (0.3608, 2.3262)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8538
Odds Ratio (OR) (95% CI)		0.9125 (0.3448, 2.4152)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8538

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0037 (-0.0434, 0.0360)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8536

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	7 (3.47)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0347 (-0.0599, -0.0094)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0071
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Myalgia	3 (1.49)	7 (3.57)
Relative Risk (RR) (95% CI)		2.4048 (0.6308, 9.1669)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1987
Odds Ratio (OR) (95% CI)		2.4568 (0.6261, 9.6401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1975
Risk Difference (RD) (95% CI)		0.0209 (-0.0100, 0.0517)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1854
Grade 1/Mild	2 (0.99)	5 (2.55)
Relative Risk (RR) (95% CI)		2.5765 (0.5058, 13.1241)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2545
Odds Ratio (OR) (95% CI)		2.6178 (0.5019, 13.6550)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2535

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0156 (-0.0103, 0.0416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2385

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	2 (1.02)
Relative Risk (RR) (95% CI)		2.0612 (0.1884, 22.5492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5535
Odds Ratio (OR) (95% CI)		2.0722 (0.1864, 23.0379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5533
Risk Difference (RD) (95% CI)		0.0053 (-0.0118, 0.0223)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5465
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [1] Relative risk from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Nervous system disorders	34 (16.83)	39 (19.90)
Relative Risk (RR) (95% CI)		1.1822 (0.7800, 1.7916)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4302
Odds Ratio (OR) (95% CI)		1.2274 (0.7380, 2.0414)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4298
Risk Difference (RD) (95% CI)		0.0307 (-0.0454, 0.1067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4295
Grade 1/Mild	25 (12.38)	27 (13.78)
Relative Risk (RR) (95% CI)		1.1131 (0.6702, 1.8485)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6790
Odds Ratio (OR) (95% CI)		1.1311 (0.6312, 2.0271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6789

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0140 (-0.0523, 0.0803)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6789

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	8 (3.96)	9 (4.59)
Relative Risk (RR) (95% CI)		1.1594 (0.4566, 2.9441)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7557
Odds Ratio (OR) (95% CI)		1.1671 (0.4410, 3.0890)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7557
Risk Difference (RD) (95% CI)		0.0063 (-0.0335, 0.0461)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7557
Grade 3/Severe	1 (0.50)	3 (1.53)
Relative Risk (RR) (95% CI)		3.0918 (0.3244, 29.4705)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3265
Odds Ratio (OR) (95% CI)		3.1244 (0.3222, 30.2956)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3257

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0104 (-0.0094, 0.0301)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3035

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Headache	22 (10.89)	25 (12.76)
Relative Risk (RR) (95% CI)		1.1712 (0.6837, 2.0061)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5651
Odds Ratio (OR) (95% CI)		1.1962 (0.6500, 2.2014)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5649
Risk Difference (RD) (95% CI)		0.0186 (-0.0448, 0.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5648
Grade 1/Mild	18 (8.91)	18 (9.18)
Relative Risk (RR) (95% CI)		1.0306 (0.5527, 1.9217)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9244
Odds Ratio (OR) (95% CI)		1.0337 (0.5211, 2.0507)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9244

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0027 (-0.0536, 0.0591)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9244

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	5 (2.55)
Relative Risk (RR) (95% CI)		1.7177 (0.4161, 7.0907)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4546
Odds Ratio (OR) (95% CI)		1.7365 (0.4093, 7.3663)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4542
Risk Difference (RD) (95% CI)		0.0107 (-0.0170, 0.0383)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4502
Grade 3/Severe	1 (0.50)	2 (1.02)
Relative Risk (RR) (95% CI)		2.0612 (0.1884, 22.5492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5535
Odds Ratio (OR) (95% CI)		2.0722 (0.1864, 23.0379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5533

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0053 (-0.0118, 0.0223)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5465

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Injury, poisoning and procedural complications	36 (17.82)	36 (18.37)
Relative Risk (RR) (95% CI)		1.0306 (0.6785, 1.5656)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8876
Odds Ratio (OR) (95% CI)		1.0375 (0.6227, 1.7285)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8876
Risk Difference (RD) (95% CI)		0.0055 (-0.0702, 0.0811)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8876
Grade 1/Mild	22 (10.89)	20 (10.20)
Relative Risk (RR) (95% CI)		0.9369 (0.5284, 1.6613)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8236
Odds Ratio (OR) (95% CI)		0.9298 (0.4902, 1.7636)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8235

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0672, 0.0535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8234

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	12 (5.94)	16 (8.16)
Relative Risk (RR) (95% CI)		1.3741 (0.6674, 2.8294)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3884
Odds Ratio (OR) (95% CI)		1.4074 (0.6479, 3.0572)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3879
Risk Difference (RD) (95% CI)		0.0222 (-0.0281, 0.0725)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3866
Grade 3/Severe	2 (0.99)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0099 (-0.0236, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Skin and subcutaneous tissue disorders	35 (17.33)	30 (15.31)
Relative Risk (RR) (95% CI)		0.8834 (0.5654, 1.3803)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5861
Odds Ratio (OR) (95% CI)		0.8623 (0.5061, 1.4692)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5858
Risk Difference (RD) (95% CI)		-0.0202 (-0.0928, 0.0524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5852
Grade 1/Mild	30 (14.85)	23 (11.73)
Relative Risk (RR) (95% CI)		0.7901 (0.4762, 1.3111)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3620
Odds Ratio (OR) (95% CI)		0.7622 (0.4256, 1.3651)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3612

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0312 (-0.0978, 0.0354)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3590

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	5 (2.48)	7 (3.57)
Relative Risk (RR) (95% CI)		1.4429 (0.4658, 4.4697)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5251
Odds Ratio (OR) (95% CI)		1.4593 (0.4552, 4.6776)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5248
Risk Difference (RD) (95% CI)		0.0110 (-0.0227, 0.0446)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5235
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Rash	9 (4.46)	12 (6.12)
Relative Risk (RR) (95% CI)		1.3741 (0.5923, 3.1882)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4592
Odds Ratio (OR) (95% CI)		1.3986 (0.5757, 3.3973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4588
Risk Difference (RD) (95% CI)		0.0167 (-0.0273, 0.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4578
Grade 1/Mild	8 (3.96)	10 (5.10)
Relative Risk (RR) (95% CI)		1.2883 (0.5192, 3.1963)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5848
Odds Ratio (OR) (95% CI)		1.3038 (0.5036, 3.3752)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5847

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0114 (-0.0295, 0.0523)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5843

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	1 (0.50)	2 (1.02)
Relative Risk (RR) (95% CI)		2.0612 (0.1884, 22.5492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5535
Odds Ratio (OR) (95% CI)		2.0722 (0.1864, 23.0379)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5533
Risk Difference (RD) (95% CI)		0.0053 (-0.0118, 0.0223)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5465
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Acne	8 (3.96)	5 (2.55)
Relative Risk (RR) (95% CI)		0.6441 (0.2144, 1.9350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4332
Odds Ratio (OR) (95% CI)		0.6348 (0.2040, 1.9752)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4327
Risk Difference (RD) (95% CI)		-0.0141 (-0.0489, 0.0207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4272
Grade 1/Mild	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	1 (0.51)
Relative Risk (RR) (95% CI)		0.5153 (0.0471, 5.6373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5870
Odds Ratio (OR) (95% CI)		0.5128 (0.0461, 5.7014)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5868
Risk Difference (RD) (95% CI)		-0.0048 (-0.0217, 0.0121)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5780
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Metabolism and nutrition disorders	18 (8.91)	20 (10.20)
Relative Risk (RR) (95% CI)		1.1451 (0.6249, 2.0985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6610
Odds Ratio (OR) (95% CI)		1.1616 (0.5947, 2.2689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6610
Risk Difference (RD) (95% CI)		0.0129 (-0.0449, 0.0707)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6609
Grade 1/Mild	12 (5.94)	15 (7.65)
Relative Risk (RR) (95% CI)		1.2883 (0.6188, 2.6819)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4983
Odds Ratio (OR) (95% CI)		1.3122 (0.5980, 2.8794)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4981

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0171 (-0.0324, 0.0666)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4975

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Hypoglycaemia	7 (3.47)	5 (2.55)
Relative Risk (RR) (95% CI)		0.7362 (0.2376, 2.2804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5954
Odds Ratio (OR) (95% CI)		0.7292 (0.2275, 2.3376)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5952
Risk Difference (RD) (95% CI)		-0.0091 (-0.0427, 0.0244)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5929
Grade 1/Mild	3 (1.49)	4 (2.04)
Relative Risk (RR) (95% CI)		1.3741 (0.3116, 6.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6746
Odds Ratio (OR) (95% CI)		1.3819 (0.3053, 6.2558)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6746

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0056 (-0.0203, 0.0314)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6740

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	4 (1.98)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0198 (-0.0390, -0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0434
Grade 3/Severe	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [1] Relative risk from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Psychiatric disorders	34 (16.83)	19 (9.69)
Relative Risk (RR) (95% CI)		0.5759 (0.3404, 0.9744)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0397
Odds Ratio (OR) (95% CI)		0.5304 (0.2912, 0.9663)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0383
Risk Difference (RD) (95% CI)		-0.0714 (-0.1375, -0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0345
Grade 1/Mild	17 (8.42)	10 (5.10)
Relative Risk (RR) (95% CI)		0.6062 (0.2847, 1.2911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1944
Odds Ratio (OR) (95% CI)		0.5851 (0.2610, 1.3115)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1931

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0331 (-0.0823, 0.0160)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1863

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	14 (6.93)	7 (3.57)
Relative Risk (RR) (95% CI)		0.5153 (0.2125, 1.2495)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1424
Odds Ratio (OR) (95% CI)		0.4974 (0.1963, 1.2599)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1408
Risk Difference (RD) (95% CI)		-0.0336 (-0.0772, 0.0100)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1311
Grade 3/Severe	3 (1.49)	2 (1.02)
Relative Risk (RR) (95% CI)		0.6871 (0.1161, 4.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6791
Odds Ratio (OR) (95% CI)		0.6838 (0.1130, 4.1374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6790

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0046 (-0.0265, 0.0172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6764

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Depression	7 (3.47)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5889 (0.1751, 1.9802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3921
Odds Ratio (OR) (95% CI)		0.5804 (0.1672, 2.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3915
Risk Difference (RD) (95% CI)		-0.0142 (-0.0463, 0.0178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3839
Grade 1/Mild	5 (2.48)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0248 (-0.0462, -0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0236

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	4 (2.04)
Relative Risk (RR) (95% CI)		2.0612 (0.3819, 11.1258)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4004
Odds Ratio (OR) (95% CI)		2.0833 (0.3772, 11.5059)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3999
Risk Difference (RD) (95% CI)		0.0105 (-0.0135, 0.0346)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3918
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Insomnia	8 (3.96)	4 (2.04)
Relative Risk (RR) (95% CI)		0.5153 (0.1577, 1.6838)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2724
Odds Ratio (OR) (95% CI)		0.5052 (0.1496, 1.7056)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2714
Risk Difference (RD) (95% CI)		-0.0192 (-0.0526, 0.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2599
Grade 1/Mild	5 (2.48)	4 (2.04)
Relative Risk (RR) (95% CI)		0.8245 (0.2247, 3.0253)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7711
Odds Ratio (OR) (95% CI)		0.8208 (0.2172, 3.1027)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7710

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0043 (-0.0335, 0.0248)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7704

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0149 (-0.0315, 0.0018)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0810
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Immune system disorders	2 (0.99)	8 (4.08)
Relative Risk (RR) (95% CI)		4.1224 (0.8865, 19.1715)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0709
Odds Ratio (OR) (95% CI)		4.2553 (0.8922, 20.2954)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0692
Risk Difference (RD) (95% CI)		0.0309 (0.0000, 0.0618)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0498
Grade 1/Mild	2 (0.99)	3 (1.53)
Relative Risk (RR) (95% CI)		1.5459 (0.2611, 9.1521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6312
Odds Ratio (OR) (95% CI)		1.5544 (0.2569, 9.4045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6310

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0054 (-0.0165, 0.0274)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6294

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	0	3 (1.53)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0153 (-0.0019, 0.0325)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0809
Grade 3/Severe	0	2 (1.02)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0102 (-0.0039, 0.0243)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Eye disorders	9 (4.46)	7 (3.57)
Relative Risk (RR) (95% CI)		0.8016 (0.3045, 2.1103)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6543
Odds Ratio (OR) (95% CI)		0.7942 (0.2899, 2.1761)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6542
Risk Difference (RD) (95% CI)		-0.0088 (-0.0474, 0.0297)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6529
Grade 1/Mild	6 (2.97)	4 (2.04)
Relative Risk (RR) (95% CI)		0.6871 (0.1969, 2.3976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5561
Odds Ratio (OR) (95% CI)		0.6806 (0.1891, 2.4494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5559

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0093 (-0.0400, 0.0214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5524

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	3 (1.53)
Relative Risk (RR) (95% CI)		1.0306 (0.2105, 5.0447)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9703
Odds Ratio (OR) (95% CI)		1.0311 (0.2056, 5.1713)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9703
Risk Difference (RD) (95% CI)		0.0005 (-0.0235, 0.0244)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9703
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Reproductive system and breast disorders	15 (7.43)	7 (3.57)
Relative Risk (RR) (95% CI)		0.4810 (0.2004, 1.1542)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1012
Odds Ratio (OR) (95% CI)		0.4617 (0.1841, 1.1582)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0996
Risk Difference (RD) (95% CI)		-0.0385 (-0.0831, 0.0060)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0897
Grade 1/Mild	12 (5.94)	5 (2.55)
Relative Risk (RR) (95% CI)		0.4294 (0.1541, 1.1964)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1059
Odds Ratio (OR) (95% CI)		0.4145 (0.1433, 1.1993)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1042

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0339 (-0.0733, 0.0055)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0915

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	3 (1.49)	2 (1.02)
Relative Risk (RR) (95% CI)		0.6871 (0.1161, 4.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6791
Odds Ratio (OR) (95% CI)		0.6838 (0.1130, 4.1374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6790
Risk Difference (RD) (95% CI)		-0.0046 (-0.0265, 0.0172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6764
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Ear and labyrinth disorders	10 (4.95)	5 (2.55)
Relative Risk (RR) (95% CI)		0.5153 (0.1794, 1.4805)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2182
Odds Ratio (OR) (95% CI)		0.5026 (0.1686, 1.4980)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2170
Risk Difference (RD) (95% CI)		-0.0240 (-0.0612, 0.0132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2059
Grade 1/Mild	8 (3.96)	5 (2.55)
Relative Risk (RR) (95% CI)		0.6441 (0.2144, 1.9350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4332
Odds Ratio (OR) (95% CI)		0.6348 (0.2040, 1.9752)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4327

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0141 (-0.0489, 0.0207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4272

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	2 (0.99)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0099 (-0.0236, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1552
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Renal and urinary disorders	16 (7.92)	5 (2.55)
Relative Risk (RR) (95% CI)		0.3221 (0.1203, 0.8622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0241
Odds Ratio (OR) (95% CI)		0.3043 (0.1093, 0.8476)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0228
Risk Difference (RD) (95% CI)		-0.0537 (-0.0970, -0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0151
Grade 1/Mild	9 (4.46)	4 (2.04)
Relative Risk (RR) (95% CI)		0.4580 (0.1434, 1.4630)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1876
Odds Ratio (OR) (95% CI)		0.4468 (0.1353, 1.4753)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1862

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0241 (-0.0588, 0.0105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1721

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 2/Moderate	7 (3.47)	1 (0.51)
Relative Risk (RR) (95% CI)		0.1472 (0.0183, 1.1857)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0719
Odds Ratio (OR) (95% CI)		0.1429 (0.0174, 1.1721)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0700
Risk Difference (RD) (95% CI)		-0.0296 (-0.0567, -0.0024)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0327
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.1.1.1
Study VX20-121-102: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any Grade 3/4/5 TEAEs	14 (6.93)	18 (9.18)
Relative Risk (RR) (95% CI)		1.3251 (0.6779, 2.5901)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4104
Odds Ratio (OR) (95% CI)		1.3579 (0.6558, 2.8119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4100
Risk Difference (RD) (95% CI)		0.0225 (-0.0310, 0.0760)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4091
Infections and infestations	3 (1.49)	7 (3.57)
Relative Risk (RR) (95% CI)		2.4048 (0.6308, 9.1669)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1987
Odds Ratio (OR) (95% CI)		2.4568 (0.6261, 9.6401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1975

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0209 (-0.0100, 0.0517)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1854

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.3
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any serious TEAEs	22 (10.89)	21 (10.71)
Relative Risk (RR) (95% CI)		0.9838 (0.5593, 1.7304)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9547
Odds Ratio (OR) (95% CI)		0.9818 (0.5213, 1.8492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9547
Risk Difference (RD) (95% CI)		-0.0018 (-0.0628, 0.0592)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9547
Infections and infestations	6 (2.97)	9 (4.59)
Relative Risk (RR) (95% CI)		1.5459 (0.5607, 4.2620)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3998
Odds Ratio (OR) (95% CI)		1.5722 (0.5489, 4.5029)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3993

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.3
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		0.0162 (-0.0213, 0.0537)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3968

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any TEAEs leading to treatment discontinuation	9 (4.46)	4 (2.04)
Relative Risk (RR) (95% CI)		0.4580 (0.1434, 1.4630)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1876
Odds Ratio (OR) (95% CI)		0.4468 (0.1353, 1.4753)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1862
Risk Difference (RD) (95% CI)		-0.0241 (-0.0588, 0.0105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1721
Investigations	3 (1.49)	2 (1.02)
Relative Risk (RR) (95% CI)		0.6871 (0.1161, 4.0676)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6791
Odds Ratio (OR) (95% CI)		0.6838 (0.1130, 4.1374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6790

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Risk Difference (RD) (95% CI)		-0.0046 (-0.0265, 0.0172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6764

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Alanine aminotransferase increased	1 (0.50)	1 (0.51)
Relative Risk (RR) (95% CI)		1.0306 (0.0649, 16.3624)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9829
Odds Ratio (OR) (95% CI)		1.0308 (0.0640, 16.5951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9829
Risk Difference (RD) (95% CI)		0.0002 (-0.0137, 0.0140)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9829
Aspartate aminotransferase increased	1 (0.50)	1 (0.51)
Relative Risk (RR) (95% CI)		1.0306 (0.0649, 16.3624)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9829
Odds Ratio (OR) (95% CI)		1.0308 (0.0640, 16.5951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9829
Risk Difference (RD) (95% CI)		0.0002 (-0.0137, 0.0140)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9829

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Blood alkaline phosphatase increased	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Blood creatine phosphokinase increased	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Pulmonary function test decreased	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Immune system disorders	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Hypersensitivity	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Infections and infestations	2 (0.99)	1 (0.51)
Relative Risk (RR) (95% CI)		0.5153 (0.0471, 5.6373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5870
Odds Ratio (OR) (95% CI)		0.5128 (0.0461, 5.7014)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5868
Risk Difference (RD) (95% CI)		-0.0048 (-0.0217, 0.0121)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5780

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- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Giardiasis	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Appendicitis	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Meningitis aseptic	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Psychiatric disorders	1 (0.50)	1 (0.51)
Relative Risk (RR) (95% CI)		1.0306 (0.0649, 16.3624)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9829
Odds Ratio (OR) (95% CI)		1.0308 (0.0640, 16.5951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9829
Risk Difference (RD) (95% CI)		0.0002 (-0.0137, 0.0140)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9829

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Anxiety	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Depression	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Suicidal ideation	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Respiratory, thoracic and mediastinal disorders	1 (0.50)	1 (0.51)
Relative Risk (RR) (95% CI)		1.0306 (0.0649, 16.3624)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9829
Odds Ratio (OR) (95% CI)		1.0308 (0.0640, 16.5951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9829
Risk Difference (RD) (95% CI)		0.0002 (-0.0137, 0.0140)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9829

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Dysphonia	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Sputum increased	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Skin and subcutaneous tissue disorders	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Rash maculo-papular	0	1 (0.51)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0051 (-0.0049, 0.0151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Gastrointestinal disorders	3 (1.49)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0149 (-0.0315, 0.0018)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0810
Abdominal pain	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Constipation	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
Gastritis	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Pancreatitis	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161
General disorders and administration site conditions	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.4
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Fatigue	1 (0.50)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0050 (-0.0146, 0.0047)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

Table 1.3.1.11
Study VX20-121-102: Summary of Death
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

Table 1.3.1.12
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events - Total and by Severity
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	70 (34.65)	57 (29.08)
Relative Risk (RR) (95% CI)		0.8392 (0.6284, 1.1207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2349
Odds Ratio (OR) (95% CI)		0.7733 (0.5065, 1.1805)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2336
Risk Difference (RD) (95% CI)		-0.0557 (-0.1471, 0.0357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2320
Subjects with non-severe events (Maximum Grade 1/2)	61 (30.20)	52 (26.53)
Relative Risk (RR) (95% CI)		0.8786 (0.6422, 1.2019)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4181
Odds Ratio (OR) (95% CI)		0.8347 (0.5393, 1.2919)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4175
Risk Difference (RD) (95% CI)		-0.0367 (-0.1252, 0.0518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4166

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.1.12
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	9 (4.46)	5 (2.55)
Relative Risk (RR) (95% CI)		0.5726 (0.1953, 1.6783)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3095
Odds Ratio (OR) (95% CI)		0.5614 (0.1848, 1.7057)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3086
Risk Difference (RD) (95% CI)		-0.0190 (-0.0551, 0.0170)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3000
Subjects with serious events	23 (11.39)	11 (5.61)
Relative Risk (RR) (95% CI)		0.4929 (0.2470, 0.9838)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0448
Odds Ratio (OR) (95% CI)		0.4627 (0.2192, 0.9770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0433
Risk Difference (RD) (95% CI)		-0.0577 (-0.1121, -0.0034)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0374

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.3533
Age at screening (<18 years vs. ≥18 years)	0.5689
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.9338
Sex (Male vs. Female)	0.0768
Region (North America vs. Rest of the World)	0.4257

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Respiratory, thoracic and mediastinal disorders	
Sinus congestion	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.0111
Age at screening (<18 years vs. ≥18 years)	0.1050
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	>0.9999
Sex (Male vs. Female)	0.3432
Region (North America vs. Rest of the World)	0.0946

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Psychiatric disorders	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.1233
Age at screening (<18 years vs. ≥18 years)	0.0539
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.2156
Sex (Male vs. Female)	0.6266
Region (North America vs. Rest of the World)	0.1936

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Renal and urinary disorders	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.5852
Age at screening (<18 years vs. ≥18 years)	0.3138
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	>0.9999
Sex (Male vs. Female)	0.1878
Region (North America vs. Rest of the World)	0.3814

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for TEAEs by SOC and PT for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs	
Prior CFTR modulator use (yes vs. no)	0.1571

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for TEAEs by SOC and PT for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Respiratory, thoracic and mediastinal disorders	
Sinus congestion	
Prior CFTR modulator use (yes vs. no)	0.4404

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for TEAEs by SOC and PT for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Psychiatric disorders	
Prior CFTR modulator use (yes vs. no)	0.3524

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for TEAEs by SOC and PT for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Renal and urinary disorders	
Prior CFTR modulator use (yes vs. no)	0.4370

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline <70 %

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with any TEAEs	111 (97.37)	99 (98.02)
Relative Risk (RR) (95% CI)		1.0067 (0.9663, 1.0488)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7498
Odds Ratio (OR) (95% CI)		1.3378 (0.2190, 8.1715)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7526
Risk Difference (RD) (95% CI)		0.0065 (-0.0335, 0.0465)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7497
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	0	7 (6.93)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline <70 %

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0693 (0.0198, 0.1188)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0061
Psychiatric disorders	21 (18.42)	7 (6.93)
Relative Risk (RR) (95% CI)		0.3762 (0.1670, 0.8478)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0184
Odds Ratio (OR) (95% CI)		0.3298 (0.1338, 0.8129)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0160
Risk Difference (RD) (95% CI)		-0.1149 (-0.2016, -0.0282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0094

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Renal and urinary disorders	11 (9.65)	2 (1.98)
Relative Risk (RR) (95% CI)		0.2052 (0.0466, 0.9039)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0363
Odds Ratio (OR) (95% CI)		0.1892 (0.0409, 0.8751)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0331
Risk Difference (RD) (95% CI)		-0.0767 (-0.1373, -0.0161)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0132

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline ≥70 %

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with any TEAEs	80 (91.95)	81 (88.04)
Relative Risk (RR) (95% CI)		0.9575 (0.8684, 1.0557)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3830
Odds Ratio (OR) (95% CI)		0.6443 (0.2378, 1.7457)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3874
Risk Difference (RD) (95% CI)		-0.0391 (-0.1266, 0.0484)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3812
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	5 (5.75)	7 (7.61)
Relative Risk (RR) (95% CI)		1.3239 (0.4365, 4.0155)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6201

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline ≥70 %

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Odds Ratio (OR) (95% CI)		1.3506 (0.4121, 4.4265)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6197
Risk Difference (RD) (95% CI)		0.0186 (-0.0544, 0.0916)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6171
Psychiatric disorders	13 (14.94)	12 (13.04)
Relative Risk (RR) (95% CI)		0.8729 (0.4216, 1.8074)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7143
Odds Ratio (OR) (95% CI)		0.8538 (0.3664, 1.9895)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7143
Risk Difference (RD) (95% CI)		-0.0190 (-0.1207, 0.0827)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7144

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Renal and urinary disorders	5 (5.75)	2 (2.17)
Relative Risk (RR) (95% CI)		0.3783 (0.0754, 1.8988)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2376
Odds Ratio (OR) (95% CI)		0.3644 (0.0688, 1.9300)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2353
Risk Difference (RD) (95% CI)		-0.0357 (-0.0930, 0.0215)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2214

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening <18 years

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any TEAEs	28 (90.32)	22 (84.62)
Relative Risk (RR) (95% CI)		0.9368 (0.7667, 1.1446)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5231
Odds Ratio (OR) (95% CI)		0.5893 (0.1192, 2.9121)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5165
Risk Difference (RD) (95% CI)		-0.0571 (-0.2305, 0.1163)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5189
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	1 (3.23)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening <18 years

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0323 (-0.0945, 0.0299)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3094
Psychiatric disorders	2 (6.45)	4 (15.38)
Relative Risk (RR) (95% CI)		2.3846 (0.4741, 11.9940)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2917
Odds Ratio (OR) (95% CI)		2.6364 (0.4421, 15.7202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2873
Risk Difference (RD) (95% CI)		0.0893 (-0.0741, 0.2528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2841

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Renal and urinary disorders	2 (6.45)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0645 (-0.1510, 0.0220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1437

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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening ≥18 years

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any TEAEs	163 (95.32)	161 (94.71)
Relative Risk (RR) (95% CI)		0.9935 (0.9464, 1.0431)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7940
Odds Ratio (OR) (95% CI)		0.8780 (0.3305, 2.3322)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7940
Risk Difference (RD) (95% CI)		-0.0062 (-0.0524, 0.0400)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7939
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	4 (2.34)	14 (8.24)
Relative Risk (RR) (95% CI)		3.5206 (1.1828, 10.4788)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0237

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening ≥18 years

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		3.7468 (1.2074, 11.6269)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0222
Risk Difference (RD) (95% CI)		0.0590 (0.0118, 0.1061)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0142
Psychiatric disorders	32 (18.71)	15 (8.82)
Relative Risk (RR) (95% CI)		0.4715 (0.2652, 0.8383)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0104
Odds Ratio (OR) (95% CI)		0.4204 (0.2184, 0.8090)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0095
Risk Difference (RD) (95% CI)		-0.0989 (-0.1713, -0.0265)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0074

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Renal and urinary disorders	14 (8.19)	5 (2.94)
Relative Risk (RR) (95% CI)		0.3592 (0.1323, 0.9754)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0445
Odds Ratio (OR) (95% CI)		0.3398 (0.1196, 0.9655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0428
Risk Difference (RD) (95% CI)		-0.0525 (-0.1008, -0.0042)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0333

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline <30 mmol/L

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any TEAEs	18 (94.74)	16 (94.12)
Relative Risk (RR) (95% CI)		0.9935 (0.8472, 1.1649)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9357
Odds Ratio (OR) (95% CI)		0.8889 (0.0513, 15.4045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9355
Risk Difference (RD) (95% CI)		-0.0062 (-0.1565, 0.1441)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9356
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline <30 mmol/L

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Psychiatric disorders	1 (5.26)	2 (11.76)
Relative Risk (RR) (95% CI)		2.2353 (0.2220, 22.5093)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4948
Odds Ratio (OR) (95% CI)		2.4000 (0.1977, 29.1311)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4919
Risk Difference (RD) (95% CI)		0.0650 (-0.1181, 0.2481)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4865

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Renal and urinary disorders	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline ≥30 mmol/L

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any TEAEs	172 (94.51)	165 (93.22)
Relative Risk (RR) (95% CI)		0.9864 (0.9355, 1.0401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6124
Odds Ratio (OR) (95% CI)		0.7994 (0.3363, 1.9004)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6124
Risk Difference (RD) (95% CI)		-0.0129 (-0.0625, 0.0368)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6121
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	5 (2.75)	13 (7.34)
Relative Risk (RR) (95% CI)		2.6734 (0.9733, 7.3434)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0565

- MedDRA version 26.1.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline ≥30 mmol/L

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Odds Ratio (OR) (95% CI)		2.8061 (0.9790, 8.0433)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0548
Risk Difference (RD) (95% CI)		0.0460 (0.0008, 0.0911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0461
Psychiatric disorders	33 (18.13)	17 (9.60)
Relative Risk (RR) (95% CI)		0.5297 (0.3064, 0.9157)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0229
Odds Ratio (OR) (95% CI)		0.4797 (0.2565, 0.8974)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0215
Risk Difference (RD) (95% CI)		-0.0853 (-0.1561, -0.0144)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0183

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Renal and urinary disorders	16 (8.79)	5 (2.82)
Relative Risk (RR) (95% CI)		0.3213 (0.1203, 0.8584)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0235
Odds Ratio (OR) (95% CI)		0.3016 (0.1080, 0.8419)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0221
Risk Difference (RD) (95% CI)		-0.0597 (-0.1075, -0.0118)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0145

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Male

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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- [2] Odds ratio from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with any TEAEs	112 (94.12)	112 (96.55)
Relative Risk (RR) (95% CI)		1.0259 (0.9694, 1.0856)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3764
Odds Ratio (OR) (95% CI)		1.7500 (0.4983, 6.1454)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3825
Risk Difference (RD) (95% CI)		0.0243 (-0.0294, 0.0781)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3748
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	2 (1.68)	9 (7.76)
Relative Risk (RR) (95% CI)		4.6164 (1.0191, 20.9114)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0472

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Male

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Odds Ratio (OR) (95% CI)		4.9206 (1.0397, 23.2863)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0445
Risk Difference (RD) (95% CI)		0.0608 (0.0069, 0.1147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0270
Psychiatric disorders	20 (16.81)	10 (8.62)
Relative Risk (RR) (95% CI)		0.5129 (0.2510, 1.0482)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0671
Odds Ratio (OR) (95% CI)		0.4670 (0.2084, 1.0466)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0644
Risk Difference (RD) (95% CI)		-0.0819 (-0.1663, 0.0025)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0573

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Renal and urinary disorders	14 (11.76)	3 (2.59)
Relative Risk (RR) (95% CI)		0.2198 (0.0649, 0.7449)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0150
Odds Ratio (OR) (95% CI)		0.1991 (0.0556, 0.7125)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0131
Risk Difference (RD) (95% CI)		-0.0918 (-0.1565, -0.0271)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0054

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Female

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with any TEAEs	79 (95.18)	71 (88.75)
Relative Risk (RR) (95% CI)		0.9324 (0.8506, 1.0221)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1354
Odds Ratio (OR) (95% CI)		0.3994 (0.1179, 1.3538)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1406
Risk Difference (RD) (95% CI)		-0.0643 (-0.1475, 0.0189)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1297
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	3 (3.61)	5 (6.25)
Relative Risk (RR) (95% CI)		1.7292 (0.4272, 6.9983)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4426

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Female

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Odds Ratio (OR) (95% CI)		1.7778 (0.4106, 7.6981)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4416
Risk Difference (RD) (95% CI)		0.0264 (-0.0402, 0.0929)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4375
Psychiatric disorders	14 (16.87)	9 (11.25)
Relative Risk (RR) (95% CI)		0.6670 (0.3060, 1.4536)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3082
Odds Ratio (OR) (95% CI)		0.6247 (0.2539, 1.5375)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3059
Risk Difference (RD) (95% CI)		-0.0562 (-0.1624, 0.0501)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3000

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Renal and urinary disorders	2 (2.41)	2 (2.50)
Relative Risk (RR) (95% CI)		1.0375 (0.1497, 7.1891)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9703
Odds Ratio (OR) (95% CI)		1.0385 (0.1427, 7.5550)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9703
Risk Difference (RD) (95% CI)		0.0009 (-0.0466, 0.0484)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9703

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = North America

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with any TEAEs	86 (94.51)	83 (95.40)
Relative Risk (RR) (95% CI)		1.0095 (0.9434, 1.0802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7845
Odds Ratio (OR) (95% CI)		1.2064 (0.3131, 4.6486)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7851
Risk Difference (RD) (95% CI)		0.0090 (-0.0553, 0.0732)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7844
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	5 (5.49)	10 (11.49)
Relative Risk (RR) (95% CI)		2.0920 (0.7450, 5.8744)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1612

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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = North America

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Odds Ratio (OR) (95% CI)		2.2338 (0.7312, 6.8235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1584
Risk Difference (RD) (95% CI)		0.0600 (-0.0218, 0.1418)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1503
Psychiatric disorders	14 (15.38)	11 (12.64)
Relative Risk (RR) (95% CI)		0.8218 (0.3949, 1.7105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5998
Odds Ratio (OR) (95% CI)		0.7961 (0.3399, 1.8642)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5993
Risk Difference (RD) (95% CI)		-0.0274 (-0.1293, 0.0744)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5979

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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Renal and urinary disorders	10 (10.99)	2 (2.30)
Relative Risk (RR) (95% CI)		0.2092 (0.0472, 0.9277)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0395
Odds Ratio (OR) (95% CI)		0.1906 (0.0405, 0.8965)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0359
Risk Difference (RD) (95% CI)		-0.0869 (-0.1585, -0.0153)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0173

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = Rest of World

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with any TEAEs	105 (94.59)	100 (91.74)
Relative Risk (RR) (95% CI)		0.9699 (0.9027, 1.0420)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4032
Odds Ratio (OR) (95% CI)		0.6349 (0.2181, 1.8486)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4048
Risk Difference (RD) (95% CI)		-0.0285 (-0.0951, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4016
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	0	4 (3.67)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
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Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = Rest of World

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0367 (0.0014, 0.0720)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0416
Psychiatric disorders	20 (18.02)	8 (7.34)
Relative Risk (RR) (95% CI)		0.4073 (0.1874, 0.8852)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0233
Odds Ratio (OR) (95% CI)		0.3604 (0.1514, 0.8581)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0211
Risk Difference (RD) (95% CI)		-0.1068 (-0.1934, -0.0201)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0157

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Renal and urinary disorders	6 (5.41)	3 (2.75)
Relative Risk (RR) (95% CI)		0.5092 (0.1306, 1.9848)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3309
Odds Ratio (OR) (95% CI)		0.4953 (0.1207, 2.0326)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3294
Risk Difference (RD) (95% CI)		-0.0265 (-0.0786, 0.0256)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3181

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2.1
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any TEAEs	169 (95.48)	164 (96.47)
Relative Risk (RR) (95% CI)		1.0104 (0.9678, 1.0548)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6386
Odds Ratio (OR) (95% CI)		1.2939 (0.4394, 3.8104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6401
Risk Difference (RD) (95% CI)		0.0099 (-0.0314, 0.0512)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6384
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	5 (2.82)	13 (7.65)
Relative Risk (RR) (95% CI)		2.7071 (0.9863, 7.4303)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0532

- MedDRA version 26.1.
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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2.1
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		2.8484 (0.9929, 8.1711)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0516
Risk Difference (RD) (95% CI)		0.0482 (0.0014, 0.0950)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0435
Psychiatric disorders	30 (16.95)	18 (10.59)
Relative Risk (RR) (95% CI)		0.6247 (0.3622, 1.0775)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0907
Odds Ratio (OR) (95% CI)		0.5803 (0.3100, 1.0860)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0888
Risk Difference (RD) (95% CI)		-0.0636 (-0.1357, 0.0085)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0837

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.1.2.1
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

System Organ Class Preferred Term	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Renal and urinary disorders	15 (8.47)	5 (2.94)
Relative Risk (RR) (95% CI)		0.3471 (0.1290, 0.9340)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0362
Odds Ratio (OR) (95% CI)		0.3273 (0.1162, 0.9214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0344
Risk Difference (RD) (95% CI)		-0.0553 (-0.1036, -0.0071)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0246

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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Table 1.3.2.1.2.1
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any TEAEs	22 (88.00)	19 (73.08)
Relative Risk (RR) (95% CI)		0.8304 (0.6310, 1.0928)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1847
Odds Ratio (OR) (95% CI)		0.3701 (0.0838, 1.6346)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1897
Risk Difference (RD) (95% CI)		-0.1492 (-0.3621, 0.0636)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1693
Respiratory, thoracic and mediastinal disorders		
Sinus congestion	0	1 (3.85)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2.1
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-102

System Organ Class Preferred Term	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0385 (-0.0355, 0.1124)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3078
Psychiatric disorders	4 (16.00)	1 (3.85)
Relative Risk (RR) (95% CI)		0.2404 (0.0288, 2.0055)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1878
Odds Ratio (OR) (95% CI)		0.2100 (0.0218, 2.0262)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1772
Risk Difference (RD) (95% CI)		-0.1215 (-0.2831, 0.0401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1405

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 1.3.2.1.2.1
Study VX20-121-102: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

System Organ Class Preferred Term	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Renal and urinary disorders	1 (4.00)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0400 (-0.1168, 0.0368)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3074

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Grade 3/4/5 TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any Grade 3/4/5 TEAEs	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.5128
Age at screening (<18 years vs. ≥18 years)	0.4712
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0136
Sex (Male vs. Female)	0.7569
Region (North America vs. Rest of the World)	0.4202

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by "*".
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.2.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for Grade 3/4/5 TEAEs by SOC and PT for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any Grade 3/4/5 TEAEs	
Prior CFTR modulator use (yes vs. no)	0.3575

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by "*".
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with any Grade 3/4/5 TEAEs	11 (9.65)	11 (10.89)
Relative Risk (RR) (95% CI)		1.1287 (0.5114, 2.4911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7644
Odds Ratio (OR) (95% CI)		1.1444 (0.4736, 2.7655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7644
Risk Difference (RD) (95% CI)		0.0124 (-0.0690, 0.0938)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7650

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with any Grade 3/4/5 TEAEs	3 (3.45)	6 (6.52)
Relative Risk (RR) (95% CI)		1.8913 (0.4881, 7.3289)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3565
Odds Ratio (OR) (95% CI)		1.9535 (0.4731, 8.0668)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3547
Risk Difference (RD) (95% CI)		0.0307 (-0.0326, 0.0941)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3418

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any Grade 3/4/5 TEAEs	2 (6.45)	1 (3.85)
Relative Risk (RR) (95% CI)		0.5962 (0.0572, 6.2086)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6653
Odds Ratio (OR) (95% CI)		0.5800 (0.0496, 6.7843)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6642
Risk Difference (RD) (95% CI)		-0.0261 (-0.1398, 0.0877)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6535

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Grade 3/4/5 TEAEs	12 (7.02)	17 (10.00)
Relative Risk (RR) (95% CI)		1.4250 (0.7021, 2.8922)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3267
Odds Ratio (OR) (95% CI)		1.4722 (0.6806, 3.1847)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3259
Risk Difference (RD) (95% CI)		0.0298 (-0.0293, 0.0890)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3231

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any Grade 3/4/5 TEAEs	0	4 (23.53)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.2353 (0.0337, 0.4369)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0222

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any Grade 3/4/5 TEAEs	14 (7.69)	13 (7.34)
Relative Risk (RR) (95% CI)		0.9548 (0.4620, 1.9734)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9006
Odds Ratio (OR) (95% CI)		0.9512 (0.4339, 2.0854)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9006
Risk Difference (RD) (95% CI)		-0.0035 (-0.0580, 0.0511)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9006

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with any Grade 3/4/5 TEAEs	7 (5.88)	10 (8.62)
Relative Risk (RR) (95% CI)		1.4655 (0.5774, 3.7196)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4212
Odds Ratio (OR) (95% CI)		1.5094 (0.5543, 4.1102)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4205
Risk Difference (RD) (95% CI)		0.0274 (-0.0389, 0.0937)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4182

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with any Grade 3/4/5 TEAEs	7 (8.43)	8 (10.00)
Relative Risk (RR) (95% CI)		1.1857 (0.4509, 3.1178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7298
Odds Ratio (OR) (95% CI)		1.2063 (0.4161, 3.4972)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7298
Risk Difference (RD) (95% CI)		0.0157 (-0.0732, 0.1045)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7297

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with any Grade 3/4/5 TEAEs	9 (9.89)	9 (10.34)
Relative Risk (RR) (95% CI)		1.0460 (0.4356, 2.5116)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9199
Odds Ratio (OR) (95% CI)		1.0513 (0.3967, 2.7859)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9199
Risk Difference (RD) (95% CI)		0.0045 (-0.0841, 0.0932)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9199

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with any Grade 3/4/5 TEAEs	5 (4.50)	9 (8.26)
Relative Risk (RR) (95% CI)		1.8330 (0.6346, 5.2950)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2629
Odds Ratio (OR) (95% CI)		1.9080 (0.6183, 5.8879)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2611
Risk Difference (RD) (95% CI)		0.0375 (-0.0270, 0.1020)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2541

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

Table 1.3.2.2.2.1
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

System Organ Class Preferred Term	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Grade 3/4/5 TEAEs	11 (6.21)	16 (9.41)
Relative Risk (RR) (95% CI)		1.5144 (0.7238, 3.1686)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2705
Odds Ratio (OR) (95% CI)		1.5679 (0.7056, 3.4837)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2696
Risk Difference (RD) (95% CI)		0.0320 (-0.0245, 0.0885)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2674

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.2.2.1
Study VX20-121-102: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

System Organ Class Preferred Term	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any Grade 3/4/5 TEAEs	3 (12.00)	2 (7.69)
Relative Risk (RR) (95% CI)		0.6410 (0.1168, 3.5191)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6088
Odds Ratio (OR) (95% CI)		0.6111 (0.0932, 4.0065)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6077
Risk Difference (RD) (95% CI)		-0.0431 (-0.2065, 0.1204)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6055

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Serious TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.4570
Age at screening (<18 years vs. ≥18 years)	0.3688
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0264
Sex (Male vs. Female)	0.8530
Region (North America vs. Rest of the World)	0.8550

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by "*".
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.3.2.3.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for Serious TEAEs by SOC and PT for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs	
Prior CFTR modulator use (yes vs. no)	0.2525

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by "*".
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with any serious TEAEs	14 (12.28)	14 (13.86)
Relative Risk (RR) (95% CI)		1.1287 (0.5657, 2.2519)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7312
Odds Ratio (OR) (95% CI)		1.1494 (0.5193, 2.5443)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7312
Risk Difference (RD) (95% CI)		0.0158 (-0.0746, 0.1062)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7318

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with any serious TEAEs	8 (9.20)	6 (6.52)
Relative Risk (RR) (95% CI)		0.7092 (0.2565, 1.9612)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5079
Odds Ratio (OR) (95% CI)		0.6890 (0.2289, 2.0732)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5074
Risk Difference (RD) (95% CI)		-0.0267 (-0.1057, 0.0522)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5068

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any serious TEAEs	3 (9.68)	1 (3.85)
Relative Risk (RR) (95% CI)		0.3974 (0.0439, 3.5952)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4115
Odds Ratio (OR) (95% CI)		0.3733 (0.0364, 3.8239)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4065
Risk Difference (RD) (95% CI)		-0.0583 (-0.1860, 0.0693)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3706

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any serious TEAEs	19 (11.11)	20 (11.76)
Relative Risk (RR) (95% CI)		1.0588 (0.5864, 1.9119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8496
Odds Ratio (OR) (95% CI)		1.0667 (0.5474, 2.0787)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8496
Risk Difference (RD) (95% CI)		0.0065 (-0.0610, 0.0741)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8496

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any serious TEAEs	1 (5.26)	5 (29.41)
Relative Risk (RR) (95% CI)		5.5882 (0.7231, 43.1879)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0991
Odds Ratio (OR) (95% CI)		7.5000 (0.7765, 72.4419)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0816
Risk Difference (RD) (95% CI)		0.2415 (0.0028, 0.4802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0474

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any serious TEAEs	21 (11.54)	15 (8.47)
Relative Risk (RR) (95% CI)		0.7345 (0.3914, 1.3783)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3366
Odds Ratio (OR) (95% CI)		0.7099 (0.3534, 1.4260)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3357
Risk Difference (RD) (95% CI)		-0.0306 (-0.0926, 0.0313)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3324

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with any serious TEAEs	11 (9.24)	10 (8.62)
Relative Risk (RR) (95% CI)		0.9326 (0.4119, 2.1118)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8671
Odds Ratio (OR) (95% CI)		0.9262 (0.3776, 2.2721)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8671
Risk Difference (RD) (95% CI)		-0.0062 (-0.0791, 0.0667)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8670

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with any serious TEAEs	11 (13.25)	11 (13.75)
Relative Risk (RR) (95% CI)		1.0375 (0.4769, 2.2571)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9260
Odds Ratio (OR) (95% CI)		1.0435 (0.4248, 2.5629)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9260
Risk Difference (RD) (95% CI)		0.0050 (-0.1000, 0.1099)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9261

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with any serious TEAEs	9 (9.89)	9 (10.34)
Relative Risk (RR) (95% CI)		1.0460 (0.4356, 2.5116)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9199
Odds Ratio (OR) (95% CI)		1.0513 (0.3967, 2.7859)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9199
Risk Difference (RD) (95% CI)		0.0045 (-0.0841, 0.0932)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9199

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with any serious TEAEs	13 (11.71)	12 (11.01)
Relative Risk (RR) (95% CI)		0.9400 (0.4490, 1.9678)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8696
Odds Ratio (OR) (95% CI)		0.9326 (0.4053, 2.1458)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8696
Risk Difference (RD) (95% CI)		-0.0070 (-0.0909, 0.0768)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8696

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

Table 1.3.2.3.2.1
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

System Organ Class Preferred Term	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any serious TEAEs	19 (10.73)	20 (11.76)
Relative Risk (RR) (95% CI)		1.0960 (0.6066, 1.9802)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7614
Odds Ratio (OR) (95% CI)		1.1088 (0.5694, 2.1592)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7614
Risk Difference (RD) (95% CI)		0.0103 (-0.0562, 0.0768)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7615

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.3.2.1
Study VX20-121-102: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

System Organ Class Preferred Term	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any serious TEAEs	3 (12.00)	1 (3.85)
Relative Risk (RR) (95% CI)		0.3205 (0.0357, 2.8799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3098
Odds Ratio (OR) (95% CI)		0.2933 (0.0284, 3.0287)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3032
Risk Difference (RD) (95% CI)		-0.0815 (-0.2288, 0.0657)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2779

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

Table 1.3.2.4.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for TEAEs Leading to Treatment Discontinuation
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs leading to treatment discontinuation	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	-
Age at screening (<18 years vs. ≥18 years)	0.2278
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	N/C
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.3.2.4.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for TEAEs Leading to Treatment Discontinuation for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs leading to treatment discontinuation	
Prior CFTR modulator use (yes vs. no)	0.1838

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any TEAEs leading to treatment discontinuation	2 (6.45)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0645 (-0.1510, 0.0220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1437

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any TEAEs leading to treatment discontinuation	7 (4.09)	4 (2.35)
Relative Risk (RR) (95% CI)		0.5748 (0.1714, 1.9275)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3697
Odds Ratio (OR) (95% CI)		0.5645 (0.1622, 1.9651)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3690
Risk Difference (RD) (95% CI)		-0.0174 (-0.0548, 0.0200)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3621

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with any TEAEs leading to treatment discontinuation	0	2 (11.76)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.1176 (-0.0355, 0.2708)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1322

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with any TEAEs leading to treatment discontinuation	9 (4.95)	2 (1.13)
Relative Risk (RR) (95% CI)		0.2285 (0.0501, 1.0428)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0567
Odds Ratio (OR) (95% CI)		0.2197 (0.0468, 1.0314)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0548
Risk Difference (RD) (95% CI)		-0.0382 (-0.0733, -0.0030)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0333

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

Table 1.3.2.4.2.1
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any TEAEs leading to treatment discontinuation	7 (3.95)	4 (2.35)
Relative Risk (RR) (95% CI)		0.5950 (0.1774, 1.9958)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4004
Odds Ratio (OR) (95% CI)		0.5852 (0.1682, 2.0363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3997
Risk Difference (RD) (95% CI)		-0.0160 (-0.0527, 0.0206)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3917

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.4.2.1
Study VX20-121-102: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with any TEAEs leading to treatment discontinuation	2 (8.00)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0800 (-0.1863, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1404

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

Table 1.3.2.12.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.3753
Age at screening (<18 years vs. ≥18 years)	0.2418
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0781
Sex (Male vs. Female)	0.8800
Region (North America vs. Rest of the World)	0.3209

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Table 1.3.2.12.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interaction for Treatment-emergent Infective Pulmonary Exacerbation Events for Subgroup Prior CFTR Modulator Use
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with serious events	
Prior CFTR modulator use (yes vs. no)	>0.9999

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with serious events	15 (13.16)	5 (4.95)
Relative Risk (RR) (95% CI)		0.3762 (0.1418, 0.9985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0497
Odds Ratio (OR) (95% CI)		0.3438 (0.1203, 0.9826)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0463
Risk Difference (RD) (95% CI)		-0.0821 (-0.1572, -0.0070)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0322

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with serious events	8 (9.20)	6 (6.52)
Relative Risk (RR) (95% CI)		0.7092 (0.2565, 1.9612)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5079
Odds Ratio (OR) (95% CI)		0.6890 (0.2289, 2.0732)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5074
Risk Difference (RD) (95% CI)		-0.0267 (-0.1057, 0.0522)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5068

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with serious events	5 (16.13)	4 (15.38)
Relative Risk (RR) (95% CI)		0.9538 (0.2853, 3.1893)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9388
Odds Ratio (OR) (95% CI)		0.9455 (0.2258, 3.9592)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9388
Risk Difference (RD) (95% CI)		-0.0074 (-0.1972, 0.1823)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9387

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with serious events	18 (10.53)	7 (4.12)
Relative Risk (RR) (95% CI)		0.3912 (0.1677, 0.9123)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0298
Odds Ratio (OR) (95% CI)		0.3650 (0.1483, 0.8983)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0283
Risk Difference (RD) (95% CI)		-0.0641 (-0.1189, -0.0092)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0220

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with serious events	4 (21.05)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.2105 (-0.3938, -0.0272)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0244

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with serious events	19 (10.44)	10 (5.65)
Relative Risk (RR) (95% CI)		0.5412 (0.2589, 1.1312)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1026
Odds Ratio (OR) (95% CI)		0.5137 (0.2319, 1.1382)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1008
Risk Difference (RD) (95% CI)		-0.0479 (-0.1038, 0.0081)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0934

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with serious events	11 (9.24)	5 (4.31)
Relative Risk (RR) (95% CI)		0.4663 (0.1672, 1.3006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1449
Odds Ratio (OR) (95% CI)		0.4423 (0.1487, 1.3152)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1423
Risk Difference (RD) (95% CI)		-0.0493 (-0.1132, 0.0145)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1298

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with serious events	12 (14.46)	6 (7.50)
Relative Risk (RR) (95% CI)		0.5188 (0.2045, 1.3156)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1669
Odds Ratio (OR) (95% CI)		0.4797 (0.1708, 1.3473)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1633
Risk Difference (RD) (95% CI)		-0.0696 (-0.1647, 0.0256)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1518

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with serious events	13 (14.29)	8 (9.20)
Relative Risk (RR) (95% CI)		0.6437 (0.2806, 1.4765)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2983
Odds Ratio (OR) (95% CI)		0.6076 (0.2386, 1.5471)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2961
Risk Difference (RD) (95% CI)		-0.0509 (-0.1450, 0.0432)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2891

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with serious events	10 (9.01)	3 (2.75)
Relative Risk (RR) (95% CI)		0.3055 (0.0864, 1.0801)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0657
Odds Ratio (OR) (95% CI)		0.2858 (0.0765, 1.0686)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0627
Risk Difference (RD) (95% CI)		-0.0626 (-0.1241, -0.0011)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0461

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-102

Table 1.3.2.12.2.1
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for Subgroup Prior CFTR Modulator Use
Safety Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with serious events	23 (12.99)	11 (6.47)
Relative Risk (RR) (95% CI)		0.4980 (0.2505, 0.9898)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0467
Odds Ratio (OR) (95% CI)		0.4632 (0.2184, 0.9825)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0449
Risk Difference (RD) (95% CI)		-0.0652 (-0.1271, -0.0034)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0386

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.3.2.12.2.1
Study VX20-121-102: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for Subgroup
Prior CFTR Modulator Use
Safety Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with serious events	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are reported only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 1.4.1.1
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with at least one Pulmonary Exacerbation	60 (29.7)	50 (25.5)
Relative Risk (RR) (95% CI)		0.8711 (0.6366, 1.1920)
P-value vs. ELX/TEZ/IVA [1]	-	0.3885
Odds Ratio (OR) (95% CI)		0.8104 (0.5172, 1.2699)
P-value vs. ELX/TEZ/IVA [2]	-	0.3590
Risk Difference (RD) (95% CI)		-0.0451 (-0.1305, 0.0403)
P-value vs. ELX/TEZ/IVA [3]	-	0.3002
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	17 (8.4)	8 (4.1)
Relative Risk (RR) (95% CI)		0.5004 (0.2216, 1.1301)
P-value vs. ELX/TEZ/IVA [1]	-	0.0958
Odds Ratio (OR) (95% CI)		0.4770 (0.2002, 1.1363)
P-value vs. ELX/TEZ/IVA [2]	-	0.0946
Risk Difference (RD) (95% CI)		N/C
P-value vs. ELX/TEZ/IVA [3]	-	N/C

- A subject is considered to have at least one Pulmonary Exacerbation (PEx) requiring IV antibiotics or hospitalization, if they had at least one PEx requiring IV antibiotics, or at least one PEx requiring hospitalization or at least one PEx requiring both IV antibiotics and hospitalization.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	26 (12.9)	10 (5.1)
Relative Risk (RR) (95% CI)		0.4038 (0.2005, 0.8133)
P-value vs. ELX/TEZ/IVA [1]	-	0.0111
Odds Ratio (OR) (95% CI)		0.3671 (0.1713, 0.7866)
P-value vs. ELX/TEZ/IVA [2]	-	0.0100
Risk Difference (RD) (95% CI)		N/C
P-value vs. ELX/TEZ/IVA [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	26 (12.9)	10 (5.1)
Relative Risk (RR) (95% CI)		0.4038 (0.2005, 0.8133)
P-value vs. ELX/TEZ/IVA [1]	-	0.0111
Odds Ratio (OR) (95% CI)		0.3671 (0.1713, 0.7866)
P-value vs. ELX/TEZ/IVA [2]	-	0.0100
Risk Difference (RD) (95% CI)		N/C
P-value vs. ELX/TEZ/IVA [3]	-	N/C

- A subject is considered to have at least one Pulmonary Exacerbation (PEx) requiring IV antibiotics or hospitalization, if they had at least one PEx requiring IV antibiotics, or at least one PEx requiring hospitalization or at least one PEx requiring both IV antibiotics and hospitalization.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 196 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	10 (5.0)	3 (1.5)
Relative Risk (RR) (95% CI)		0.2973 (0.0833, 1.0609)
P-value vs. ELX/TEZ/IVA [1]	-	0.0616
Odds Ratio (OR) (95% CI)		0.2881 (0.0776, 1.0688)
P-value vs. ELX/TEZ/IVA [2]	-	0.0628
Risk Difference (RD) (95% CI)		N/C
P-value vs. ELX/TEZ/IVA [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization but not IV Antibiotics	0	0
Relative Risk (RR) (95% CI)		- (-, -)
P-value vs. ELX/TEZ/IVA [1]	-	-
Odds Ratio (OR) (95% CI)		- (-, -)
P-value vs. ELX/TEZ/IVA [2]	-	-
Risk Difference (RD) (95% CI)		- (-, -)
P-value vs. ELX/TEZ/IVA [3]	-	-

- A subject is considered to have at least one Pulmonary Exacerbation (PEx) requiring IV antibiotics or hospitalization, if they had at least one PEx requiring IV antibiotics, or at least one PEx requiring hospitalization or at least one PEx requiring both IV antibiotics and hospitalization.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, age at screening (<18 vs ≥18 years) treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, and treatment*subgroup, with adjustment for baseline $ppFEV_1$and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Subgroup	P-value for Interaction
Subjects with at least one Pulmonary Exacerbation	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9656
Age at screening (<18 years vs. ≥18 years) [2]	0.2895
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0767
Sex (Male vs. Female) [1]	0.4917
Region (North America vs. Rest of the World) [1]	0.9768
Prior CFTR modulator use (yes vs. no) [1]	0.4889
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.2984
Age at screening (<18 years vs. ≥18 years) [2]	0.9038
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	N/C
Sex (Male vs. Female) [1]	0.4802*
Region (North America vs. Rest of the World) [1]	0.9365
Prior CFTR modulator use (yes vs. no) [1]	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, age at screening (<18 vs ≥18 years) treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, and treatment*subgroup, with adjustment for baseline $ppFEV_1$and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 1.4.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, age at screening (<18 vs ≥18 years) treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, and treatment*subgroup, with adjustment for baseline $ppFEV_1$and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-102

Subgroup	P-value for Interaction
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3051
Age at screening (<18 years vs. ≥18 years) [2]	0.7347
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	N/C
Sex (Male vs. Female) [1]	0.6099
Region (North America vs. Rest of the World) [1]	0.9984
Prior CFTR modulator use (yes vs. no) [1]	0.1349
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3051
Age at screening (<18 years vs. ≥18 years) [2]	0.7347
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	N/C
Sex (Male vs. Female) [1]	0.6099
Region (North America vs. Rest of the World) [1]	0.9984
Prior CFTR modulator use (yes vs. no) [1]	0.1349

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, age at screening (<18 vs ≥18 years) treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, and treatment*subgroup, with adjustment for baseline $ppFEV_1$and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 1.4.1.1.1
Study VX20-121-102: Treatment by Subgroup Factor Interactions for Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	N/C
Age at screening (<18 years vs. ≥18 years) [2]	>0.9999
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	N/C
Sex (Male vs. Female) [1]	N/C
Region (North America vs. Rest of the World) [1]	N/C
Prior CFTR modulator use (yes vs. no) [1]	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, age at screening (<18 vs ≥18 years) treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, and treatment*subgroup, with adjustment for baseline $ppFEV_1$and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Percent predicted FEV1 at Baseline <70%

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with at least one Pulmonary Exacerbation	41 (36.0)	32 (31.7)
Relative Risk (RR) (95% CI)		0.8796 (0.6028, 1.2836)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5059
Odds Ratio (OR) (95% CI)		0.8161 (0.4585, 1.4528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4899
Risk Difference (RD) (95% CI)		-0.0584 (-0.1897, 0.0728)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.3828
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	11 (9.6)	3 (3.0)
Relative Risk (RR) (95% CI)		0.3239 (0.0928, 1.1305)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0771
Odds Ratio (OR) (95% CI)		0.3019 (0.0811, 1.1243)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0742
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Percent predicted FEV1 at Baseline <70%

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	19 (16.7)	5 (5.0)
Relative Risk (RR) (95% CI)		0.3021 (0.1166, 0.7825)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0137
Odds Ratio (OR) (95% CI)		0.2637 (0.0940, 0.7396)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0113
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	19 (16.7)	5 (5.0)
Relative Risk (RR) (95% CI)		0.3021 (0.1166, 0.7825)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0137
Odds Ratio (OR) (95% CI)		0.2637 (0.0940, 0.7396)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0113
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Percent predicted FEV1 at Baseline <70%

	ELX/TEZ/IVA N = 114 n (%)	VNZ/TEZ/D-IVA N = 101 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	9 (7.9)	2 (2.0)
Relative Risk (RR) (95% CI)		0.2454 (0.0541, 1.1132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0686
Odds Ratio (OR) (95% CI)		0.2318 (0.0485, 1.1083)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0671
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Percent predicted FEV1 at Baseline ≥70%

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with at least one Pulmonary Exacerbation	19 (21.8)	18 (19.6)
Relative Risk (RR) (95% CI)		0.8747 (0.4943, 1.5479)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6457
Odds Ratio (OR) (95% CI)		0.8382 (0.4041, 1.7385)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6354
Risk Difference (RD) (95% CI)		-0.0335 (-0.1518, 0.0849)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.5794
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	6 (6.9)	5 (5.4)
Relative Risk (RR) (95% CI)		0.7344 (0.2111, 2.5552)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6275*
Odds Ratio (OR) (95% CI)		0.7190 (0.2065, 2.5040)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6044
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Percent predicted FEV1 at Baseline ≥70%

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	7 (8.0)	5 (5.4)
Relative Risk (RR) (95% CI)		0.6429 (0.1981, 2.0861)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4620*
Odds Ratio (OR) (95% CI)		0.6196 (0.1852, 2.0725)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4371
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	7 (8.0)	5 (5.4)
Relative Risk (RR) (95% CI)		0.6429 (0.1981, 2.0861)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4620*
Odds Ratio (OR) (95% CI)		0.6196 (0.1852, 2.0725)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4371
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Percent predicted FEV1 at Baseline ≥70%

	ELX/TEZ/IVA N = 87 n (%)	VNZ/TEZ/D-IVA N = 92 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	1 (1.1)	1 (1.1)
Relative Risk (RR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	N/C
Odds Ratio (OR) (95% CI)		0.4200 (0.0136, 12.9961)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6204
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with at least one Pulmonary Exacerbation	6 (19.4)	2 (7.7)
Relative Risk (RR) (95% CI)		0.3989 (0.0868, 1.8342)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2378
Odds Ratio (OR) (95% CI)		0.3507 (0.0626, 1.9639)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2332
Risk Difference (RD) (95% CI)		-0.1208 (-0.3136, 0.0720)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.2195
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	2 (6.5)	1 (3.8)
Relative Risk (RR) (95% CI)		0.3728 (0.0293, 4.7470)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4472*
Odds Ratio (OR) (95% CI)		0.3601 (0.0217, 5.9849)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4763
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	2 (6.5)	1 (3.8)
Relative Risk (RR) (95% CI)		0.3728 (0.0293, 4.7470)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4472*
Odds Ratio (OR) (95% CI)		0.3601 (0.0217, 5.9849)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4763
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	2 (6.5)	1 (3.8)
Relative Risk (RR) (95% CI)		0.3728 (0.0293, 4.7470)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4472*
Odds Ratio (OR) (95% CI)		0.3601 (0.0217, 5.9849)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4763
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 31 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with at least one Pulmonary Exacerbation	54 (31.6)	48 (28.2)
Relative Risk (RR) (95% CI)		0.9069 (0.6569, 1.2520)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5526
Odds Ratio (OR) (95% CI)		0.8666 (0.5417, 1.3862)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5501
Risk Difference (RD) (95% CI)		-0.0300 (-0.1274, 0.0674)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.5455
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	15 (8.8)	7 (4.1)
Relative Risk (RR) (95% CI)		0.4869 (0.2038, 1.1636)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1054
Odds Ratio (OR) (95% CI)		0.4636 (0.1835, 1.1714)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.1041
Risk Difference (RD) (95% CI)		-0.0454 (-0.0967, 0.0060)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.0834

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	24 (14.0)	9 (5.3)
Relative Risk (RR) (95% CI)		0.3863 (0.1851, 0.8060)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0113
Odds Ratio (OR) (95% CI)		0.3488 (0.1565, 0.7771)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0100
Risk Difference (RD) (95% CI)		-0.0903 (-0.1545, -0.0260)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.0059
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	24 (14.0)	9 (5.3)
Relative Risk (RR) (95% CI)		0.3863 (0.1851, 0.8060)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0113
Odds Ratio (OR) (95% CI)		0.3488 (0.1565, 0.7771)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0100
Risk Difference (RD) (95% CI)		-0.0903 (-0.1545, -0.0260)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.0059

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 171 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	10 (5.8)	3 (1.8)
Relative Risk (RR) (95% CI)		0.2973 (0.0833, 1.0609)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0616
Odds Ratio (OR) (95% CI)		0.2881 (0.0776, 1.0688)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0628
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with at least one Pulmonary Exacerbation	7 (36.8)	2 (11.8)
Relative Risk (RR) (95% CI)		0.3332 (0.0795, 1.3966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1328*
Odds Ratio (OR) (95% CI)		0.2151 (0.0300, 1.5409)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.1261
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	2 (10.5)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	5 (26.3)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	5 (26.3)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 19 n (%)	VNZ/TEZ/D-IVA N = 17 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	3 (15.8)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with at least one Pulmonary Exacerbation	53 (29.1)	48 (27.1)
Relative Risk (RR) (95% CI)		0.9465 (0.6838, 1.3100)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7401
Odds Ratio (OR) (95% CI)		0.9065 (0.5673, 1.4486)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6816
Risk Difference (RD) (95% CI)		-0.0234 (-0.1134, 0.0666)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.6103
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	15 (8.2)	8 (4.5)
Relative Risk (RR) (95% CI)		0.5664 (0.2471, 1.2983)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1792
Odds Ratio (OR) (95% CI)		0.5469 (0.2248, 1.3303)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.1833
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	21 (11.5)	10 (5.6)
Relative Risk (RR) (95% CI)		0.5066 (0.2469, 1.0395)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0637
Odds Ratio (OR) (95% CI)		0.4739 (0.2151, 1.0441)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0639
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	21 (11.5)	10 (5.6)
Relative Risk (RR) (95% CI)		0.5066 (0.2469, 1.0395)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0637
Odds Ratio (OR) (95% CI)		0.4739 (0.2151, 1.0441)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0639
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 182 n (%)	VNZ/TEZ/D-IVA N = 177 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	7 (3.8)	3 (1.7)
Relative Risk (RR) (95% CI)		0.4494 (0.1182, 1.7093)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2406
Odds Ratio (OR) (95% CI)		0.4383 (0.1108, 1.7343)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2398
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with at least one Pulmonary Exacerbation	29 (24.4)	29 (25.0)
Relative Risk (RR) (95% CI)		1.0018 (0.6427, 1.5614)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9938
Odds Ratio (OR) (95% CI)		0.9934 (0.5428, 1.8183)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.9830
Risk Difference (RD) (95% CI)		-0.0030 (-0.1126, 0.1066)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.9571
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	6 (5.0)	4 (3.4)
Relative Risk (RR) (95% CI)		0.7314 (0.2102, 2.5443)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6229*
Odds Ratio (OR) (95% CI)		0.7205 (0.1922, 2.7012)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6269
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	12 (10.1)	4 (3.4)
Relative Risk (RR) (95% CI)		0.3254 (0.1080, 0.9808)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0461
Odds Ratio (OR) (95% CI)		0.2991 (0.0924, 0.9679)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0440
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	12 (10.1)	4 (3.4)
Relative Risk (RR) (95% CI)		0.3254 (0.1080, 0.9808)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0461
Odds Ratio (OR) (95% CI)		0.2991 (0.0924, 0.9679)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0440
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 116 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	6 (5.0)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with at least one Pulmonary Exacerbation	31 (37.3)	21 (26.3)
Relative Risk (RR) (95% CI)		0.7945 (0.5097, 1.2383)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3096
Odds Ratio (OR) (95% CI)		0.6725 (0.3364, 1.3442)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2615
Risk Difference (RD) (95% CI)		-0.0831 (-0.2269, 0.0607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.2574
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	11 (13.3)	4 (5.0)
Relative Risk (RR) (95% CI)		0.3850 (0.1277, 1.1601)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0899
Odds Ratio (OR) (95% CI)		0.3512 (0.1056, 1.1679)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0878
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	14 (16.9)	6 (7.5)
Relative Risk (RR) (95% CI)		0.4782 (0.1941, 1.1779)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1087
Odds Ratio (OR) (95% CI)		0.4202 (0.1505, 1.1729)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0978
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	14 (16.9)	6 (7.5)
Relative Risk (RR) (95% CI)		0.4782 (0.1941, 1.1779)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1087
Odds Ratio (OR) (95% CI)		0.4202 (0.1505, 1.1729)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0978
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 83 n (%)	VNZ/TEZ/D-IVA N = 80 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	4 (4.8)	3 (3.8)
Relative Risk (RR) (95% CI)		0.9025 (0.2118, 3.8462)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8897
Odds Ratio (OR) (95% CI)		0.8877 (0.1882, 4.1865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8803
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with at least one Pulmonary Exacerbation	25 (27.5)	21 (24.1)
Relative Risk (RR) (95% CI)		0.8921 (0.5422, 1.4679)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6532
Odds Ratio (OR) (95% CI)		0.8252 (0.4155, 1.6389)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5832
Risk Difference (RD) (95% CI)		-0.0424 (-0.1698, 0.0851)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.5148
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	11 (12.1)	5 (5.7)
Relative Risk (RR) (95% CI)		0.4995 (0.1824, 1.3682)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1770
Odds Ratio (OR) (95% CI)		0.4667 (0.1538, 1.4158)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.1783
Risk Difference (RD) (95% CI)		-0.0605 (-0.1408, 0.0199)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.1402

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	13 (14.3)	5 (5.7)
Relative Risk (RR) (95% CI)		0.4209 (0.1575, 1.1249)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0845
Odds Ratio (OR) (95% CI)		0.3812 (0.1288, 1.1277)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0814
Risk Difference (RD) (95% CI)		-0.0827 (-0.1679, 0.0025)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.0573
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	13 (14.3)	5 (5.7)
Relative Risk (RR) (95% CI)		0.4209 (0.1575, 1.1249)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0845
Odds Ratio (OR) (95% CI)		0.3812 (0.1288, 1.1277)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0814
Risk Difference (RD) (95% CI)		-0.0827 (-0.1679, 0.0025)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.0573

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 91 n (%)	VNZ/TEZ/D-IVA N = 87 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	2 (2.2)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with at least one Pulmonary Exacerbation	35 (31.5)	29 (26.6)
Relative Risk (RR) (95% CI)		0.8694 (0.5804, 1.3022)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4971
Odds Ratio (OR) (95% CI)		0.8118 (0.4469, 1.4745)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4935
Risk Difference (RD) (95% CI)		-0.0523 (-0.1685, 0.0638)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.3772
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	6 (5.4)	3 (2.8)
Relative Risk (RR) (95% CI)		0.5184 (0.1336, 2.0123)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3424
Odds Ratio (OR) (95% CI)		0.5015 (0.1213, 2.0722)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.3404
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	13 (11.7)	5 (4.6)
Relative Risk (RR) (95% CI)		0.4011 (0.1491, 1.0786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0703
Odds Ratio (OR) (95% CI)		0.3664 (0.1248, 1.0757)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0677
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	13 (11.7)	5 (4.6)
Relative Risk (RR) (95% CI)		0.4011 (0.1491, 1.0786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0703
Odds Ratio (OR) (95% CI)		0.3664 (0.1248, 1.0757)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0677
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 111 n (%)	VNZ/TEZ/D-IVA N = 109 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	8 (7.2)	3 (2.8)
Relative Risk (RR) (95% CI)		0.3874 (0.1061, 1.4144)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1512
Odds Ratio (OR) (95% CI)		0.3692 (0.0947, 1.4396)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.1512
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with at least one Pulmonary Exacerbation	54 (30.5)	43 (25.3)
Relative Risk (RR) (95% CI)		0.8371 (0.5986, 1.1707)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2989
Odds Ratio (OR) (95% CI)		0.7712 (0.4779, 1.2446)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2874
Risk Difference (RD) (95% CI)		-0.0497 (-0.1430, 0.0437)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.2970
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	17 (9.6)	8 (4.7)
Relative Risk (RR) (95% CI)		0.5045 (0.2247, 1.1326)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0973
Odds Ratio (OR) (95% CI)		0.4771 (0.1991, 1.1431)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0969
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	25 (14.1)	8 (4.7)
Relative Risk (RR) (95% CI)		0.3396 (0.1579, 0.7303)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0057
Odds Ratio (OR) (95% CI)		0.3038 (0.1325, 0.6966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0049
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	25 (14.1)	8 (4.7)
Relative Risk (RR) (95% CI)		0.3396 (0.1579, 0.7303)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0057
Odds Ratio (OR) (95% CI)		0.3038 (0.1325, 0.6966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0049
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 177 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	9 (5.1)	1 (0.6)
Relative Risk (RR) (95% CI)		0.1114 (0.0143, 0.8680)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0362
Odds Ratio (OR) (95% CI)		0.1058 (0.0132, 0.8477)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0344
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with at least one Pulmonary Exacerbation	6 (24.0)	7 (26.9)
Relative Risk (RR) (95% CI)		1.2077 (0.5010, 2.9113)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6743
Odds Ratio (OR) (95% CI)		1.2019 (0.3178, 4.5464)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7864
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	1 (4.0)	2 (7.7)
Relative Risk (RR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	N/C
Odds Ratio (OR) (95% CI)		2.0553 (0.1583, 26.6906)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5818
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	1 (4.0)	2 (7.7)
Relative Risk (RR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	N/C
Odds Ratio (OR) (95% CI)		2.0553 (0.1583, 26.6906)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5818
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 1.4.1.1.2
Study VX20-121-102: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 25 n (%)	VNZ/TEZ/D-IVA N = 26 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	1 (4.0)	2 (7.7)
Relative Risk (RR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	N/C
Odds Ratio (OR) (95% CI)		2.0553 (0.1583, 26.6906)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5818
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 14.2.8.1.1
Summary of CFQ-R Respiratory Domain Score and Change from Baseline at Each Visit
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline	n	197	192
	Mean (SD)	82.9 (15.7)	85.8 (14.7)
	Median	83.3	88.9
	Min, max	22.2, 100.0	27.8, 100.0
Week 8	n	198	193
	Mean (SD)	81.1 (18.0)	85.0 (15.7)
	Median	83.3	88.9
	Min, max	0.0, 100.0	22.2, 100.0
Change at Week 8	n	194	190
	Mean (SD)	-2.0 (16.8)	-0.7 (16.6)
	Median	0.0	0.0
	Min, max	-77.8, 33.3	-61.1, 72.2
Week 16	n	198	194
	Mean (SD)	80.6 (18.8)	85.9 (16.1)
	Median	83.3	88.9
	Min, max	11.1, 100.0	0.0, 100.0
Change at Week 16	n	194	190
	Mean (SD)	-2.2 (17.0)	0.6 (15.9)
	Median	0.0	0.0
	Min, max	-83.3, 61.1	-61.1, 50.0

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.1.1
Summary of CFQ-R Respiratory Domain Score and Change from Baseline at Each Visit
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 24	n	198	192
	Mean (SD)	81.7 (18.6)	85.8 (16.3)
	Median	83.3	88.9
	Min, max	11.1, 100.0	16.7, 100.0
Change at Week 24	n	194	188
	Mean (SD)	-1.3 (16.7)	0.2 (17.5)
	Median	0.0	0.0
	Min, max	-77.8, 55.6	-55.6, 72.2
Week 52	n	192	184
	Mean (SD)	81.8 (16.7)	87.1 (13.4)
	Median	83.3	88.9
	Min, max	5.6, 100.0	44.4, 100.0
Change at Week 52	n	188	180
	Mean (SD)	-1.2 (14.6)	1.5 (14.7)
	Median	0.0	0.0
	Min, max	-50.0, 44.4	-38.9, 72.2

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Physical

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline	n	197	192
	Mean (SD)	82.5 (18.6)	83.2 (19.8)
	Median	87.5	91.7
	Min, max	20.8, 100.0	4.2, 100.0
Week 8	n	199	193
	Mean (SD)	80.8 (20.8)	83.3 (20.3)
	Median	87.5	91.7
	Min, max	0.0, 100.0	8.3, 100.0
Change at Week 8	n	195	190
	Mean (SD)	-2.0 (16.6)	0.2 (12.9)
	Median	0.0	0.0
	Min, max	-87.5, 58.3	-75.0, 62.5
Week 16	n	198	194
	Mean (SD)	80.8 (20.8)	82.8 (20.4)
	Median	87.5	91.1
	Min, max	4.2, 100.0	4.2, 100.0
Change at Week 16	n	194	190
	Mean (SD)	-2.0 (15.4)	0.3 (14.3)
	Median	0.0	0.0
	Min, max	-83.3, 62.5	-87.5, 37.5

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Physical

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 24	n	198	193
	Mean (SD)	82.6 (19.1)	83.2 (21.3)
	Median	87.5	91.7
	Min, max	4.2, 100.0	4.2, 100.0
Change at Week 24	n	194	189
	Mean (SD)	-0.3 (13.7)	0.5 (13.2)
	Median	0.0	0.0
	Min, max	-62.5, 62.5	-50.0, 66.7
Week 52	n	193	184
	Mean (SD)	83.8 (18.6)	84.7 (18.9)
	Median	91.7	91.7
	Min, max	12.5, 100.0	4.2, 100.0
Change at Week 52	n	189	180
	Mean (SD)	1.1 (12.6)	2.0 (12.1)
	Median	0.0	0.0
	Min, max	-33.3, 58.3	-58.3, 33.3

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Vitality

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline	n	189	187
	Mean (SD)	66.8 (17.7)	69.7 (20.1)
	Median	66.7	75.0
	Min, max	16.7, 100.0	0.0, 100.0
Week 8	n	191	188
	Mean (SD)	65.1 (18.9)	67.9 (19.7)
	Median	66.7	66.7
	Min, max	25.0, 100.0	0.0, 100.0
Change at Week 8	n	188	185
	Mean (SD)	-2.1 (17.2)	-1.6 (18.0)
	Median	0.0	0.0
	Min, max	-66.7, 41.7	-50.0, 66.7
Week 16	n	189	189
	Mean (SD)	64.5 (20.4)	67.3 (20.6)
	Median	66.7	66.7
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 16	n	186	186
	Mean (SD)	-2.4 (16.4)	-1.7 (16.3)
	Median	0.0	0.0
	Min, max	-66.7, 33.3	-50.0, 50.0

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Vitality

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 24	n	189	188
	Mean (SD)	64.2 (21.0)	67.6 (20.5)
	Median	66.7	66.7
	Min, max	0.0, 100.0	16.7, 100.0
Change at Week 24	n	186	185
	Mean (SD)	-2.9 (16.5)	-2.0 (17.0)
	Median	0.0	0.0
	Min, max	-50.0, 41.7	-58.3, 66.7
Week 52	n	184	179
	Mean (SD)	66.9 (18.6)	68.9 (20.0)
	Median	66.7	66.7
	Min, max	16.7, 100.0	0.0, 100.0
Change at Week 52	n	181	176
	Mean (SD)	-0.3 (14.9)	-0.6 (18.1)
	Median	0.0	0.0
	Min, max	-50.0, 41.7	-50.0, 66.7

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Emotion

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline	n	197	192
	Mean (SD)	80.8 (18.3)	82.2 (17.5)
	Median	86.7	86.7
	Min, max	6.7, 100.0	20.0, 100.0
Week 8	n	199	193
	Mean (SD)	81.5 (17.2)	83.4 (16.4)
	Median	86.7	86.7
	Min, max	26.7, 100.0	26.7, 100.0
Change at Week 8	n	195	190
	Mean (SD)	0.3 (11.4)	1.2 (10.9)
	Median	0.0	0.0
	Min, max	-46.7, 33.3	-33.3, 53.3
Week 16	n	198	194
	Mean (SD)	81.8 (18.5)	82.4 (16.4)
	Median	86.7	86.7
	Min, max	6.7, 100.0	6.7, 100.0
Change at Week 16	n	194	190
	Mean (SD)	0.6 (13.1)	0.7 (11.5)
	Median	0.0	0.0
	Min, max	-46.7, 46.7	-33.3, 60.0

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Emotion

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 24	n	198	193
	Mean (SD)	81.6 (16.4)	82.6 (17.9)
	Median	86.7	86.7
	Min, max	20.0, 100.0	6.7, 100.0
Change at Week 24	n	194	189
	Mean (SD)	0.6 (13.7)	0.7 (13.1)
	Median	0.0	0.0
	Min, max	-40.0, 53.3	-46.7, 60.0
Week 52	n	193	184
	Mean (SD)	81.2 (18.6)	82.9 (16.0)
	Median	86.7	86.7
	Min, max	13.3, 100.0	13.3, 100.0
Change at Week 52	n	189	180
	Mean (SD)	0.3 (12.8)	1.2 (13.3)
	Median	0.0	0.0
	Min, max	-46.7, 40.0	-37.5, 60.0

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Body

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline	n	197	192
	Mean (SD)	76.6 (21.9)	77.8 (23.0)
	Median	77.8	88.9
	Min, max	11.1, 100.0	0.0, 100.0
Week 8	n	199	193
	Mean (SD)	78.2 (21.6)	79.4 (22.0)
	Median	77.8	88.9
	Min, max	11.1, 100.0	11.1, 100.0
Change at Week 8	n	195	190
	Mean (SD)	1.8 (13.6)	1.4 (12.5)
	Median	0.0	0.0
	Min, max	-44.4, 44.4	-33.3, 44.4
Week 16	n	198	194
	Mean (SD)	77.7 (21.6)	80.3 (21.4)
	Median	77.8	88.9
	Min, max	11.1, 100.0	11.1, 100.0
Change at Week 16	n	194	190
	Mean (SD)	1.2 (14.1)	2.7 (13.8)
	Median	0.0	0.0
	Min, max	-44.4, 33.3	-44.4, 66.7

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Body

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 24	n	198	193
	Mean (SD)	76.4 (22.3)	79.6 (22.7)
	Median	77.8	88.9
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 24	n	194	189
	Mean (SD)	-0.2 (16.5)	2.1 (14.4)
	Median	0.0	0.0
	Min, max	-100.0, 44.4	-44.4, 55.6
Week 52	n	193	184
	Mean (SD)	78.8 (20.7)	80.3 (20.6)
	Median	77.8	88.9
	Min, max	22.2, 100.0	11.1, 100.0
Change at Week 52	n	189	180
	Mean (SD)	1.8 (14.6)	2.2 (14.2)
	Median	0.0	0.0
	Min, max	-44.4, 33.3	-44.4, 55.6

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Eat

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline	n	197	192
	Mean (SD)	92.8 (14.4)	91.1 (16.5)
	Median	100.0	100.0
	Min, max	33.3, 100.0	0.0, 100.0
Week 8	n	199	193
	Mean (SD)	92.3 (15.2)	91.4 (16.7)
	Median	100.0	100.0
	Min, max	22.2, 100.0	0.0, 100.0
Change at Week 8	n	195	190
	Mean (SD)	-0.6 (11.8)	0.2 (10.9)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-44.4, 55.6
Week 16	n	198	194
	Mean (SD)	92.0 (14.1)	90.5 (17.0)
	Median	100.0	100.0
	Min, max	33.3, 100.0	0.0, 100.0
Change at Week 16	n	194	190
	Mean (SD)	-1.3 (11.7)	-0.1 (12.1)
	Median	0.0	0.0
	Min, max	-44.4, 44.4	-44.4, 44.4

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Eat

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 24	n	198	193
	Mean (SD)	93.0 (14.5)	90.4 (18.1)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 24	n	194	189
	Mean (SD)	-0.2 (12.4)	-0.4 (10.6)
	Median	0.0	0.0
	Min, max	-66.7, 44.4	-44.4, 44.4
Week 52	n	193	184
	Mean (SD)	93.7 (12.5)	91.2 (18.3)
	Median	100.0	100.0
	Min, max	44.4, 100.0	0.0, 100.0
Change at Week 52	n	189	180
	Mean (SD)	0.5 (10.3)	0.2 (12.1)
	Median	0.0	0.0
	Min, max	-33.3, 44.4	-44.4, 66.7

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Treatment Burden

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline	n	197	192
	Mean (SD)	70.4 (20.1)	72.3 (19.8)
	Median	66.7	77.8
	Min, max	11.1, 100.0	0.0, 100.0
Week 8	n	198	193
	Mean (SD)	71.4 (19.9)	73.4 (19.1)
	Median	66.7	77.8
	Min, max	22.2, 100.0	22.2, 100.0
Change at Week 8	n	194	190
	Mean (SD)	0.9 (13.1)	1.1 (14.5)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-44.4, 100.0
Week 16	n	198	194
	Mean (SD)	70.9 (20.4)	73.2 (20.7)
	Median	66.7	77.8
	Min, max	0.0, 100.0	11.1, 100.0
Change at Week 16	n	194	190
	Mean (SD)	0.3 (14.7)	1.5 (15.0)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-55.6, 88.9

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Treatment Burden

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 24	n	198	193
	Mean (SD)	72.7 (20.3)	73.2 (20.0)
	Median	66.7	77.8
	Min, max	11.1, 100.0	11.1, 100.0
Change at Week 24	n	194	189
	Mean (SD)	2.1 (14.2)	1.1 (14.5)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-55.6, 55.6
Week 52	n	193	184
	Mean (SD)	73.7 (19.9)	76.3 (19.0)
	Median	77.8	77.8
	Min, max	11.1, 100.0	11.1, 100.0
Change at Week 52	n	189	180
	Mean (SD)	3.2 (16.0)	4.4 (15.4)
	Median	0.0	0.0
	Min, max	-33.3, 66.7	-55.6, 100.0

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Health Perceptions

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline	n	189	187
	Mean (SD)	71.1 (19.2)	73.9 (19.5)
	Median	66.7	77.8
	Min, max	11.1, 100.0	0.0, 100.0
Week 8	n	191	188
	Mean (SD)	70.4 (19.2)	73.2 (19.4)
	Median	66.7	66.7
	Min, max	11.1, 100.0	11.1, 100.0
Change at Week 8	n	188	185
	Mean (SD)	-1.0 (15.2)	-0.7 (12.6)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-44.4, 44.4
Week 16	n	189	189
	Mean (SD)	71.3 (20.0)	72.8 (20.2)
	Median	66.7	66.7
	Min, max	0.0, 100.0	11.1, 100.0
Change at Week 16	n	186	186
	Mean (SD)	-0.4 (13.8)	-1.0 (14.9)
	Median	0.0	0.0
	Min, max	-66.7, 44.4	-55.6, 44.4

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Health Perceptions

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 24	n	189	188
	Mean (SD)	70.3 (20.5)	74.2 (20.6)
	Median	66.7	77.8
	Min, max	11.1, 100.0	11.1, 100.0
Change at Week 24	n	186	185
	Mean (SD)	-1.3 (13.9)	0.2 (14.1)
	Median	0.0	0.0
	Min, max	-66.7, 33.3	-33.3, 44.4
Week 52	n	184	179
	Mean (SD)	72.7 (20.0)	75.0 (20.1)
	Median	72.2	77.8
	Min, max	11.1, 100.0	0.0, 100.0
Change at Week 52	n	181	176
	Mean (SD)	1.2 (12.9)	1.1 (15.0)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-44.4, 44.4

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Weight

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline	n	189	187
	Mean (SD)	84.8 (26.9)	82.4 (29.0)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Week 8	n	190	188
	Mean (SD)	85.4 (25.5)	83.3 (27.9)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 8	n	187	185
	Mean (SD)	0.5 (20.3)	0.9 (21.8)
	Median	0.0	0.0
	Min, max	-66.7, 66.7	-66.7, 66.7
Week 16	n	189	189
	Mean (SD)	82.5 (28.5)	82.9 (28.9)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 16	n	186	186
	Mean (SD)	-2.7 (24.5)	0.7 (23.7)
	Median	0.0	0.0
	Min, max	-66.7, 66.7	-66.7, 66.7

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Weight

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 24	n	189	187
	Mean (SD)	84.8 (27.2)	83.2 (29.8)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 24	n	186	184
	Mean (SD)	-0.2 (26.5)	0.5 (22.4)
	Median	0.0	0.0
	Min, max	-100.0, 100.0	-66.7, 66.7
Week 52	n	183	179
	Mean (SD)	86.2 (24.8)	82.5 (27.2)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 52	n	180	176
	Mean (SD)	1.1 (24.9)	-0.2 (21.8)
	Median	0.0	0.0
	Min, max	-66.7, 100.0	-66.7, 100.0

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Digestion

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline	n	197	191
	Mean (SD)	82.7 (18.3)	85.0 (15.7)
	Median	88.9	88.9
	Min, max	22.2, 100.0	33.3, 100.0
Week 8	n	198	193
	Mean (SD)	81.8 (19.4)	86.9 (15.8)
	Median	88.9	88.9
	Min, max	11.1, 100.0	22.2, 100.0
Change at Week 8	n	194	189
	Mean (SD)	-1.3 (17.0)	1.9 (12.6)
	Median	0.0	0.0
	Min, max	-66.7, 66.7	-44.4, 44.4
Week 16	n	198	194
	Mean (SD)	81.5 (19.7)	83.9 (18.4)
	Median	88.9	88.9
	Min, max	0.0, 100.0	22.2, 100.0
Change at Week 16	n	194	189
	Mean (SD)	-1.4 (18.0)	-0.9 (12.2)
	Median	0.0	0.0
	Min, max	-66.7, 66.7	-33.3, 33.3

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Digestion

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 24	n	198	191
	Mean (SD)	82.3 (18.6)	86.3 (15.0)
	Median	88.9	88.9
	Min, max	22.2, 100.0	44.4, 100.0
Change at Week 24	n	194	187
	Mean (SD)	-0.5 (15.7)	1.2 (12.1)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-33.3, 44.4
Week 52	n	192	184
	Mean (SD)	82.6 (18.2)	82.4 (17.7)
	Median	88.9	88.9
	Min, max	22.2, 100.0	22.2, 100.0
Change at Week 52	n	188	179
	Mean (SD)	0.0 (16.4)	-2.2 (12.6)
	Median	0.0	0.0
	Min, max	-55.6, 66.7	-66.7, 33.3

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Role

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline	n	189	186
	Mean (SD)	87.7 (16.9)	87.4 (15.8)
	Median	91.7	91.7
	Min, max	8.3, 100.0	16.7, 100.0
Week 8	n	190	188
	Mean (SD)	87.4 (14.6)	88.1 (15.2)
	Median	91.7	91.7
	Min, max	8.3, 100.0	33.3, 100.0
Change at Week 8	n	187	184
	Mean (SD)	-0.7 (12.8)	0.6 (12.6)
	Median	0.0	0.0
	Min, max	-58.3, 50.0	-50.0, 58.3
Week 16	n	189	189
	Mean (SD)	86.1 (17.7)	88.6 (14.1)
	Median	91.7	91.7
	Min, max	0.0, 100.0	41.7, 100.0
Change at Week 16	n	186	185
	Mean (SD)	-1.7 (15.8)	1.9 (12.6)
	Median	0.0	0.0
	Min, max	-66.7, 91.7	-50.0, 58.3

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Role

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 24	n	189	187
	Mean (SD)	87.0 (15.7)	88.1 (14.8)
	Median	91.7	91.7
	Min, max	8.3, 100.0	33.3, 100.0
Change at Week 24	n	186	183
	Mean (SD)	-0.9 (14.1)	1.0 (13.5)
	Median	0.0	0.0
	Min, max	-58.3, 75.0	-50.0, 66.7
Week 52	n	183	179
	Mean (SD)	88.8 (14.8)	88.7 (14.8)
	Median	91.7	91.7
	Min, max	16.7, 100.0	33.3, 100.0
Change at Week 52	n	180	175
	Mean (SD)	1.1 (12.3)	1.8 (14.6)
	Median	0.0	0.0
	Min, max	-33.3, 66.7	-58.3, 75.0

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Baseline	n	197	192
	Mean (SD)	74.3 (17.2)	75.1 (18.4)
	Median	77.8	77.8
	Min, max	22.2, 100.0	16.7, 100.0
Week 8	n	199	193
	Mean (SD)	75.7 (15.9)	76.1 (18.3)
	Median	77.8	77.8
	Min, max	38.9, 100.0	22.2, 100.0
Change at Week 8	n	195	190
	Mean (SD)	1.1 (13.9)	0.9 (13.4)
	Median	0.0	0.0
	Min, max	-38.9, 38.9	-77.8, 44.4
Week 16	n	198	194
	Mean (SD)	74.9 (17.3)	74.8 (19.5)
	Median	77.8	77.8
	Min, max	11.1, 100.0	16.7, 100.0
Change at Week 16	n	194	190
	Mean (SD)	0.1 (14.7)	-0.2 (14.3)
	Median	0.0	0.0
	Min, max	-61.1, 50.0	-61.1, 44.4

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

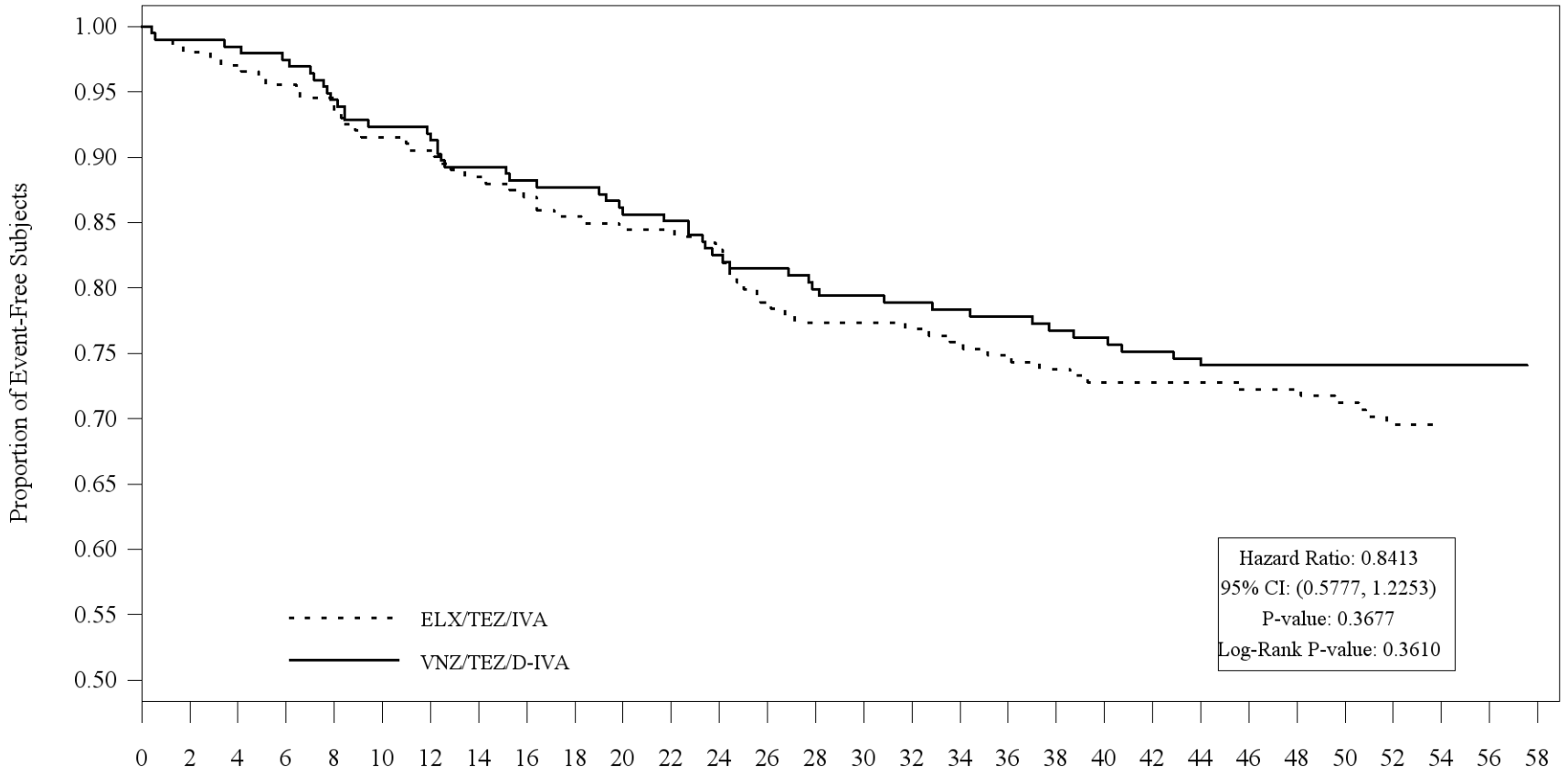
Visit	Statistics	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 196
Week 24	n	198	193
	Mean (SD)	76.5 (16.2)	77.0 (18.6)
	Median	77.8	77.8
	Min, max	27.8, 100.0	22.2, 100.0
Change at Week 24	n	194	189
	Mean (SD)	1.8 (13.4)	2.0 (12.8)
	Median	0.0	0.0
	Min, max	-33.3, 38.9	-33.3, 55.6
Week 52	n	193	184
	Mean (SD)	77.7 (16.2)	77.4 (17.5)
	Median	77.8	77.8
	Min, max	27.8, 100.0	22.2, 100.0
Change at Week 52	n	189	180
	Mean (SD)	3.2 (13.4)	2.7 (14.2)
	Median	0.0	0.0
	Min, max	-38.9, 44.4	-55.6, 44.4

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Zusatzanalysen zur Studie VX20-121-102

Figure 1.2.1.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52
Full Analysis Set

Zusatzanalysen zur Studie VX20-121-102



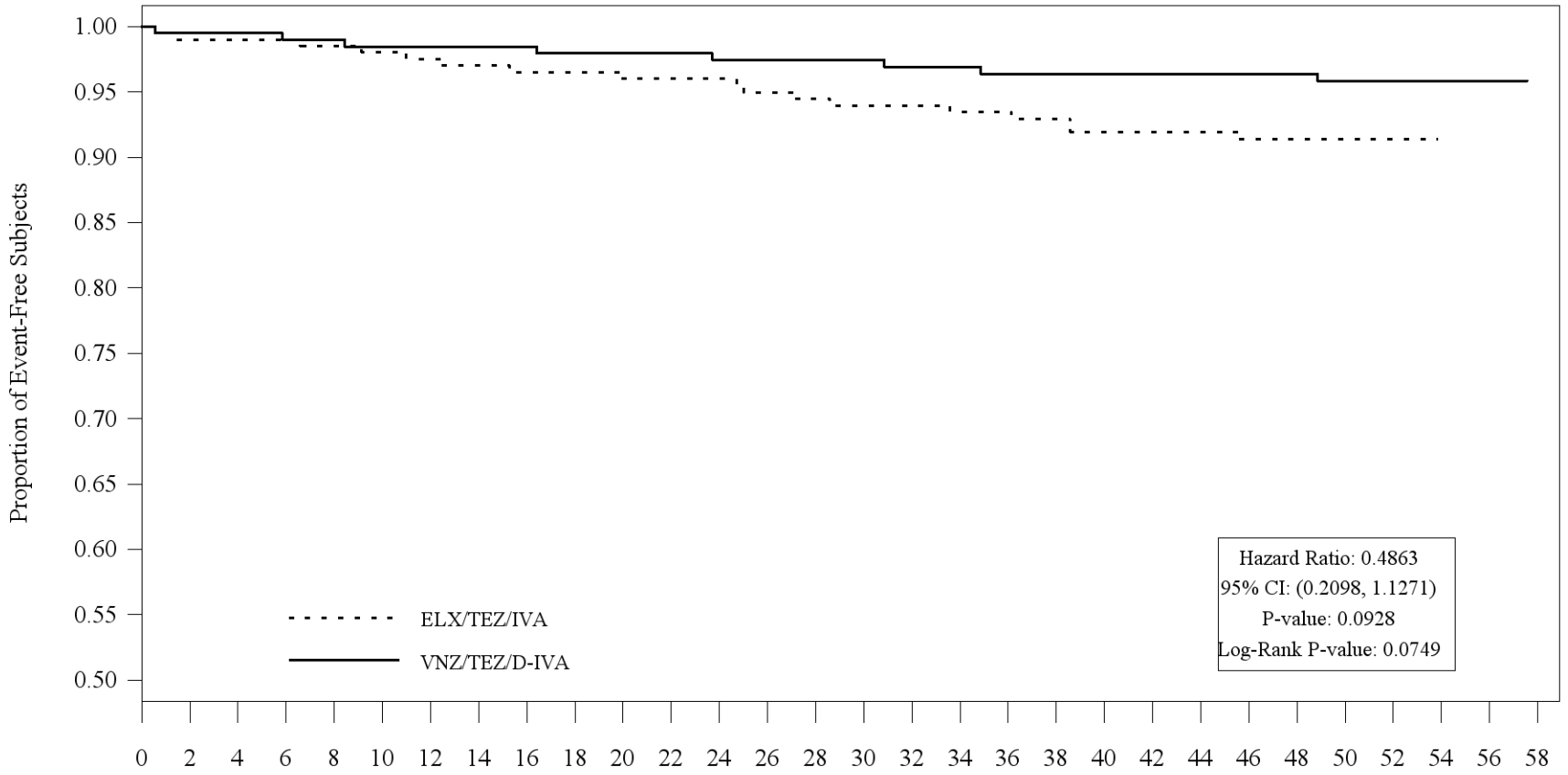
ELX/TEZ/IVA - Number of patients					
at risk	202	179	164	146	139
with event(s)	0	19	34	50	55
censored	0	4	4	6	8
VNZ/TEZ/D-IVA - Number of patients					
at risk	196	179	159	147	139
with event(s)	0	17	34	43	50
censored	0	0	3	6	7

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Zusatzanalysen zur Studie VX20-121-102

Figure 1.2.1.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Zusatzanalysen zur Studie VX20-121-102

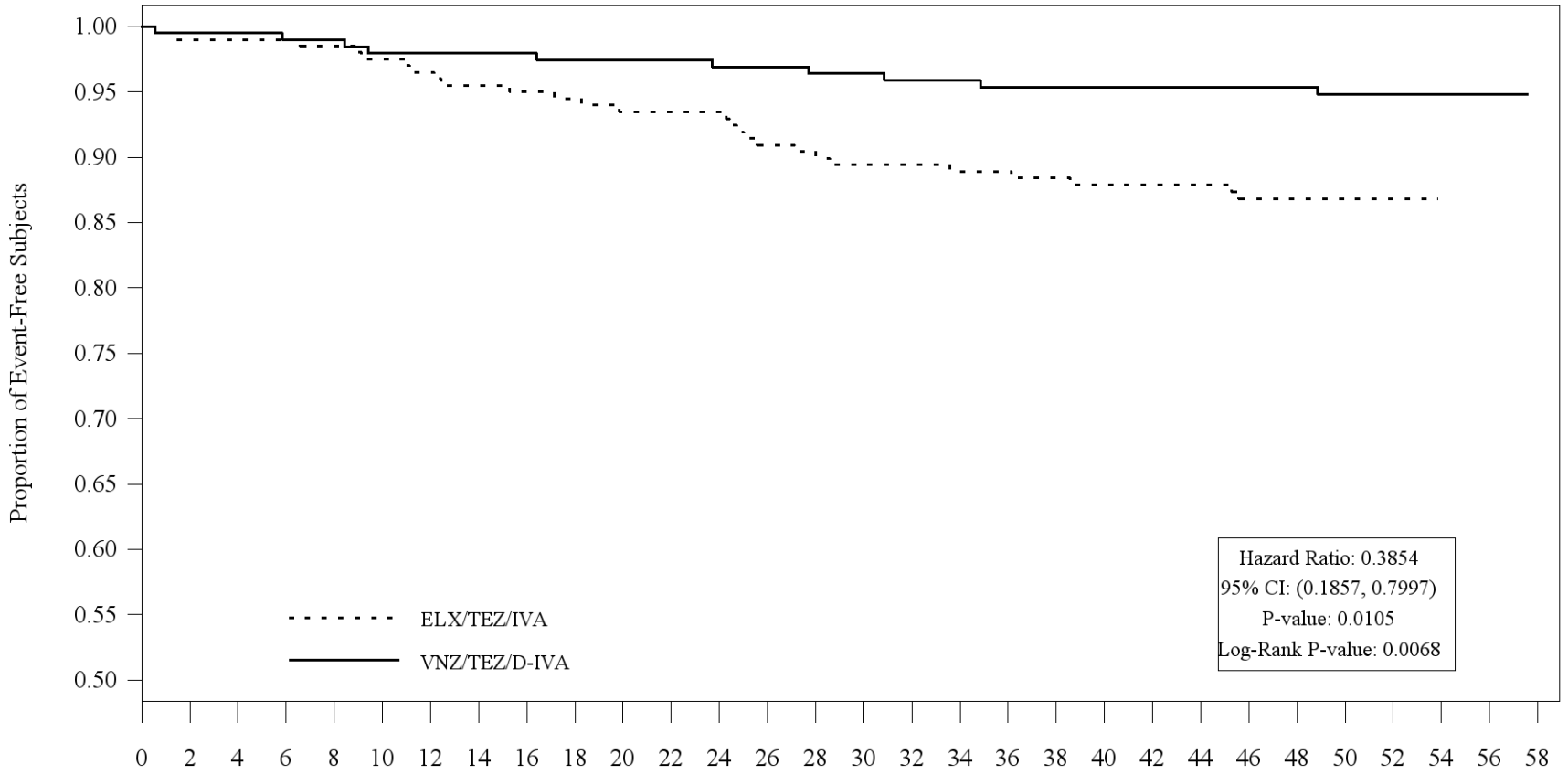


ELX/TEZ/IVA - Number of patients					
at risk	202	193	190	182	175
with event(s)	0	5	8	13	17
censored	0	4	4	7	10
VNZ/TEZ/D-IVA - Number of patients					
at risk	196	192	188	182	181
with event(s)	0	3	5	7	7
censored	0	1	3	7	8

Zusatzanalysen zur Studie VX20-121-102

Figure 1.2.1.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	202	191	185	173	166
with event(s)	0	7	13	22	26
censored	0	4	4	7	10
VNZ/TEZ/D-IVA - Number of patients					
at risk	196	191	187	180	179
with event(s)	0	4	6	9	9
censored	0	1	3	7	8

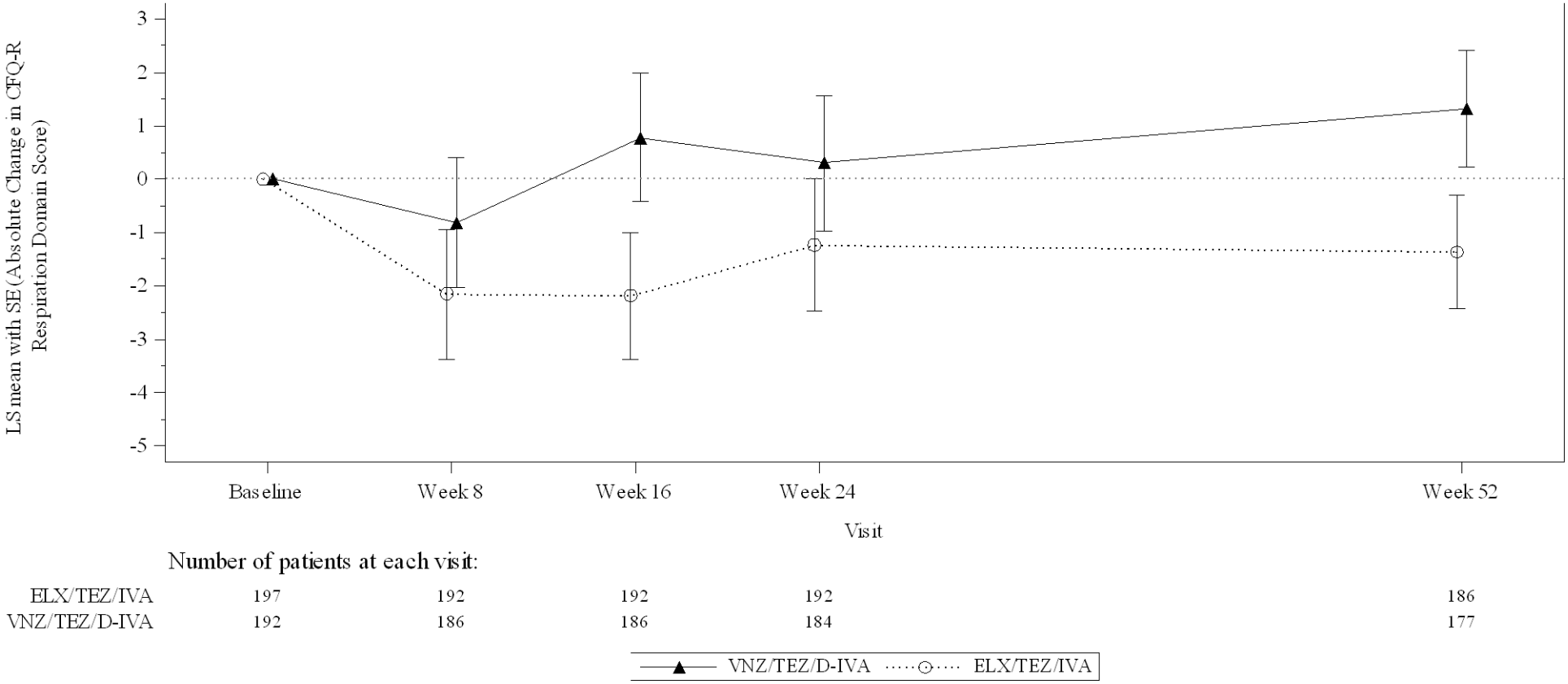
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

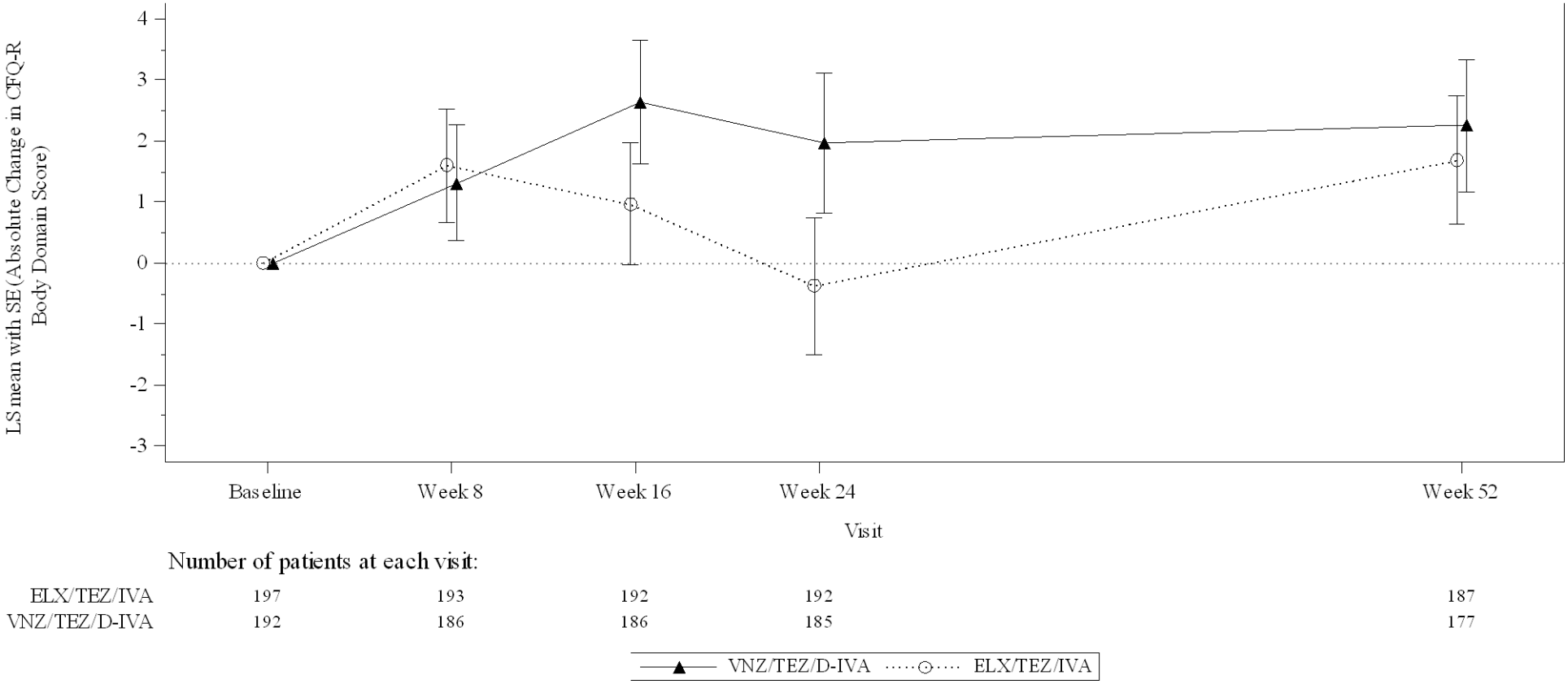
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Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

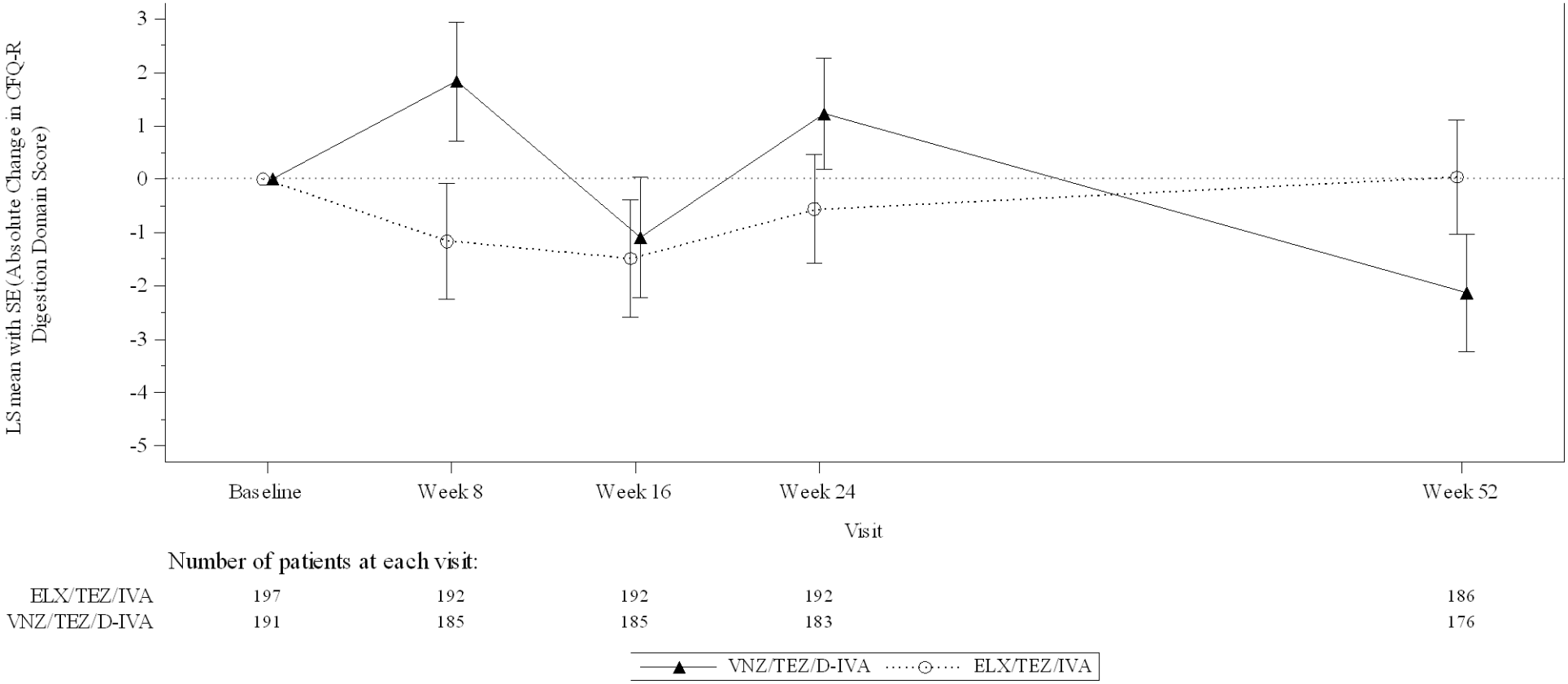
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Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

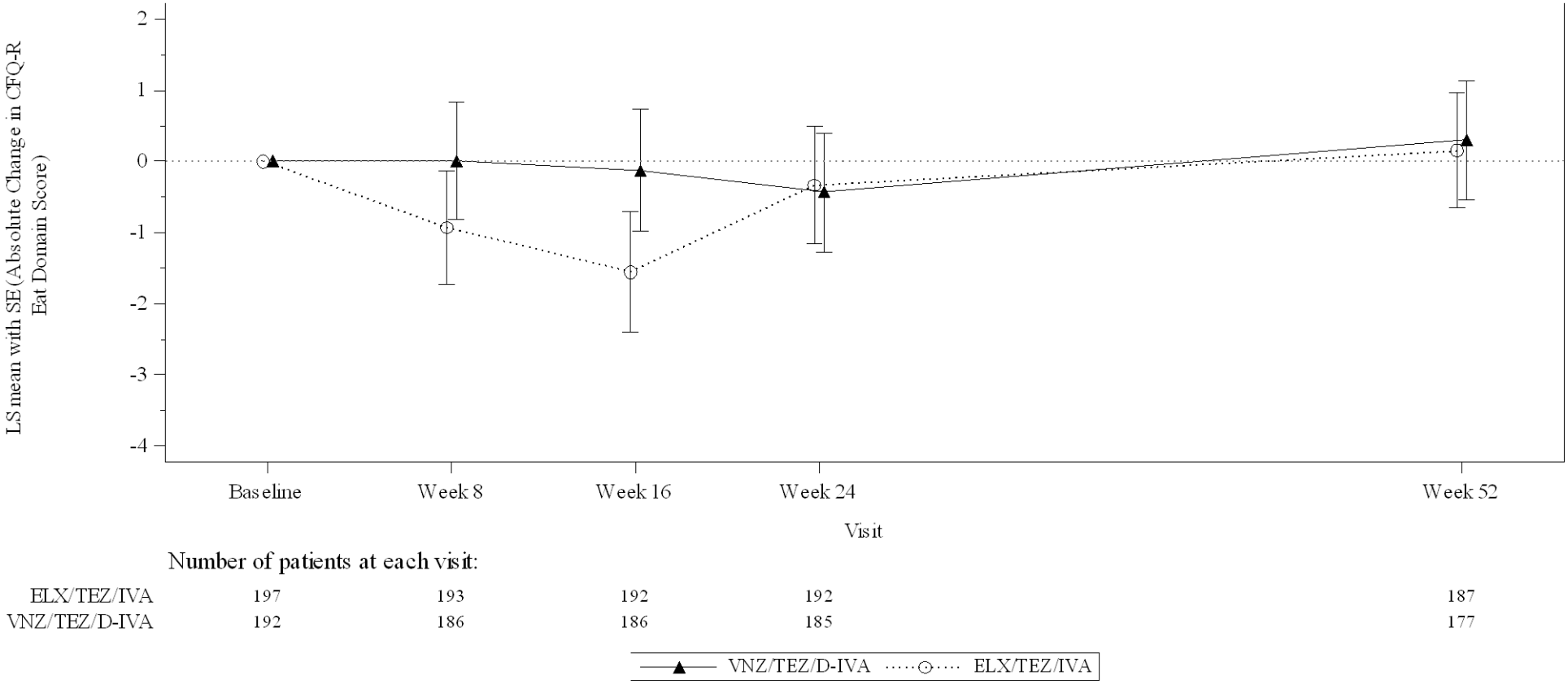
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Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

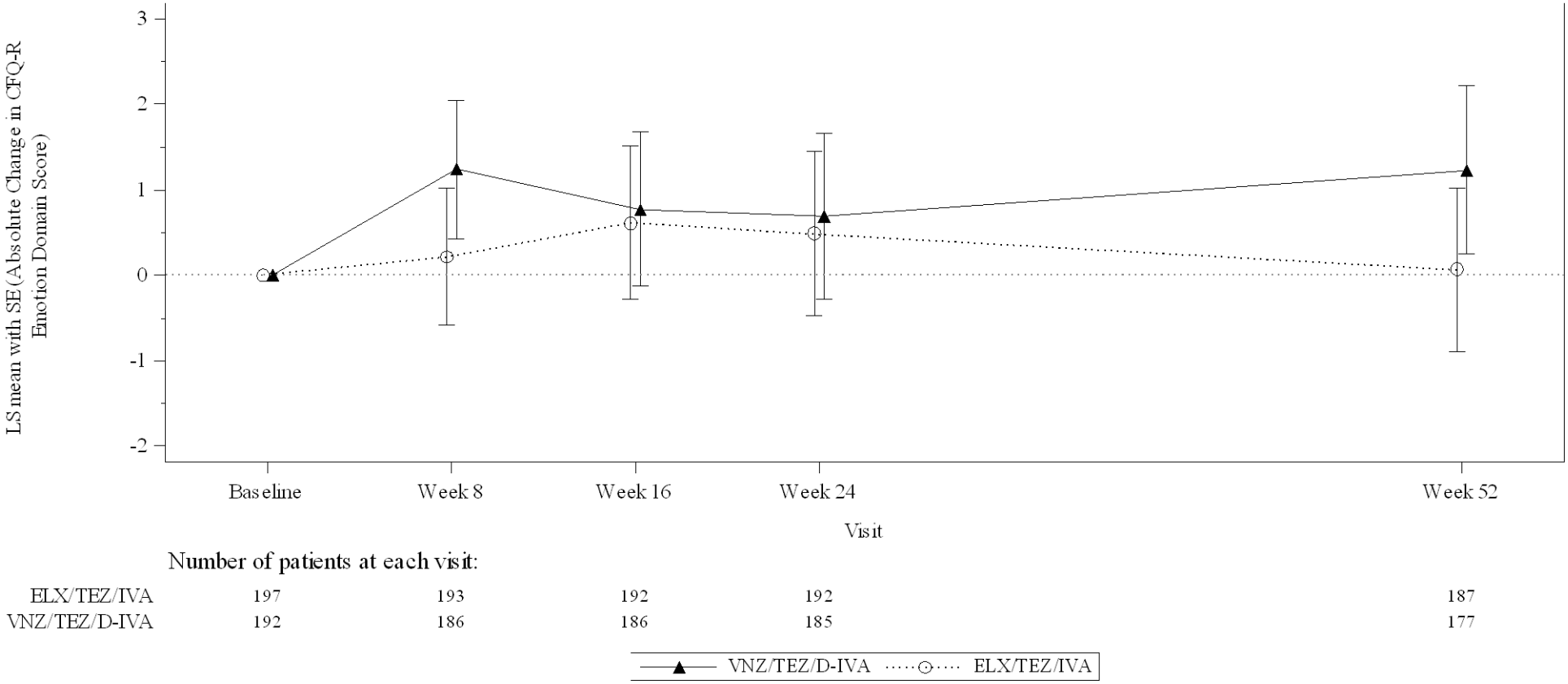
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Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

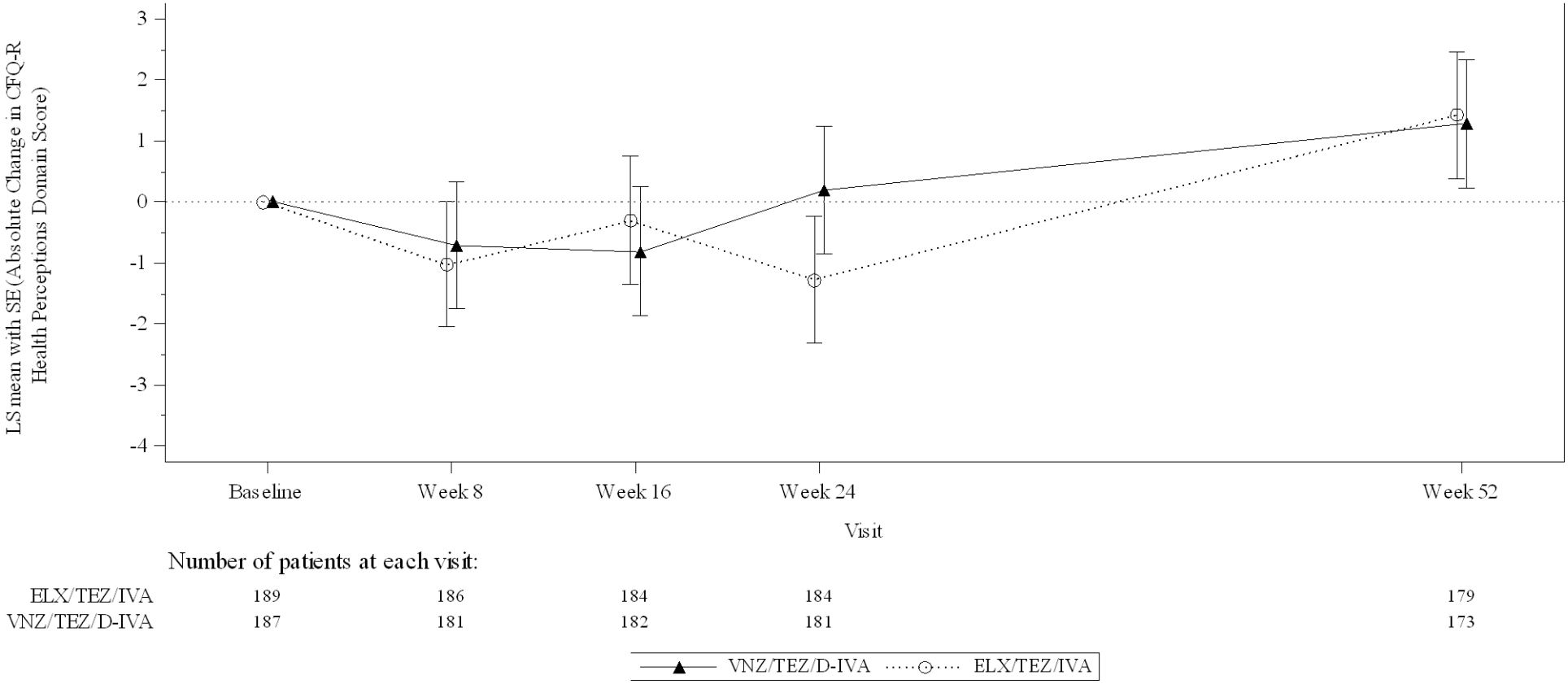
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Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

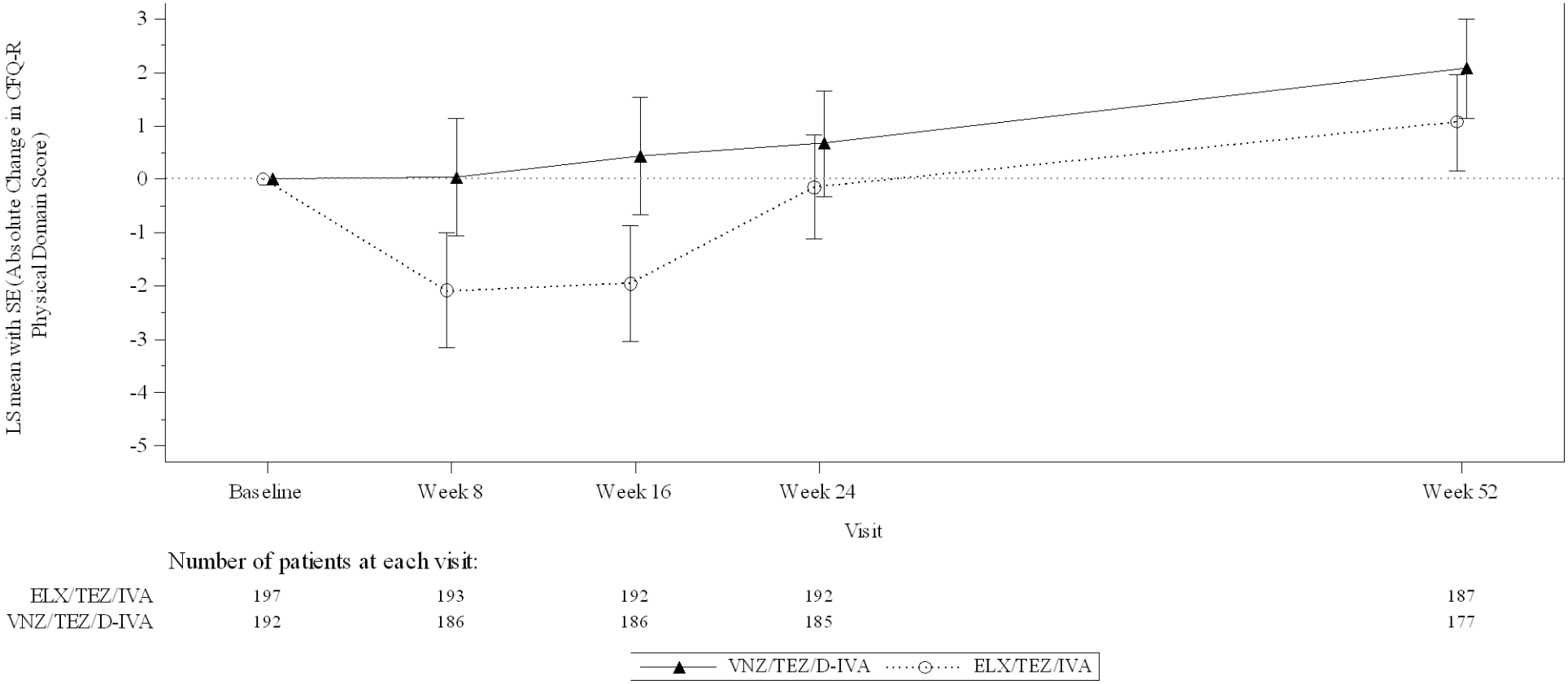
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Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

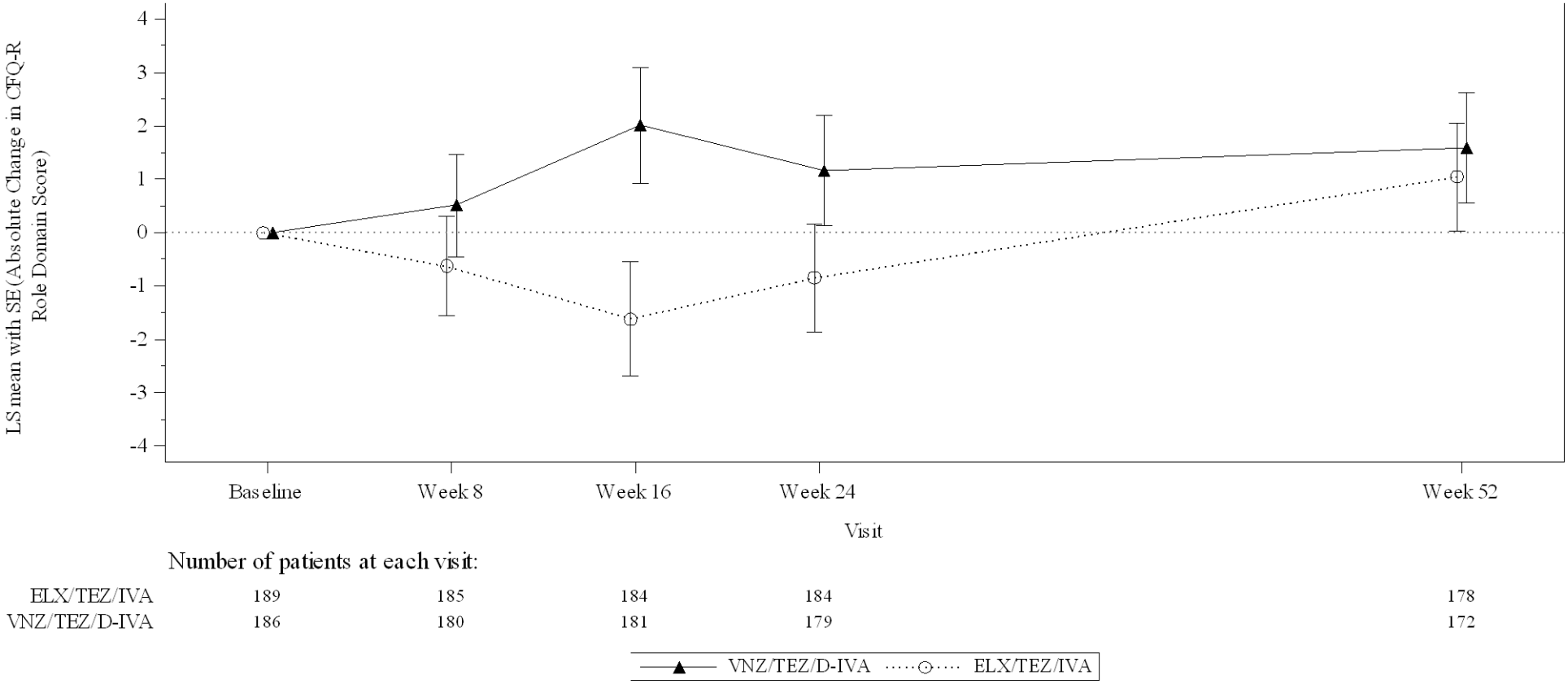
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Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

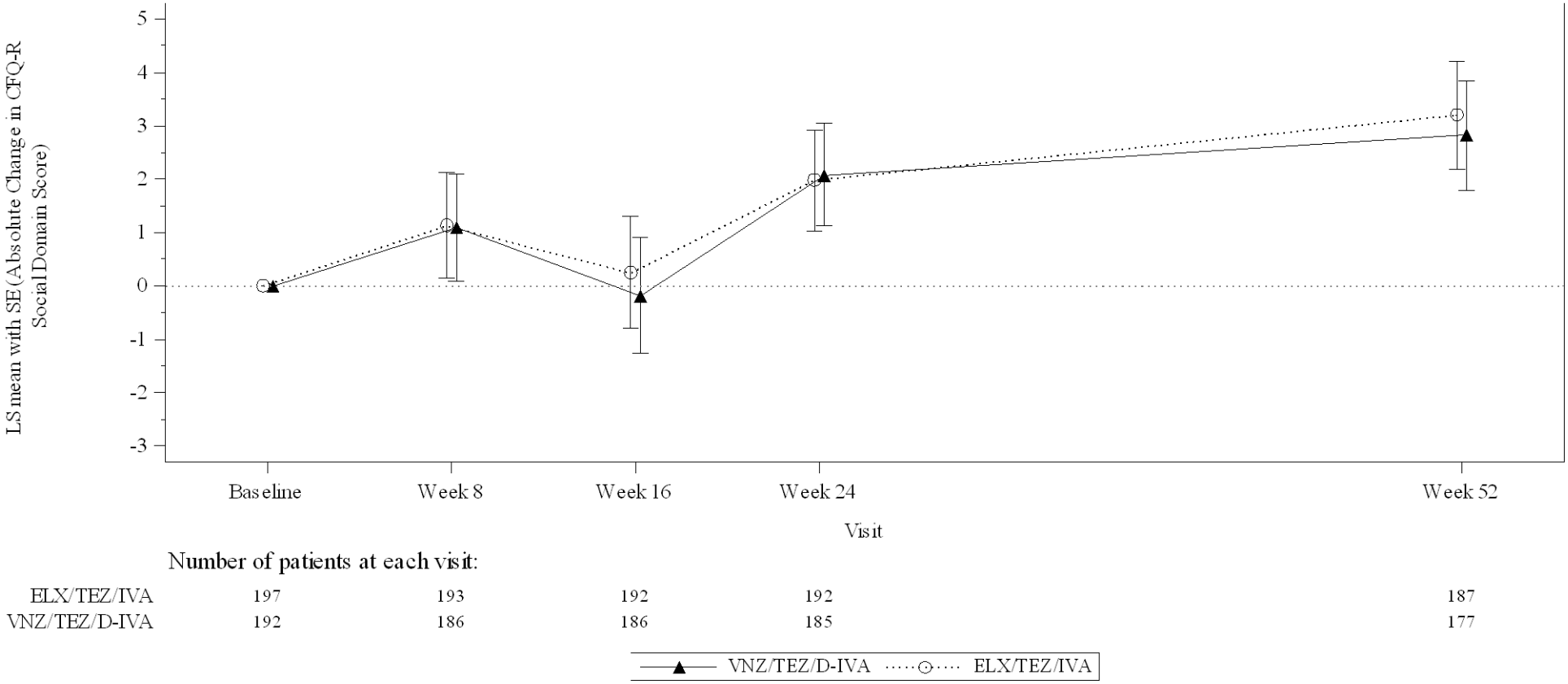
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Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

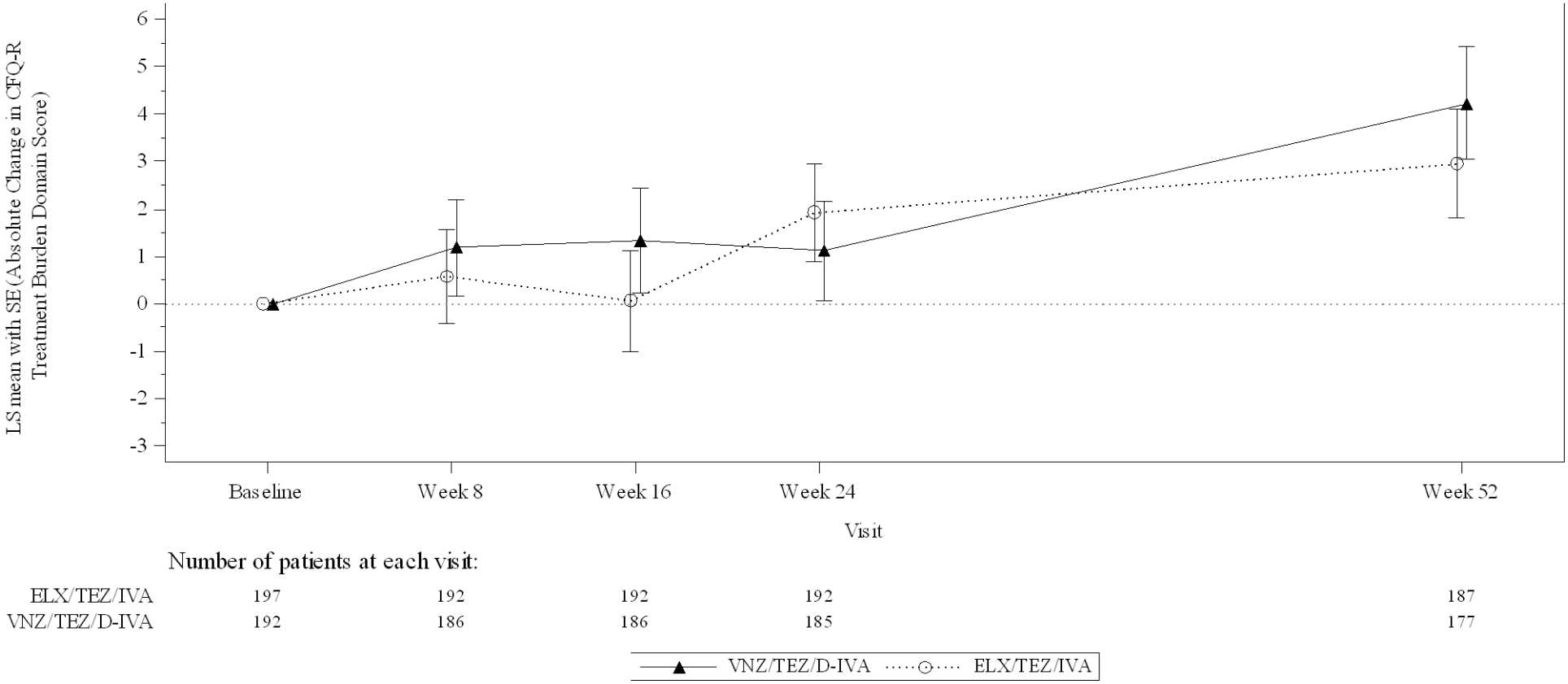
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Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

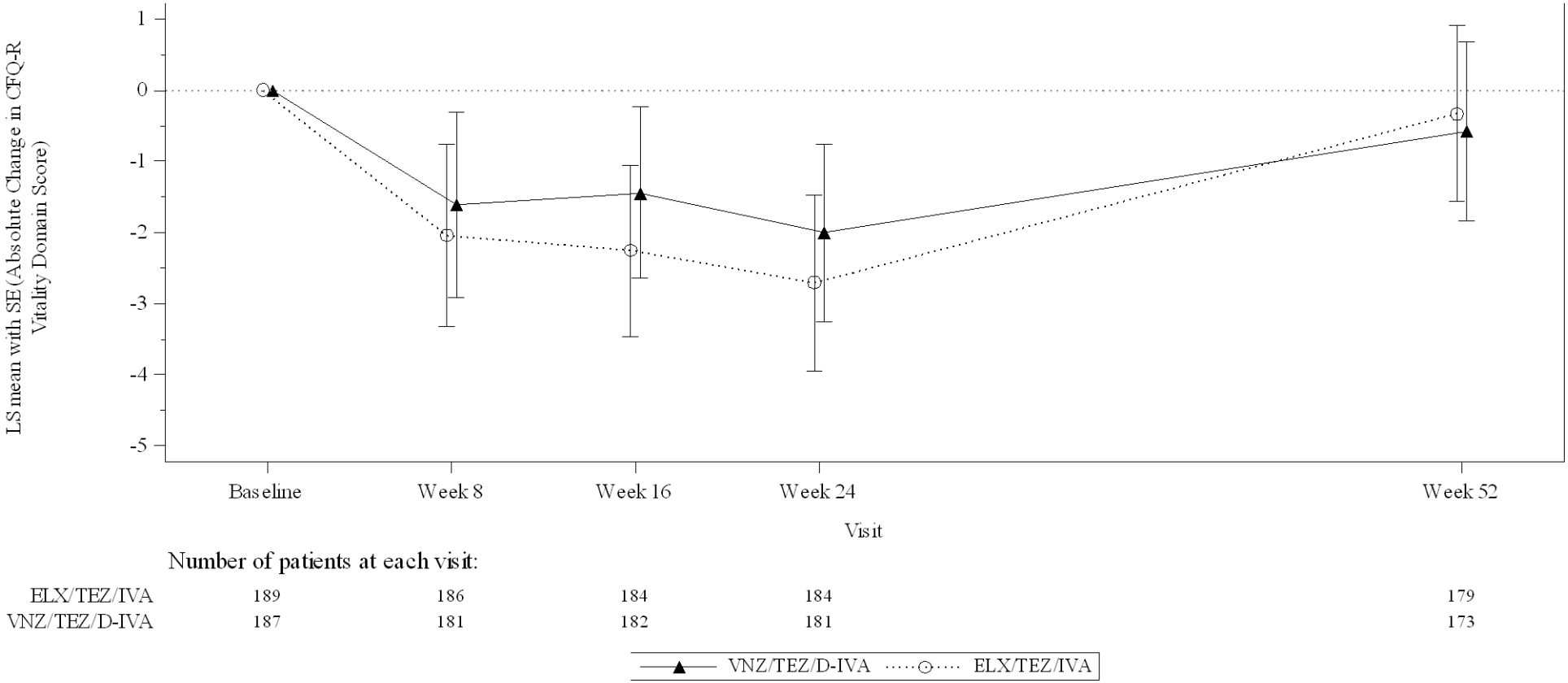
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Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

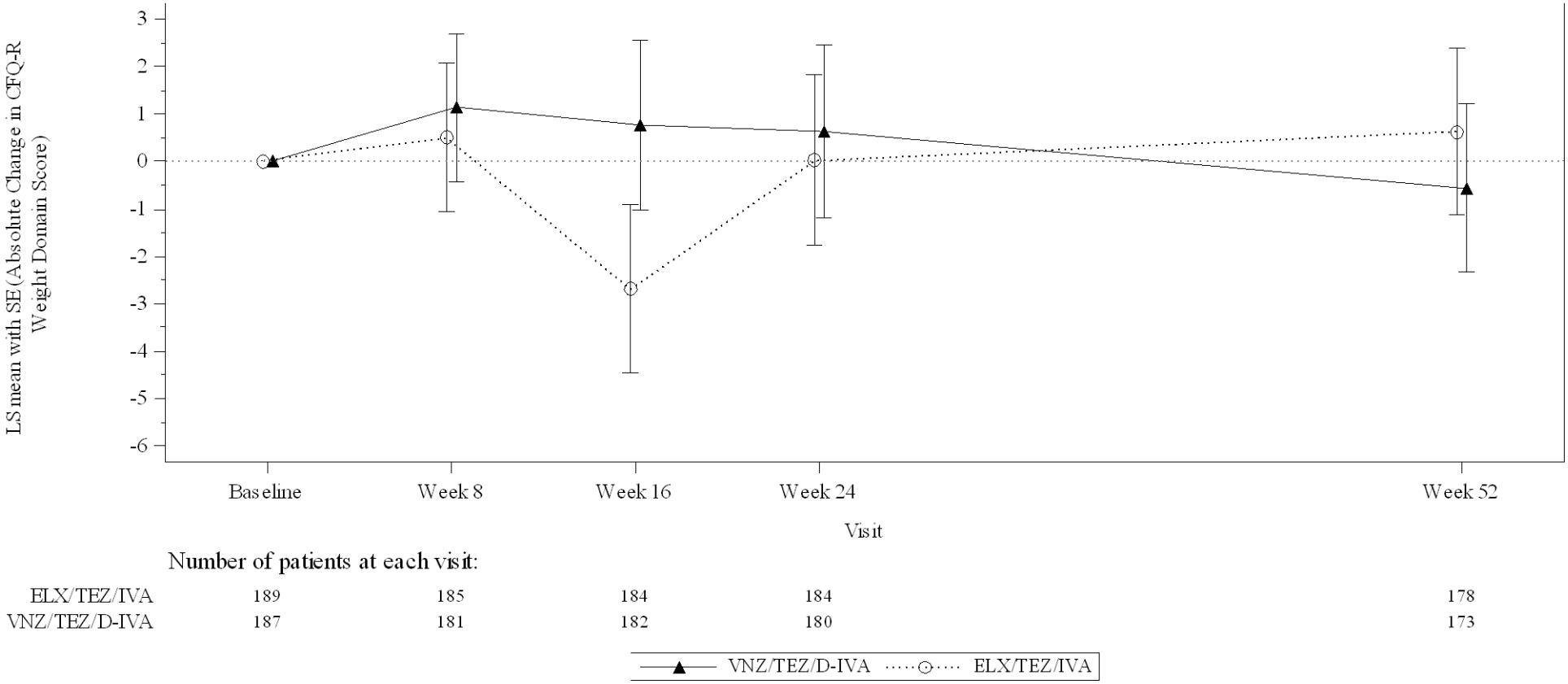
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Figure 1.2.1.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

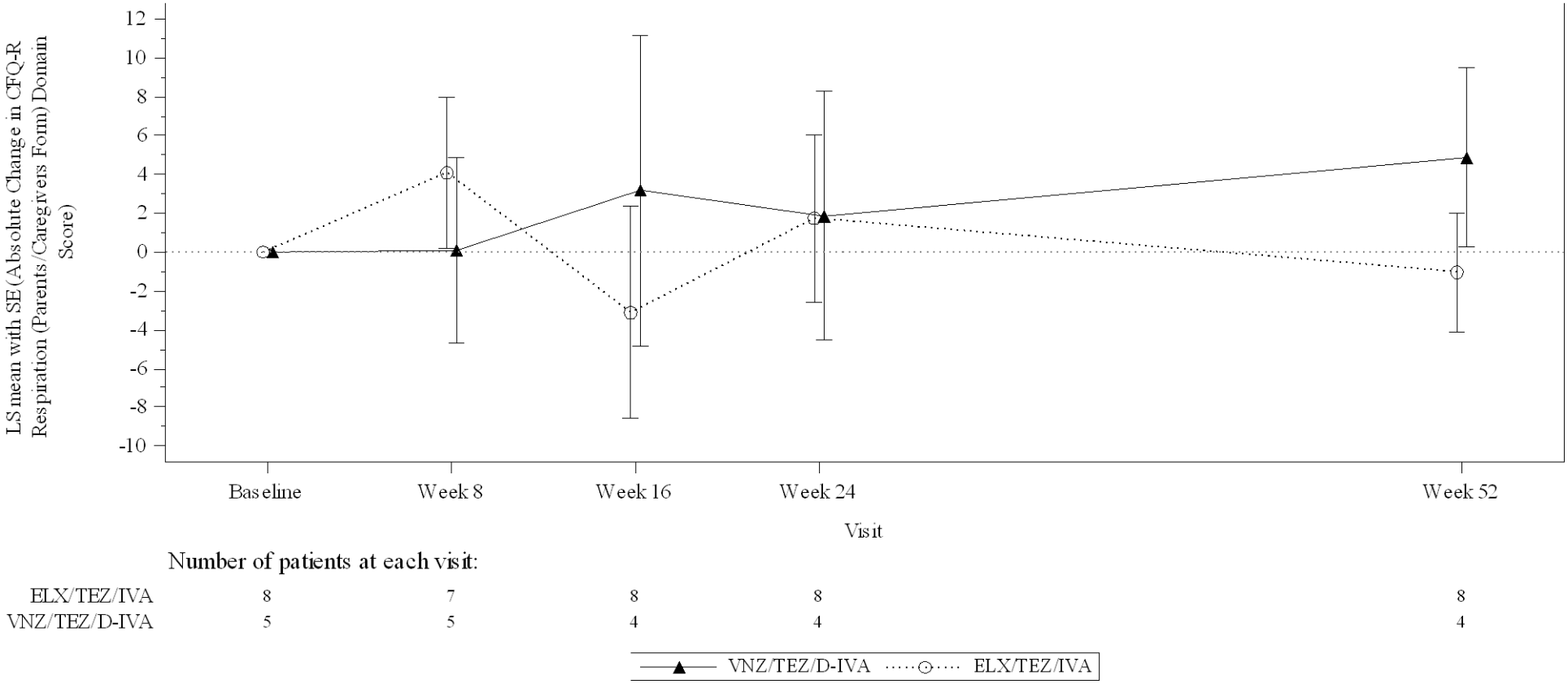
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Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

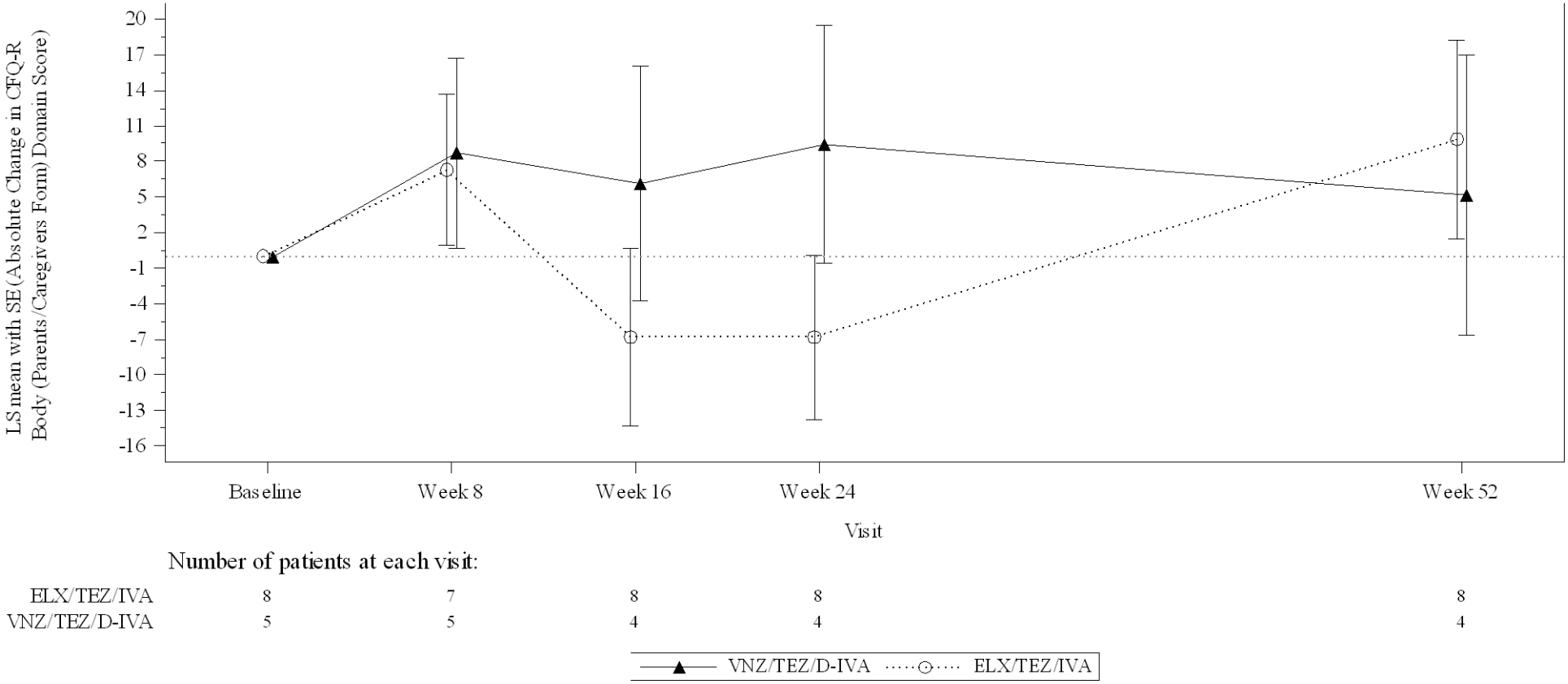
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Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

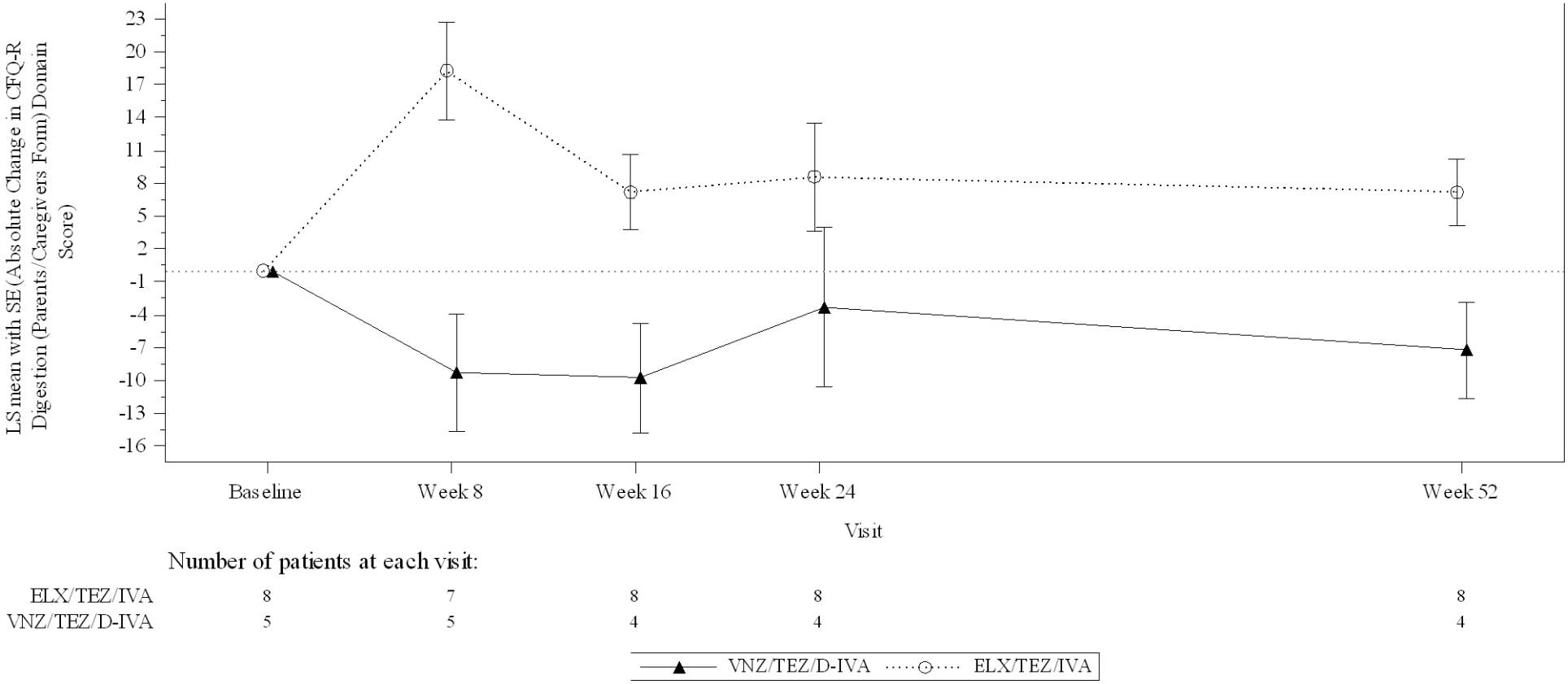
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Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

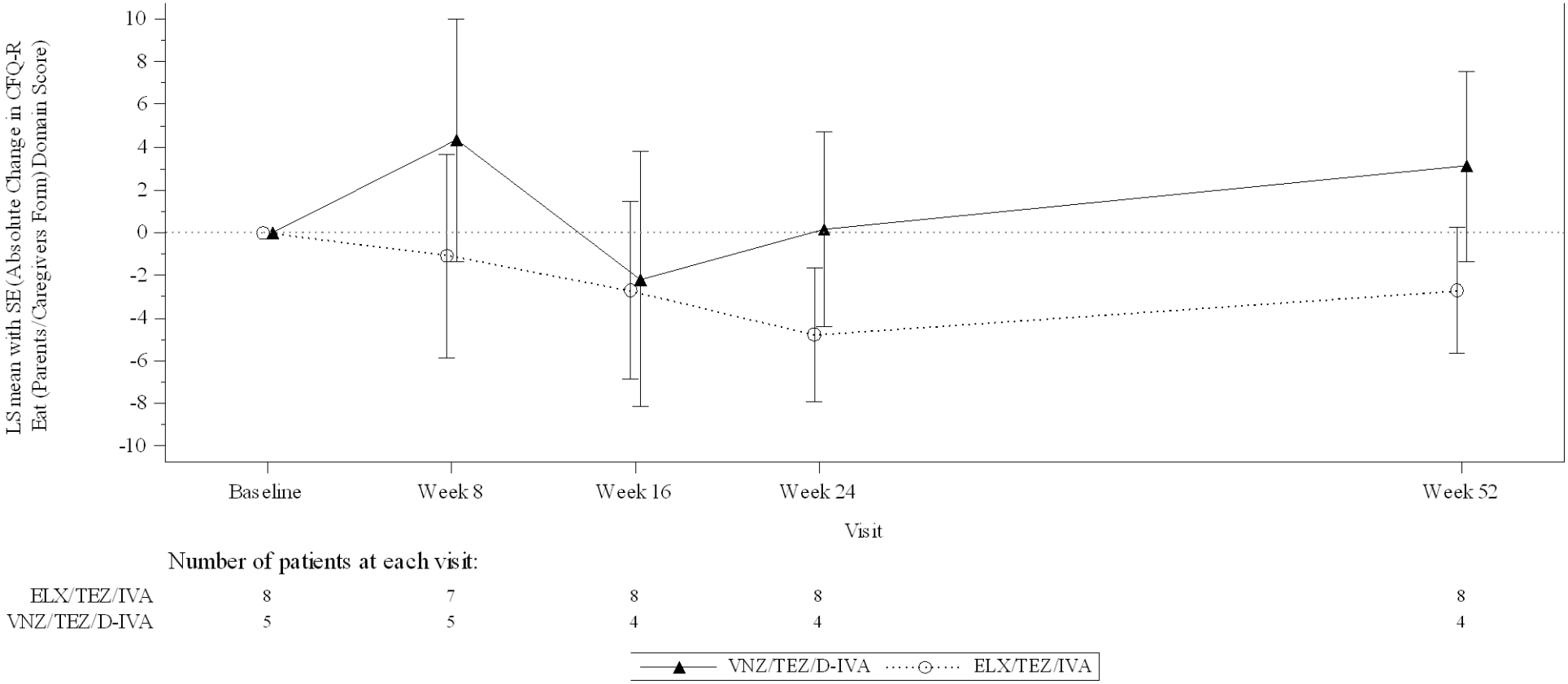
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Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

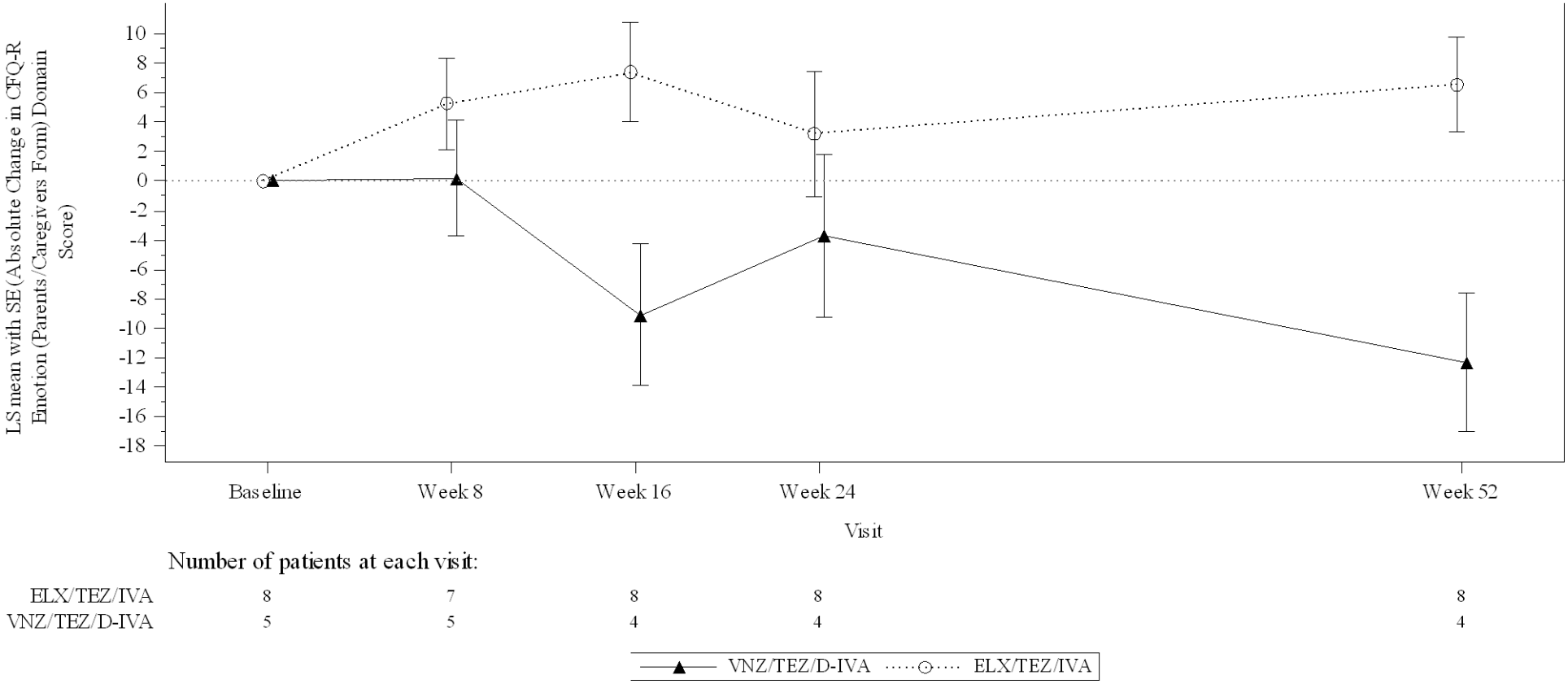
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Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

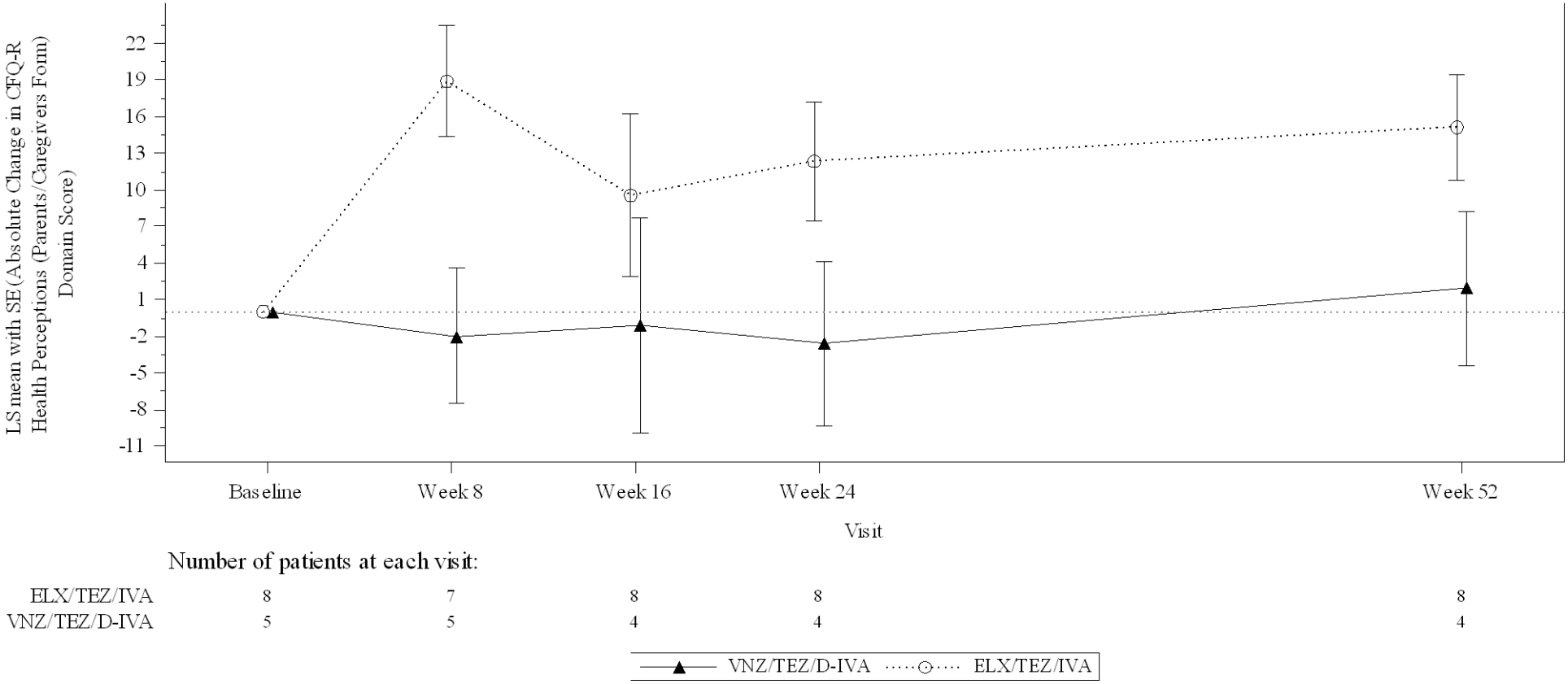
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Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

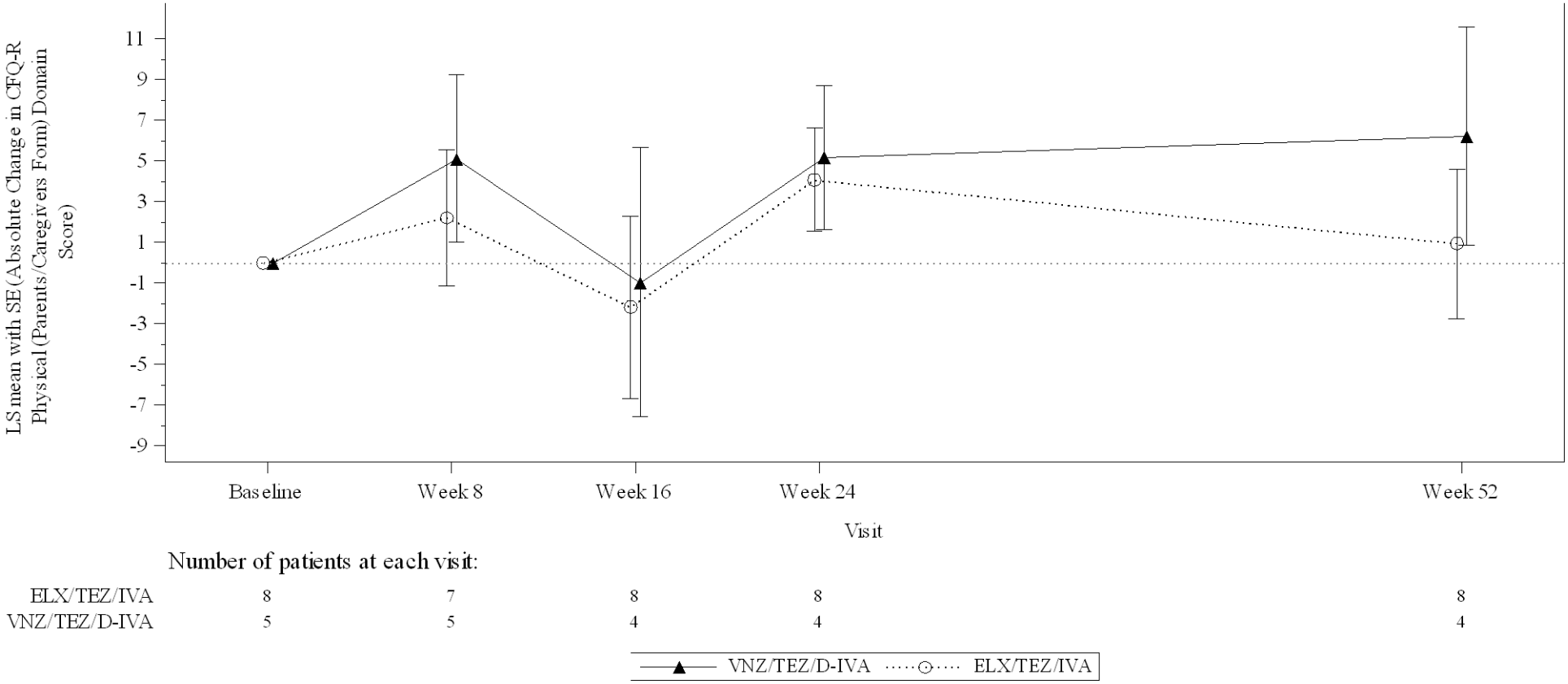
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Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

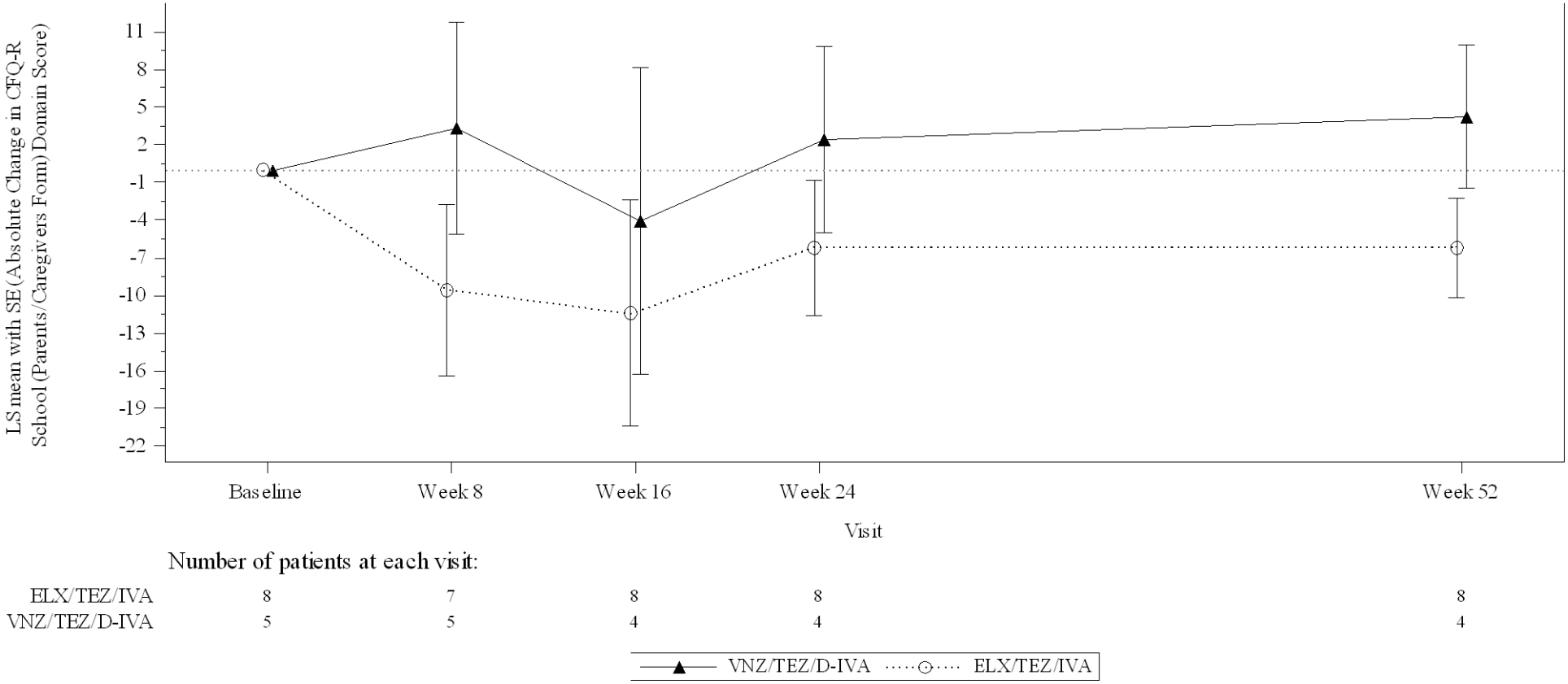
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Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

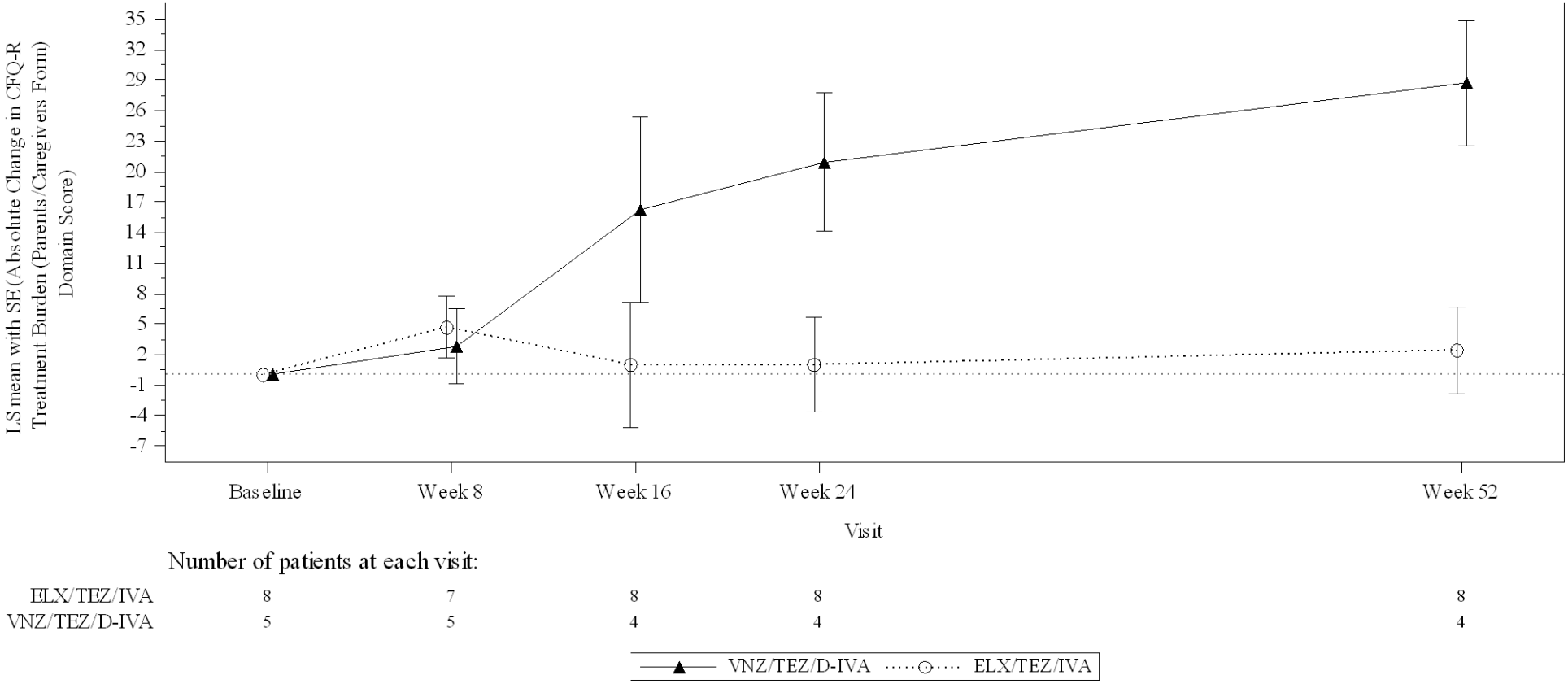
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Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

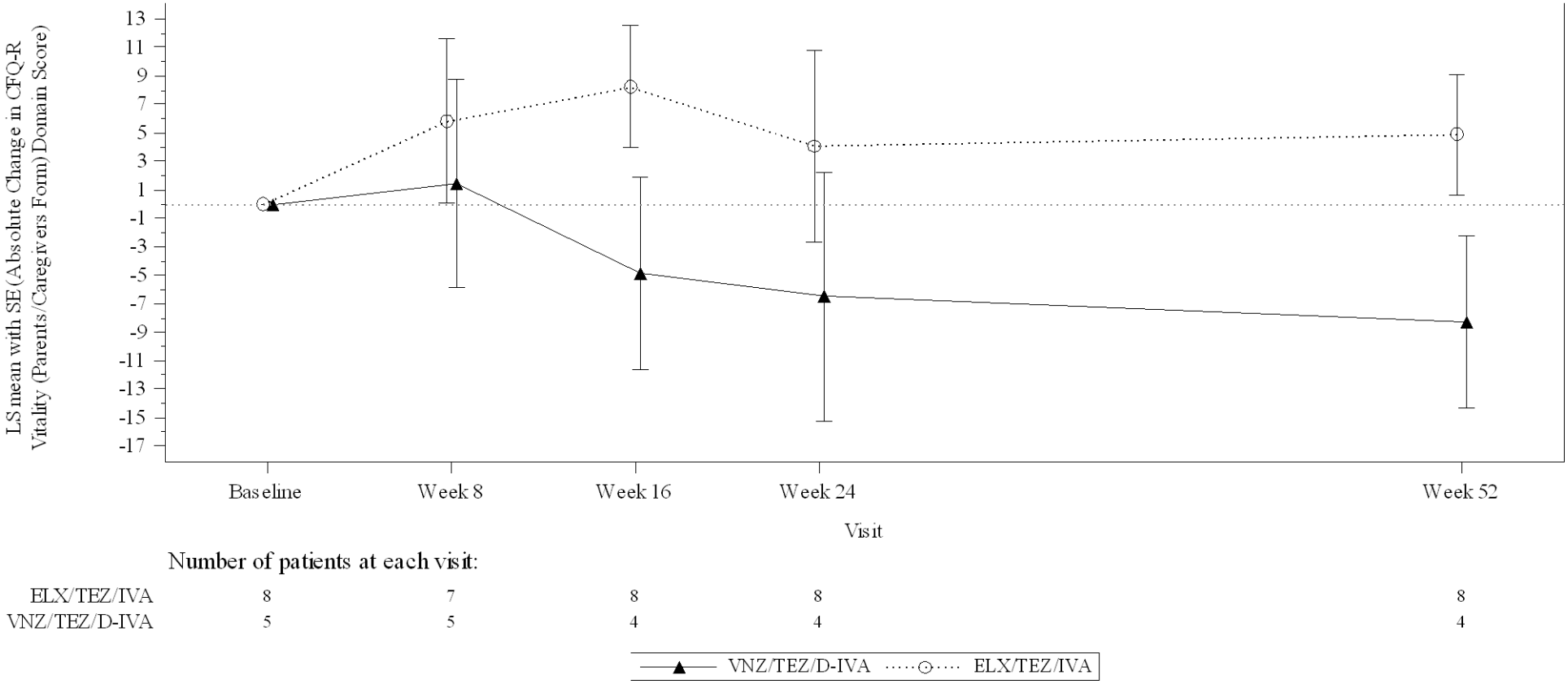
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Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

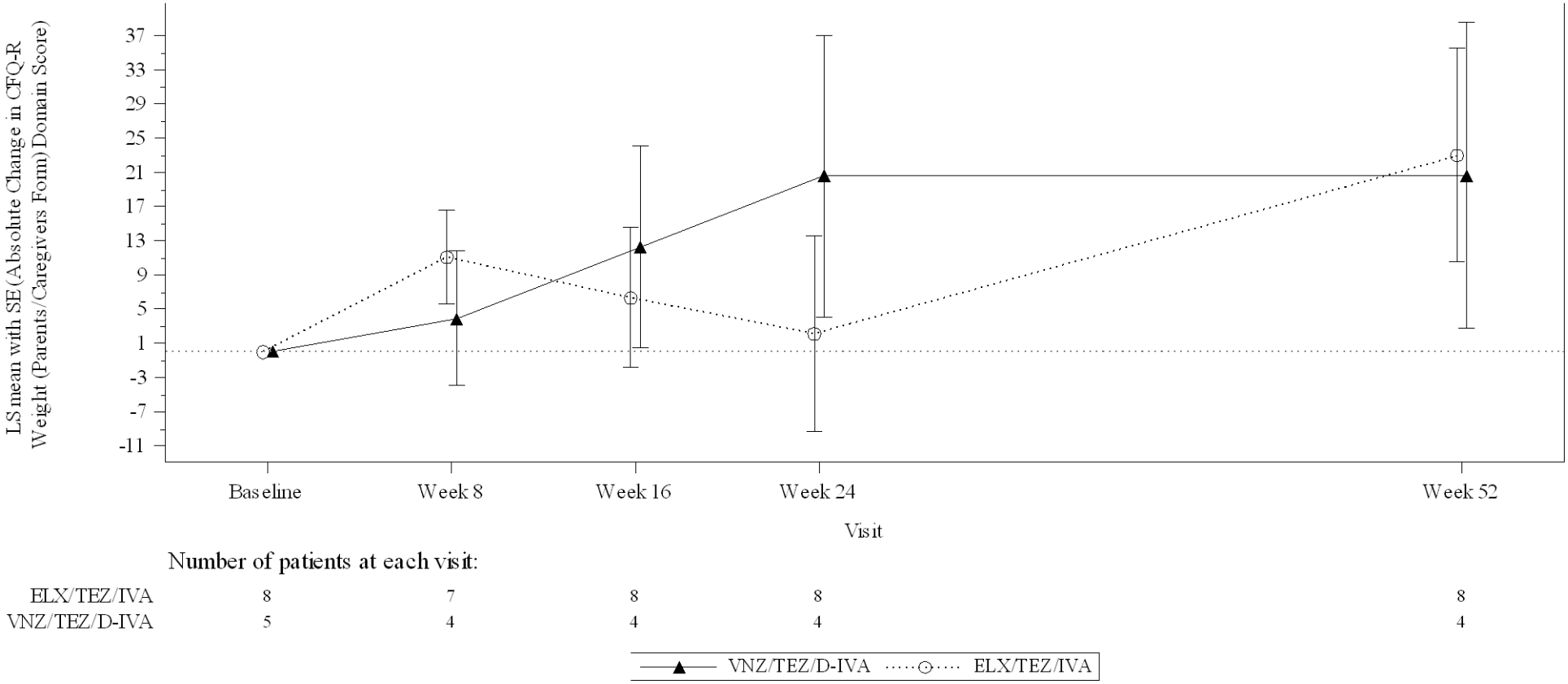
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Figure 1.2.1.9.6
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-102

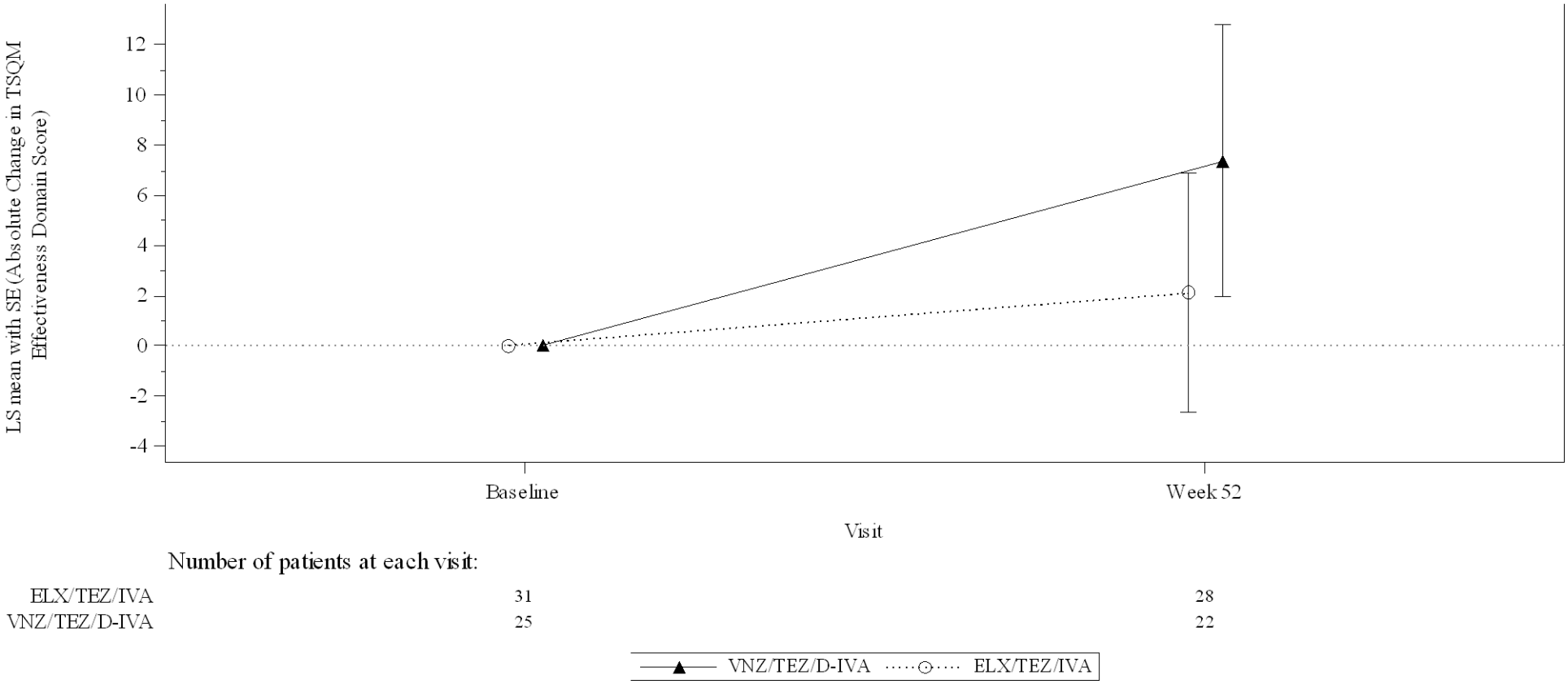


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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Figure 1.2.1.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness



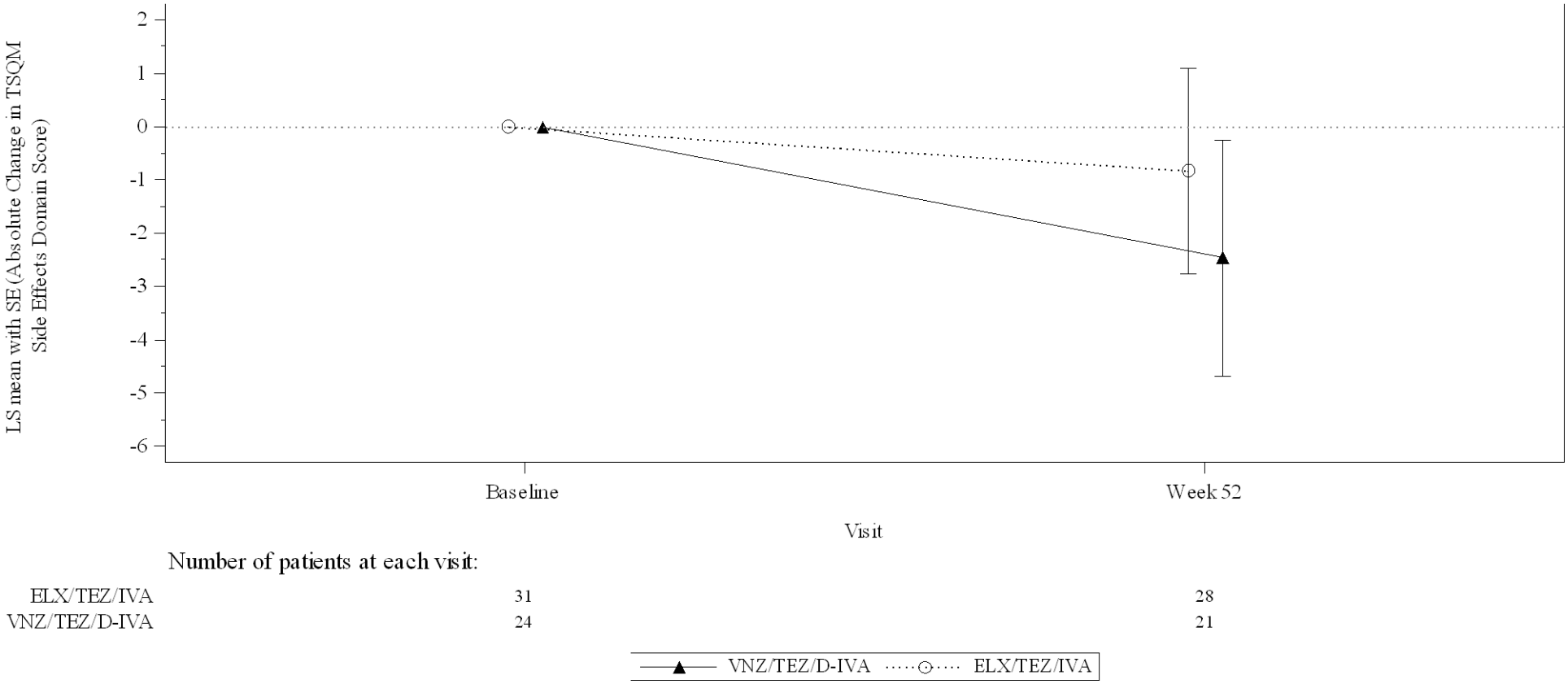
Number of patients at each visit:

	Baseline	Week 52
ELX/TEZ/IVA	31	28
VNZ/TEZ/D-IVA	25	22

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 1.2.1.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

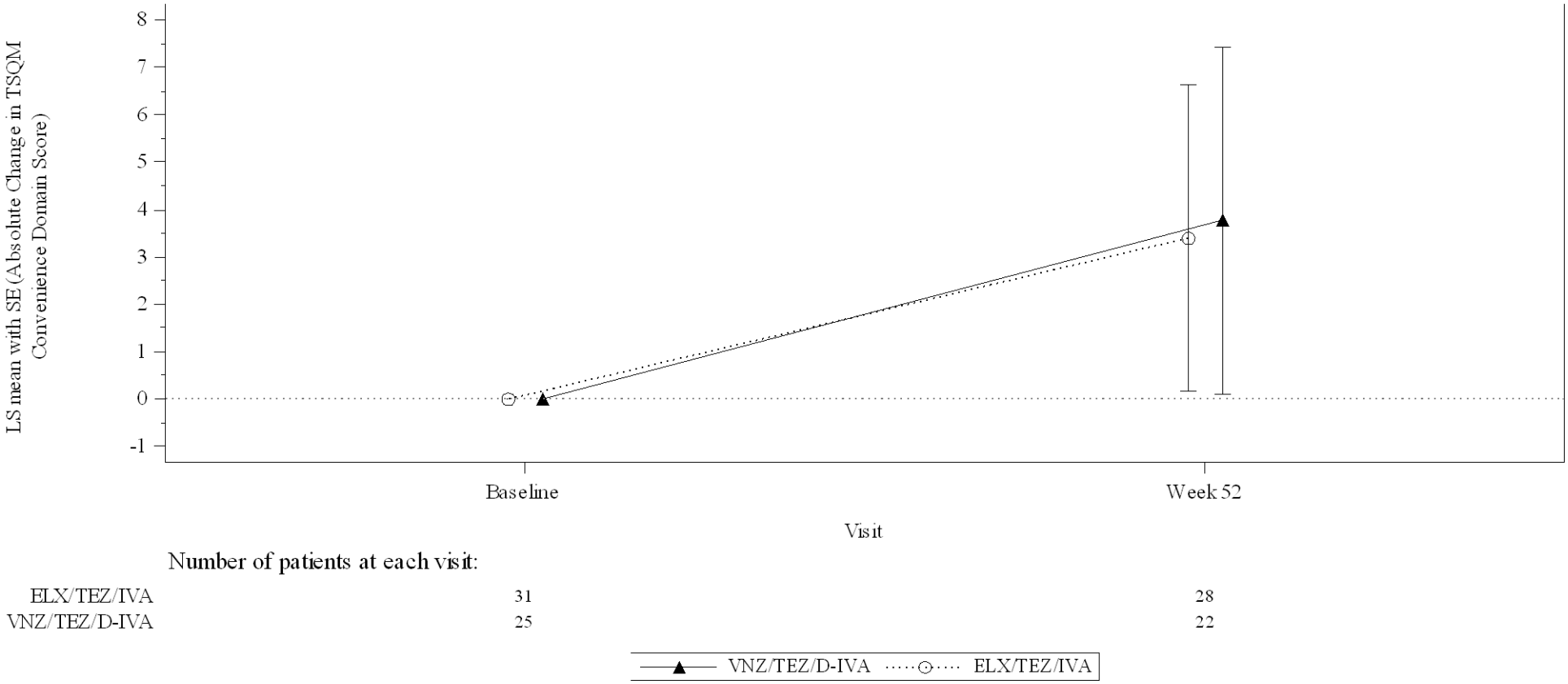
Domain: Side Effects



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 1.2.1.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

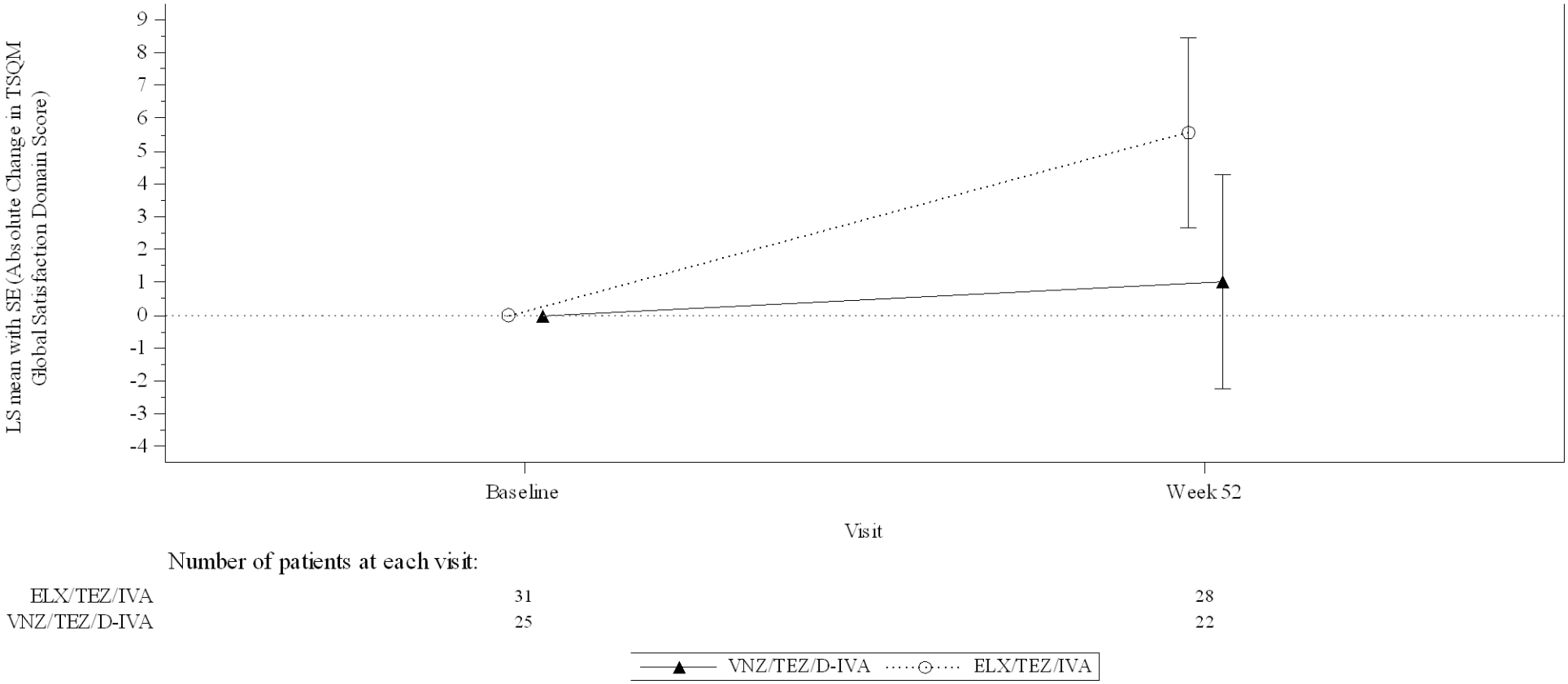
Domain: Convenience



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 1.2.1.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction



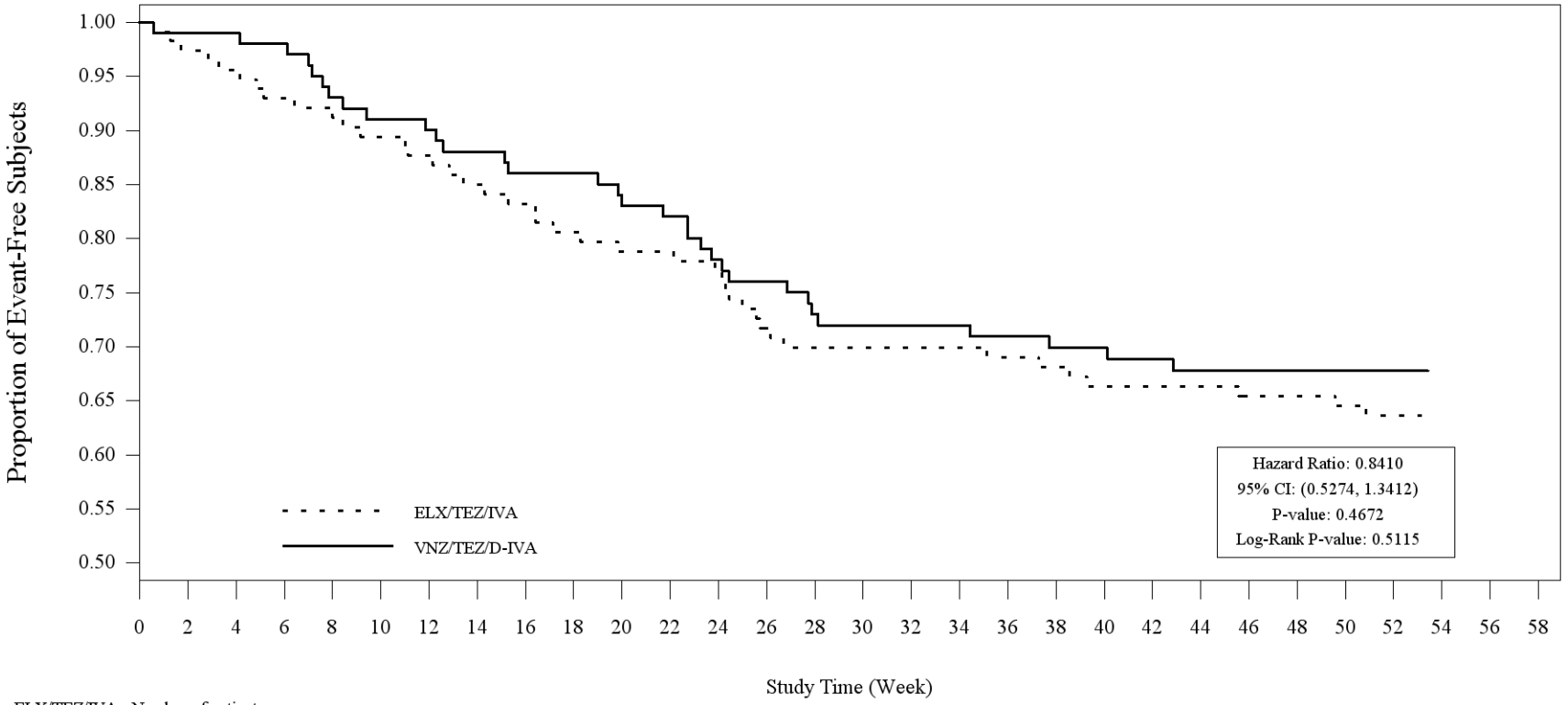
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: $ppFEV_1$ at Baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	114	99	87	77	73
with event(s)	0	14	26	35	39
censored	0	1	1	2	2
VNZ/TEZ/D-IVA - Number of patients					
at risk	101	90	78	68	64
with event(s)	0	10	22	29	32
censored	0	1	1	4	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

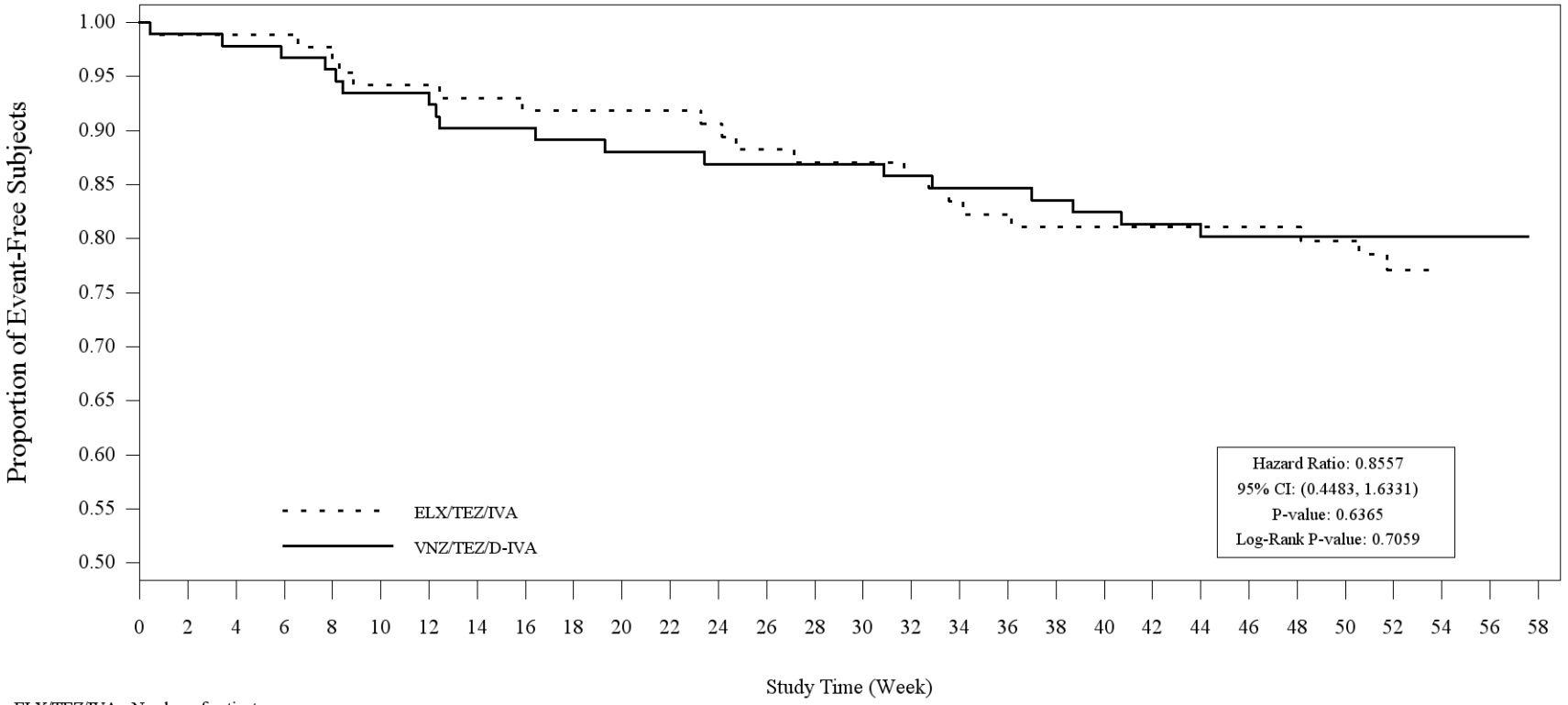
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Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: $ppFEV_1$ at Baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	87	79	76	68	65
with event(s)	0	5	8	15	16
censored	0	3	3	4	6
VNZ/TEZ/D-IVA - Number of patients					
at risk	92	86	78	76	72
with event(s)	0	7	12	14	18
censored	0	-1	2	2	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

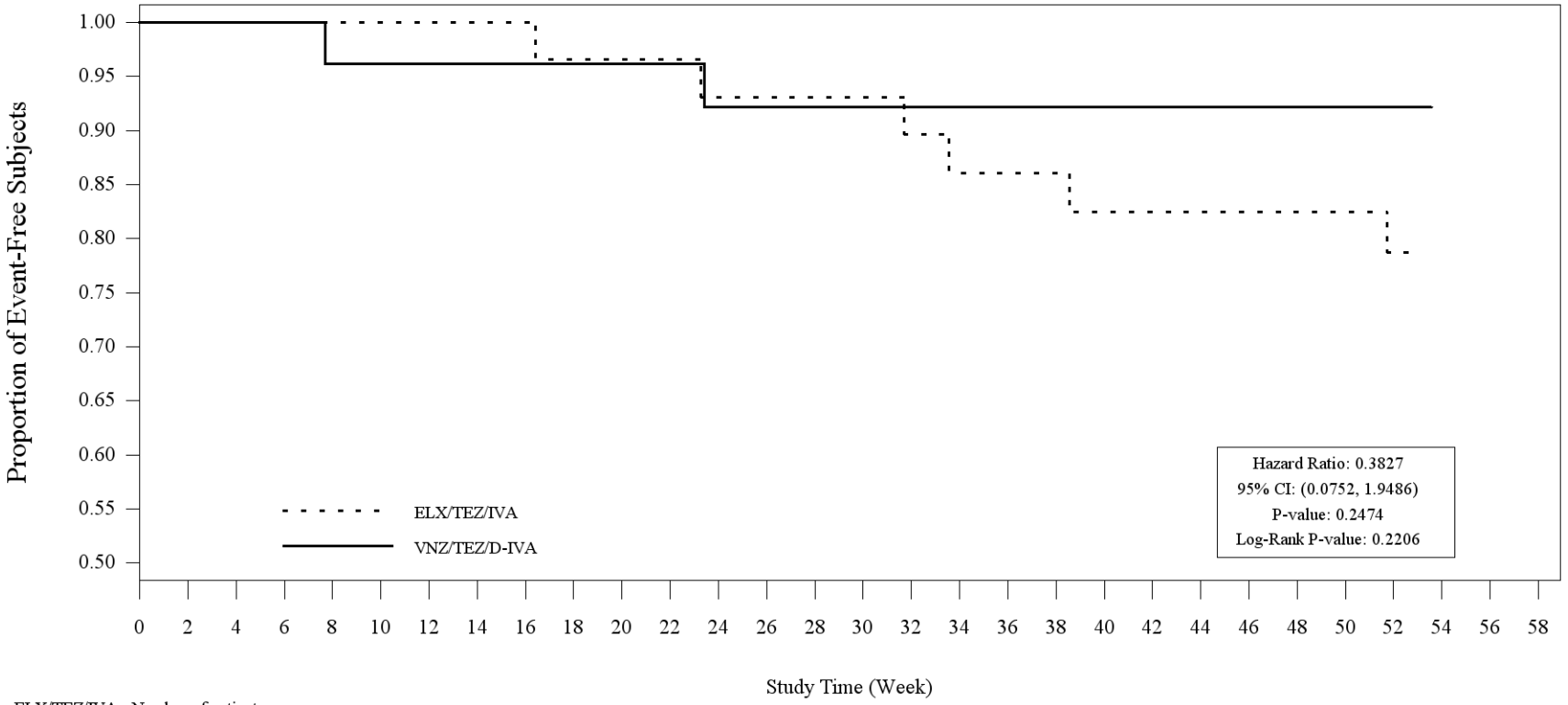
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Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening < 18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	31	29	27	24	22
with event(s)	0	0	2	4	5
censored	0	2	2	3	4
VNZ/TEZ/D-IVA - Number of patients					
at risk	26	25	23	23	23
with event(s)	0	1	2	2	2
censored	0	0	1	1	1

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

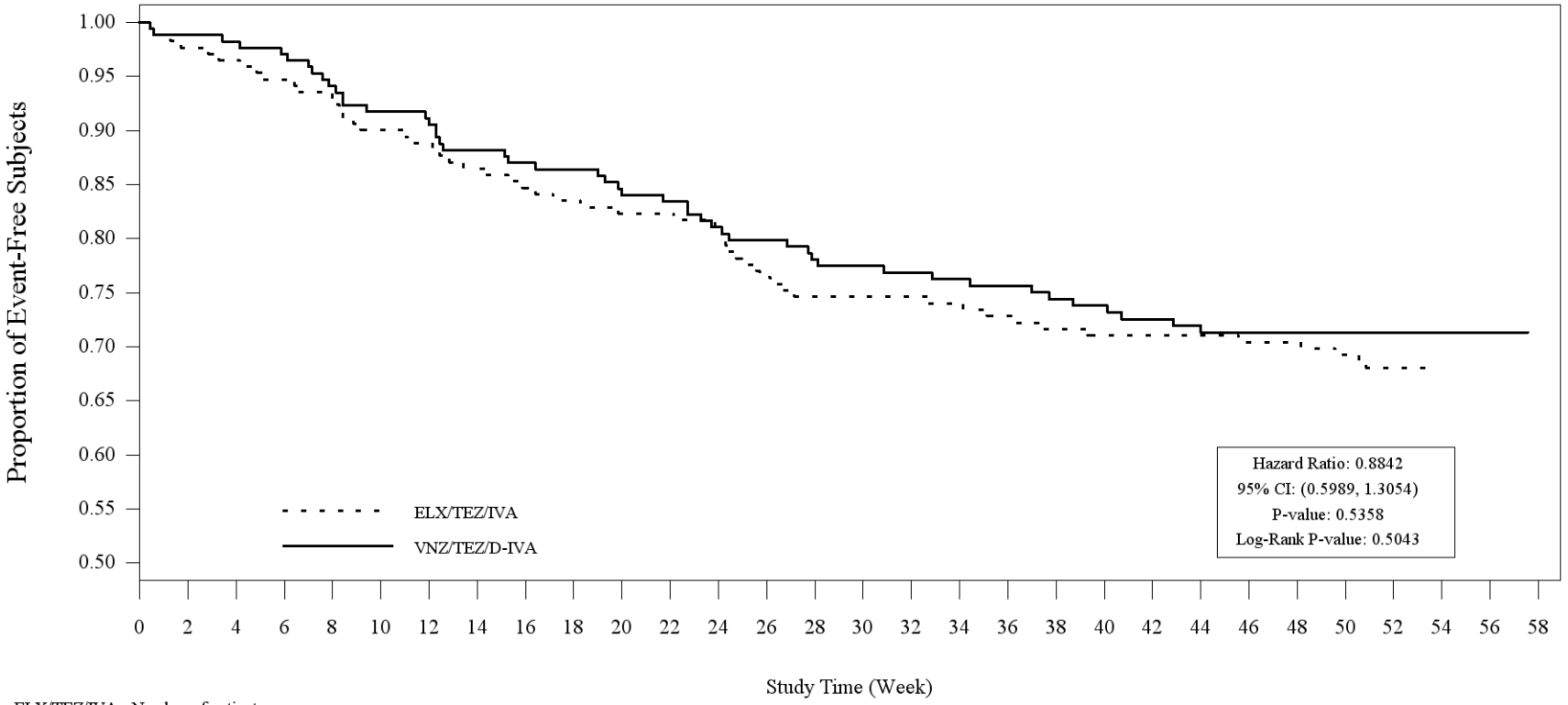
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Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening ≥ 18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	171	150	137	122	117
with event(s)	0	19	32	46	50
censored	0	2	2	3	4
VNZ/TEZ/D-IVA - Number of patients					
at risk	170	154	136	124	116
with event(s)	0	16	32	41	48
censored	0	0	2	5	6

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

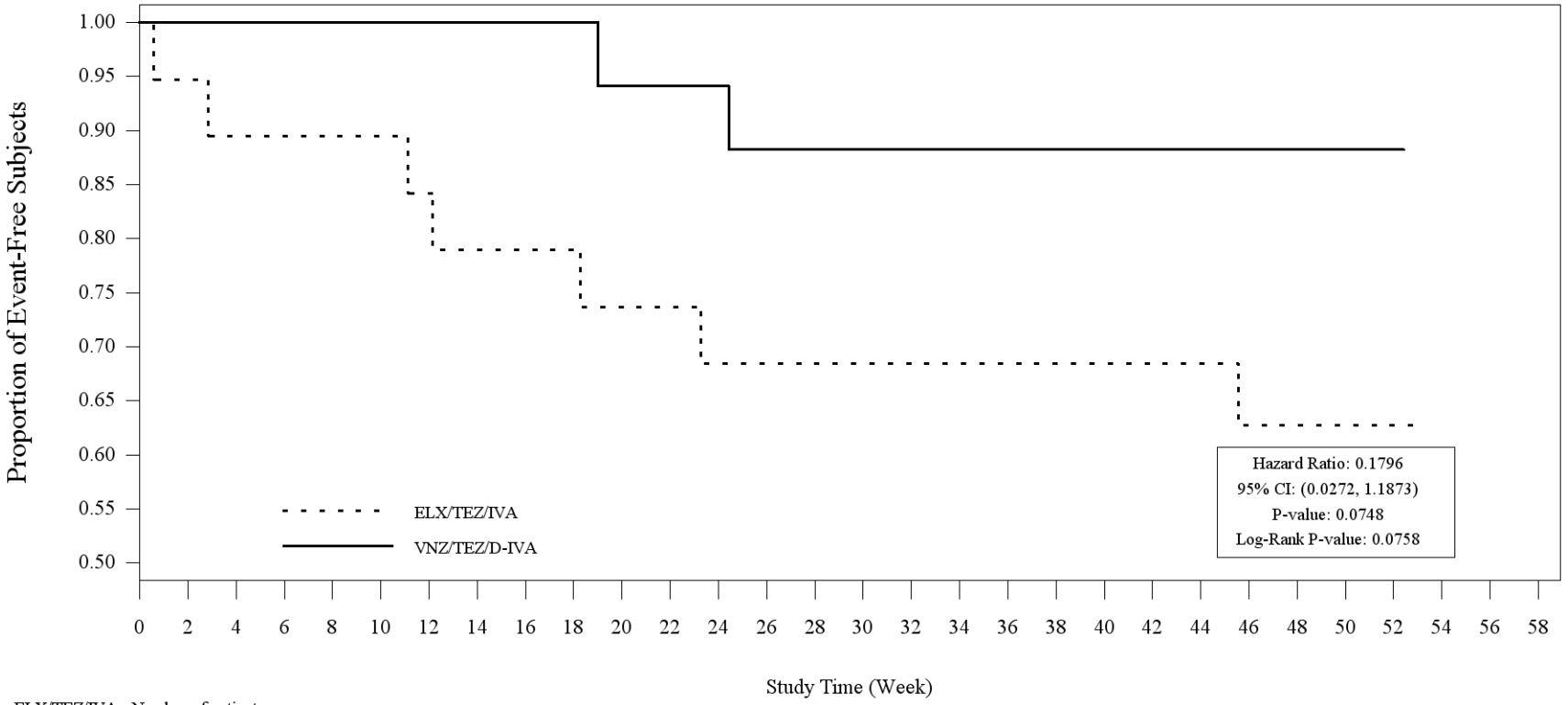
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Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	19	16	13	12	11
with event(s)	0	3	6	6	7
censored	0	0	0	1	1
VNZ/TEZ/D-IVA - Number of patients					
at risk	17	17	16	13	13
with event(s)	0	0	1	2	2
censored	0	0	0	2	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

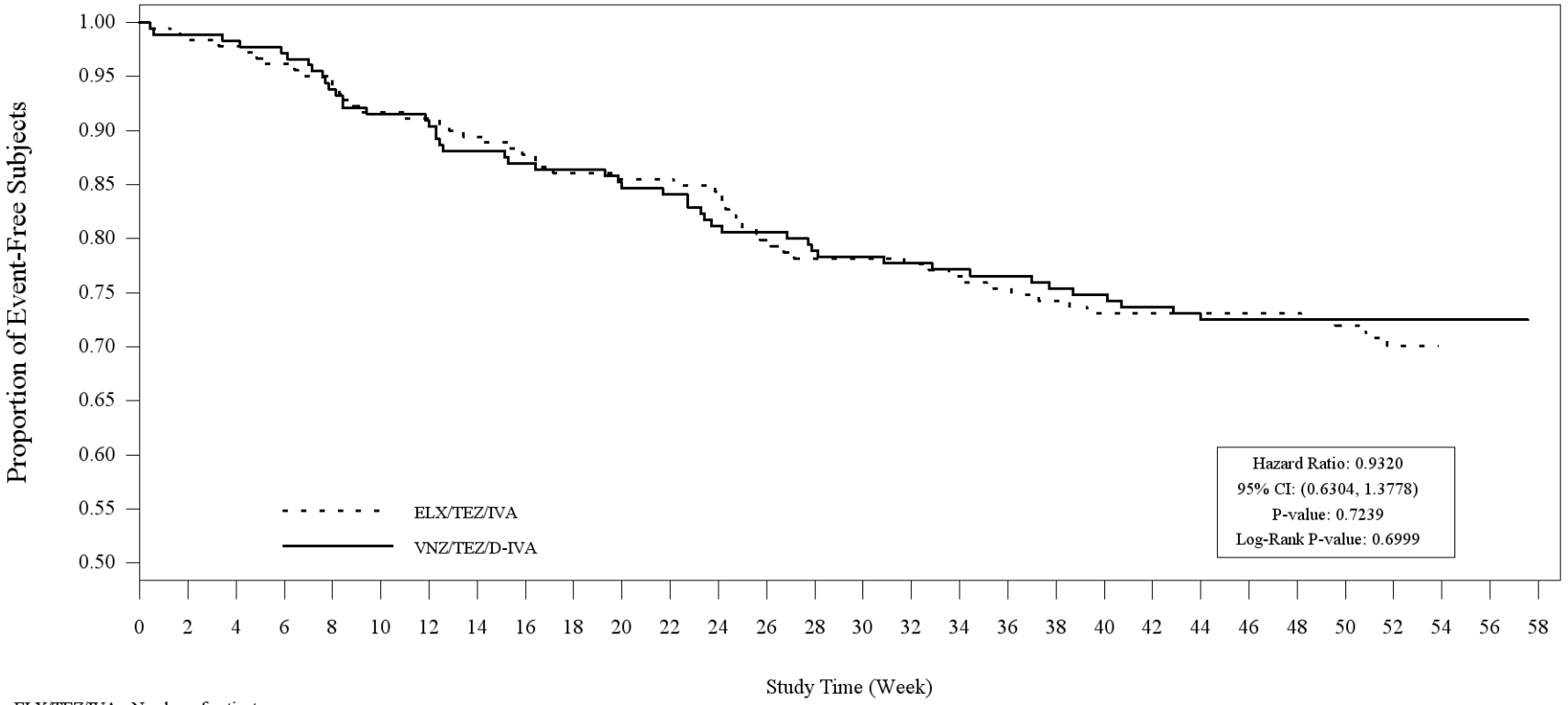
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Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	182	162	150	133	127
with event(s)	0	16	28	44	48
censored	0	4	4	5	7
VNZ/TEZ/D-IVA - Number of patients					
at risk	177	160	141	132	125
with event(s)	0	17	33	41	48
censored	0	0	3	4	4

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

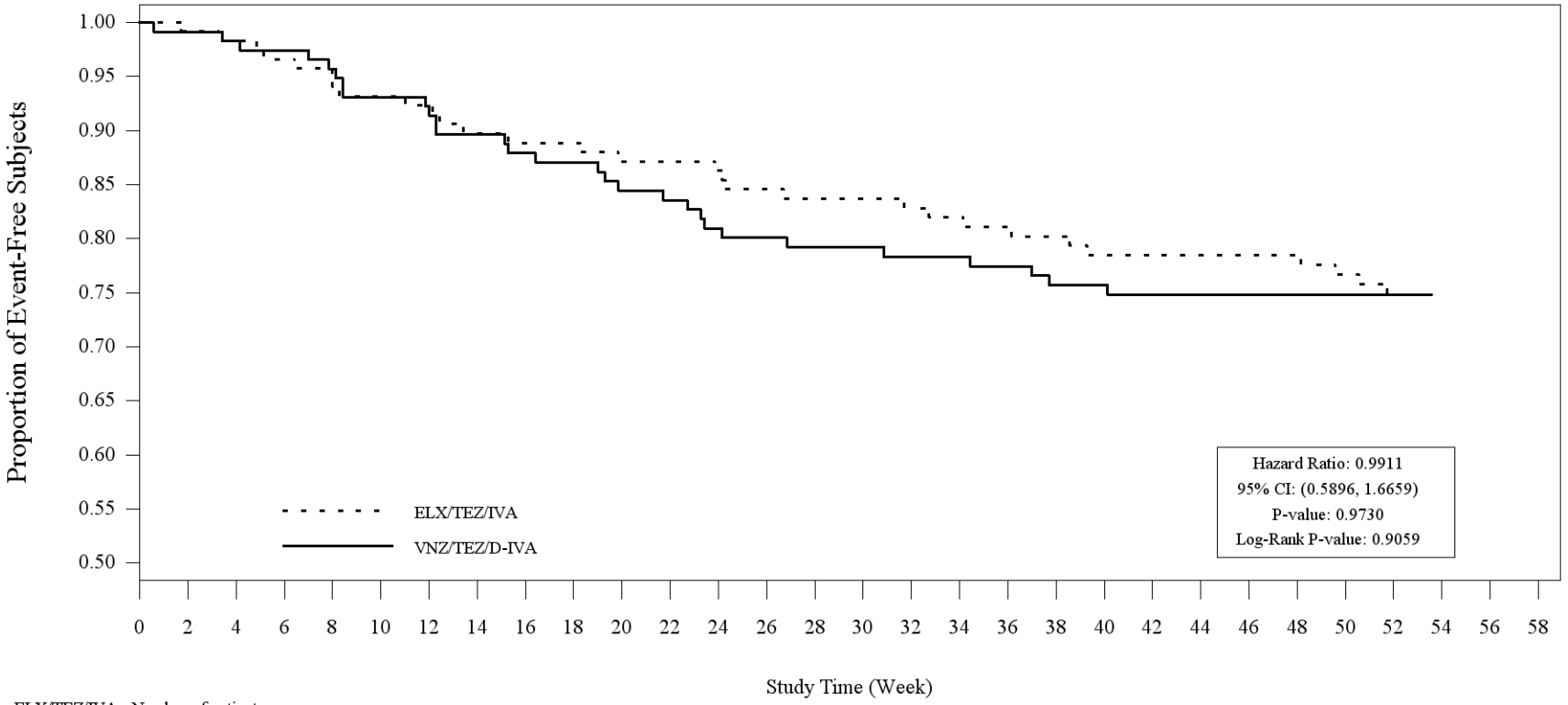
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Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	119	107	100	93	89
with event(s)	0	9	16	22	25
censored	0	3	3	4	5
VNZ/TEZ/D-IVA - Number of patients					
at risk	116	107	93	88	85
with event(s)	0	10	22	26	29
censored	0	-1	1	2	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

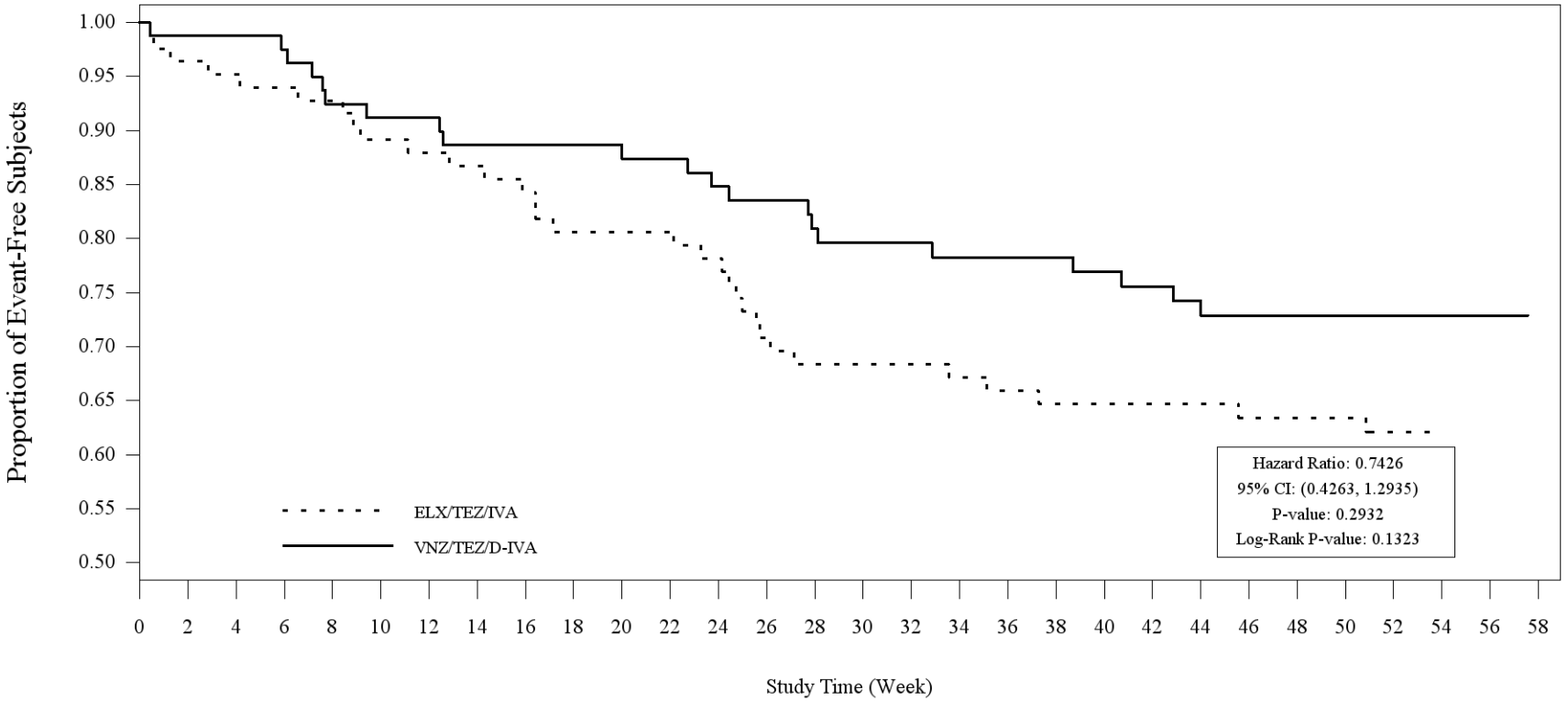
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Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	83	72	64	53	50
with event(s)	0	10	18	28	30
censored	0	1	1	2	3
VNZ/TEZ/D-IVA - Number of patients					
at risk	80	72	66	59	54
with event(s)	0	7	12	17	21
censored	0	1	2	4	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

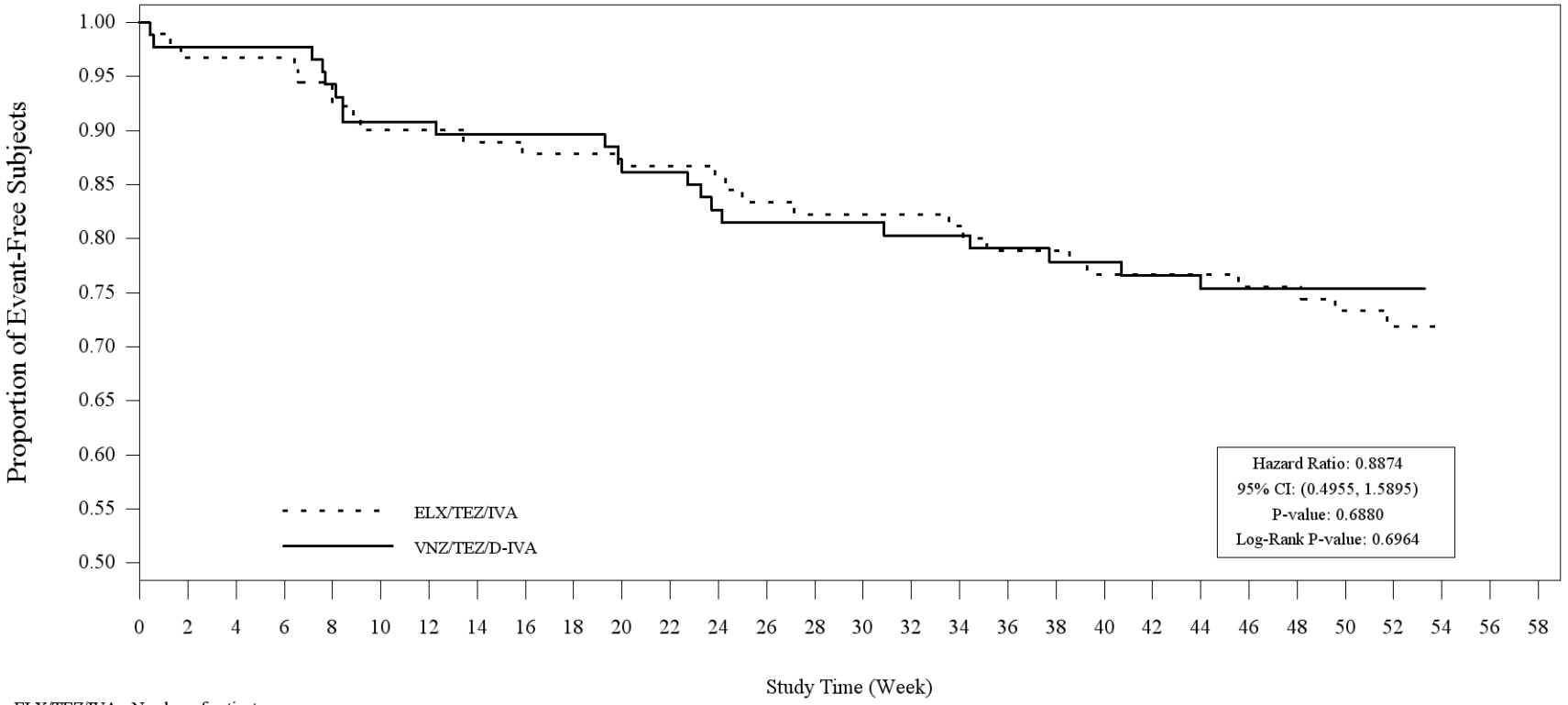
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Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	91	81	77	71	67
with event(s)	0	9	13	19	22
censored	0	1	1	1	2
VNZ/TEZ/D-IVA - Number of patients					
at risk	87	79	71	65	61
with event(s)	0	8	15	18	21
censored	0	0	1	4	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

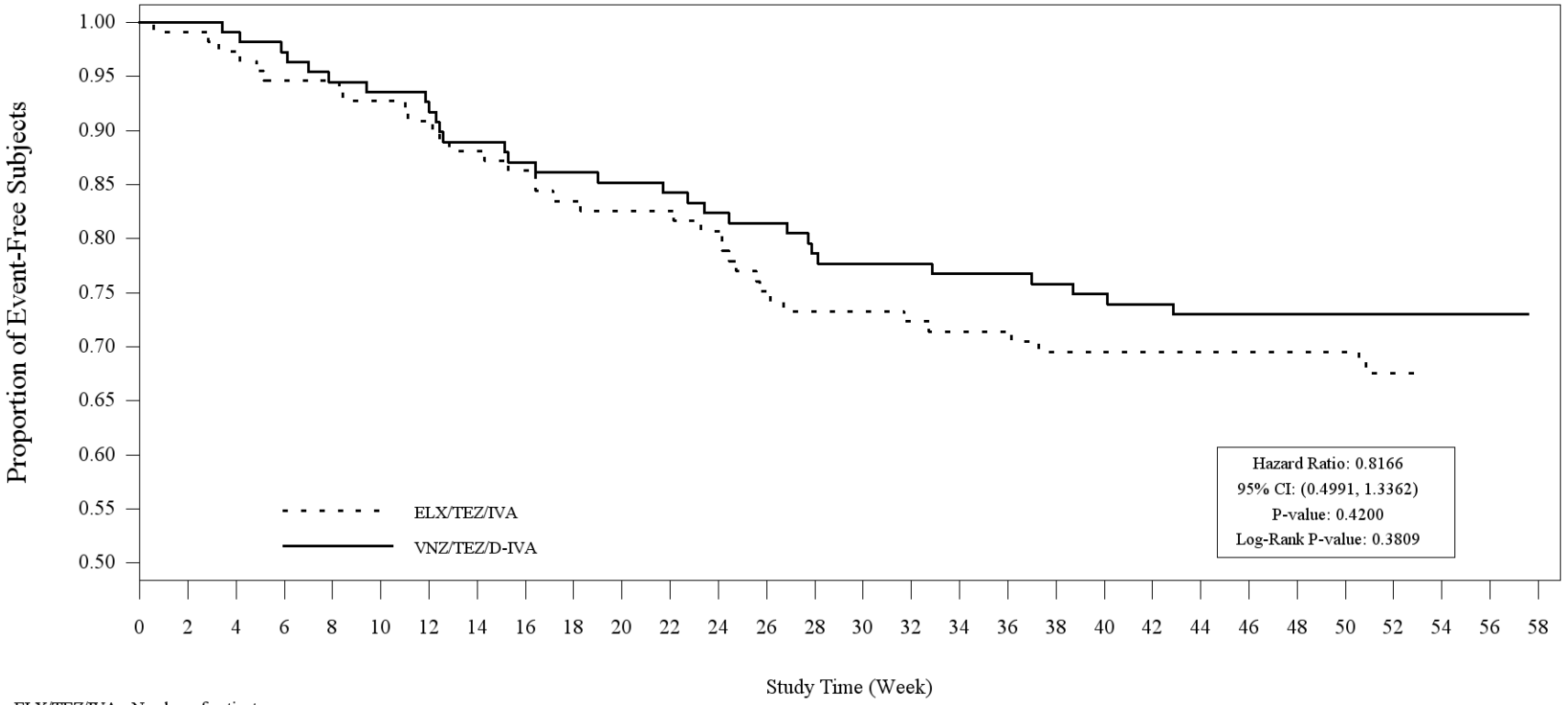
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Figure 1.2.2.6.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = Rest of the World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	111	98	87	75	72
with event(s)	0	10	21	31	33
censored	0	3	3	5	6
VNZ/TEZ/D-IVA - Number of patients					
at risk	109	100	88	82	78
with event(s)	0	9	19	25	29
censored	0	0	2	2	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

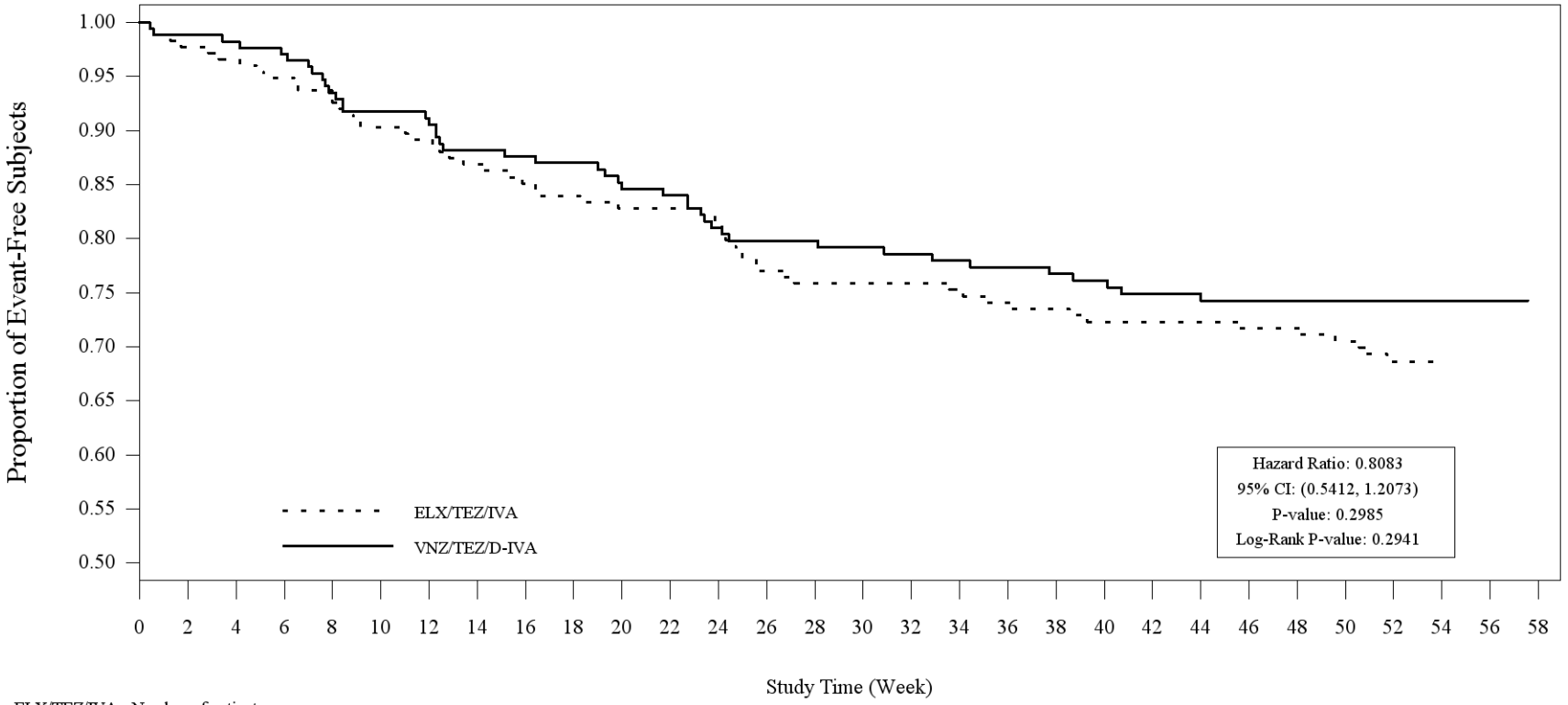
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Figure 1.2.2.6.2.1
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Subgroup: Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	177	154	141	126	120
with event(s)	0	19	32	45	49
censored	0	4	4	6	8
VNZ/TEZ/D-IVA - Number of patients					
at risk	170	154	135	126	120
with event(s)	0	16	32	38	43
censored	0	0	3	6	7

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.

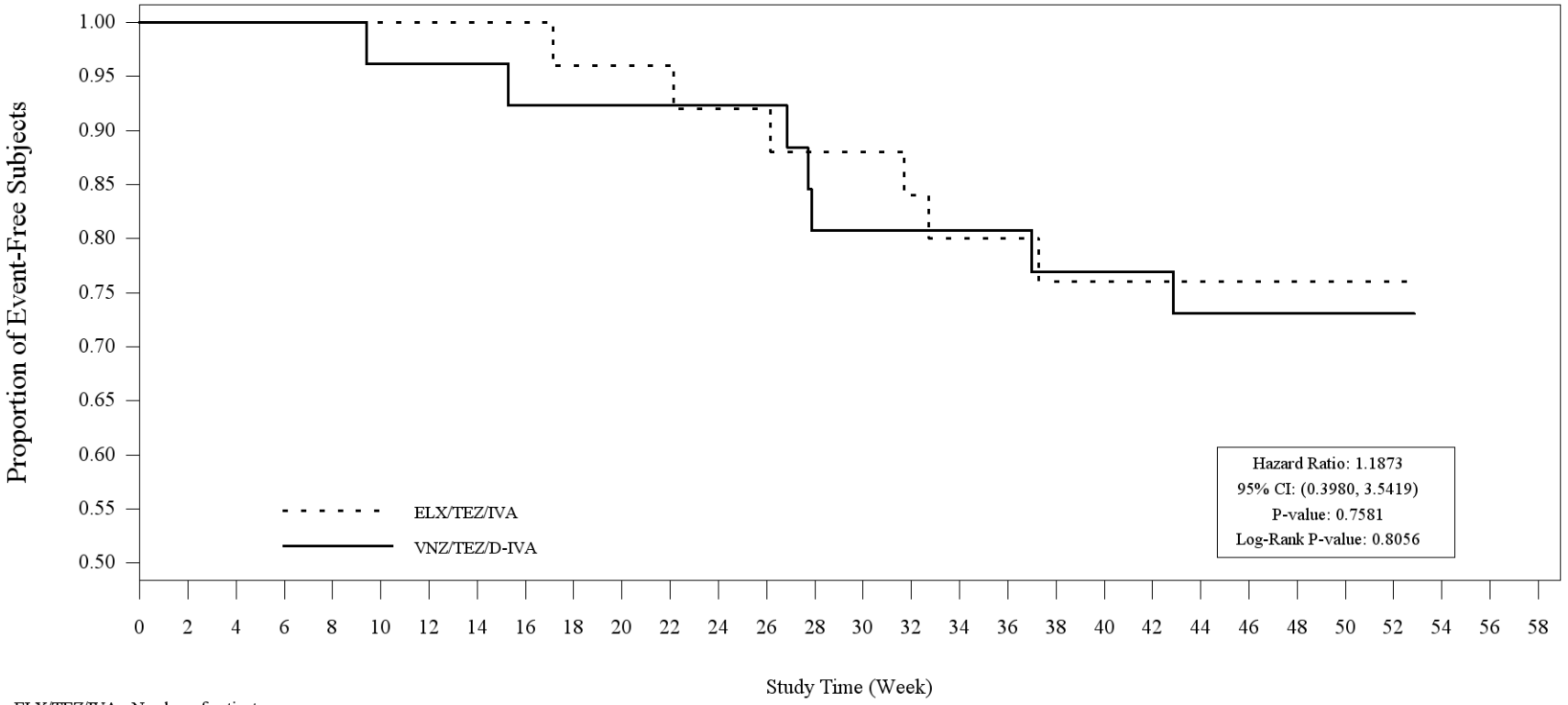
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Figure 1.2.2.6.2.1
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Subgroup: Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	25	25	23	20	19
with event(s)	0	0	2	5	6
censored	0	0	0	0	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	26	25	24	21	19
with event(s)	0	1	2	5	7
censored	0	0	0	0	0

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.

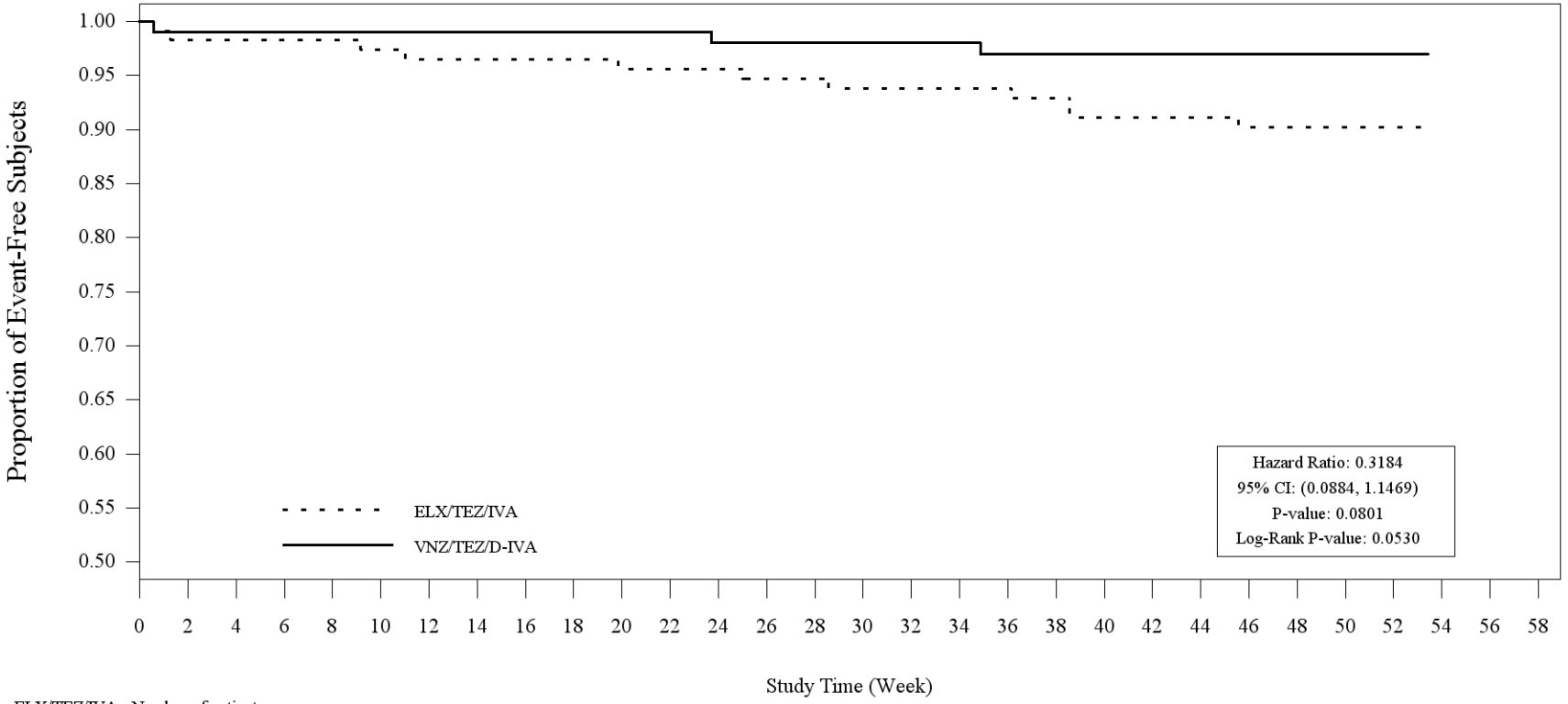
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Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: $ppFEV_1$ at Baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	114	109	108	105	100
with event(s)	0	4	5	7	11
censored	0	1	1	2	3
VNZ/TEZ/D-IVA - Number of patients					
at risk	101	99	98	93	92
with event(s)	0	1	2	3	3
censored	0	1	1	5	6

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

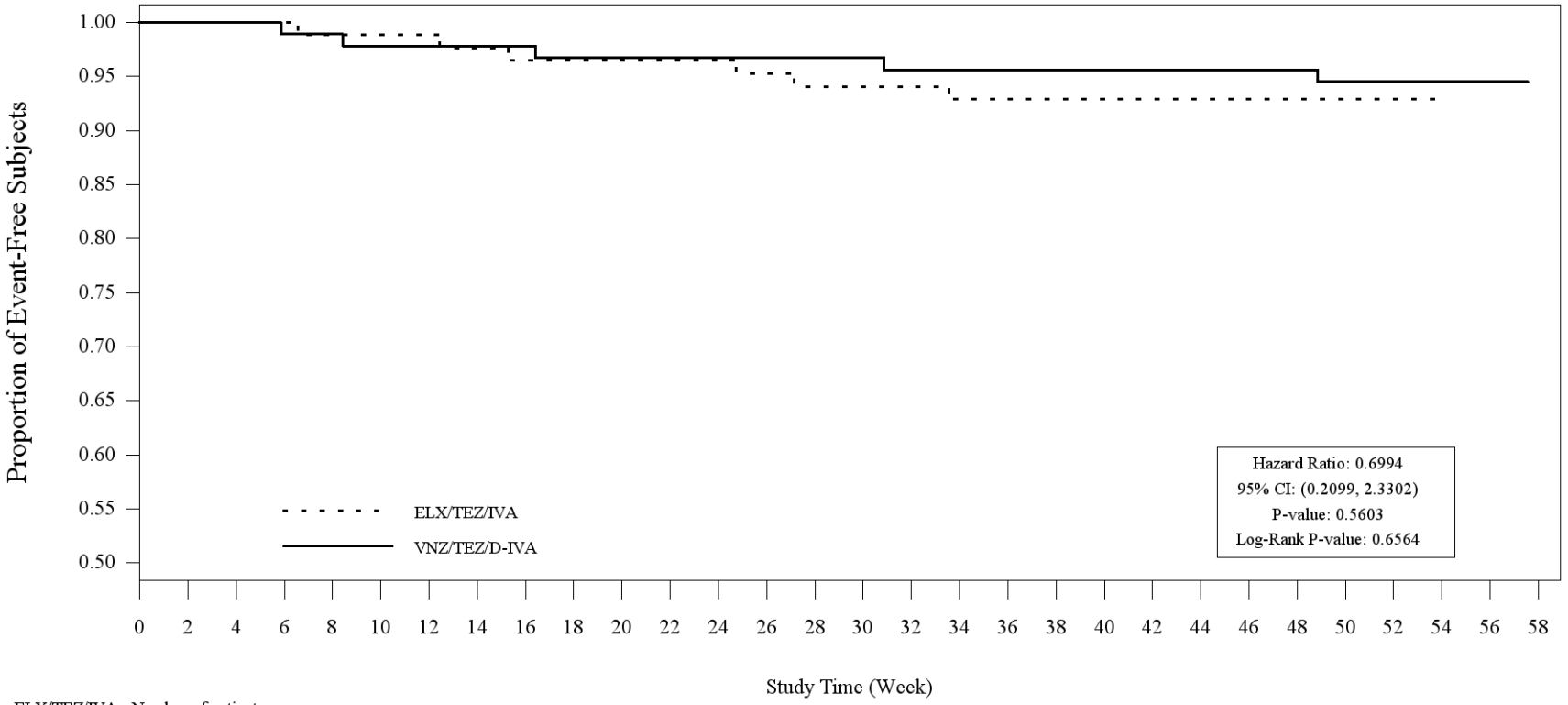
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Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: $ppFEV_1$ at Baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	87	83	81	76	74
with event(s)	0	1	3	6	6
censored	0	3	3	5	7
VNZ/TEZ/D-IVA - Number of patients					
at risk	92	90	87	86	86
with event(s)	0	2	3	4	4
censored	0	0	2	2	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

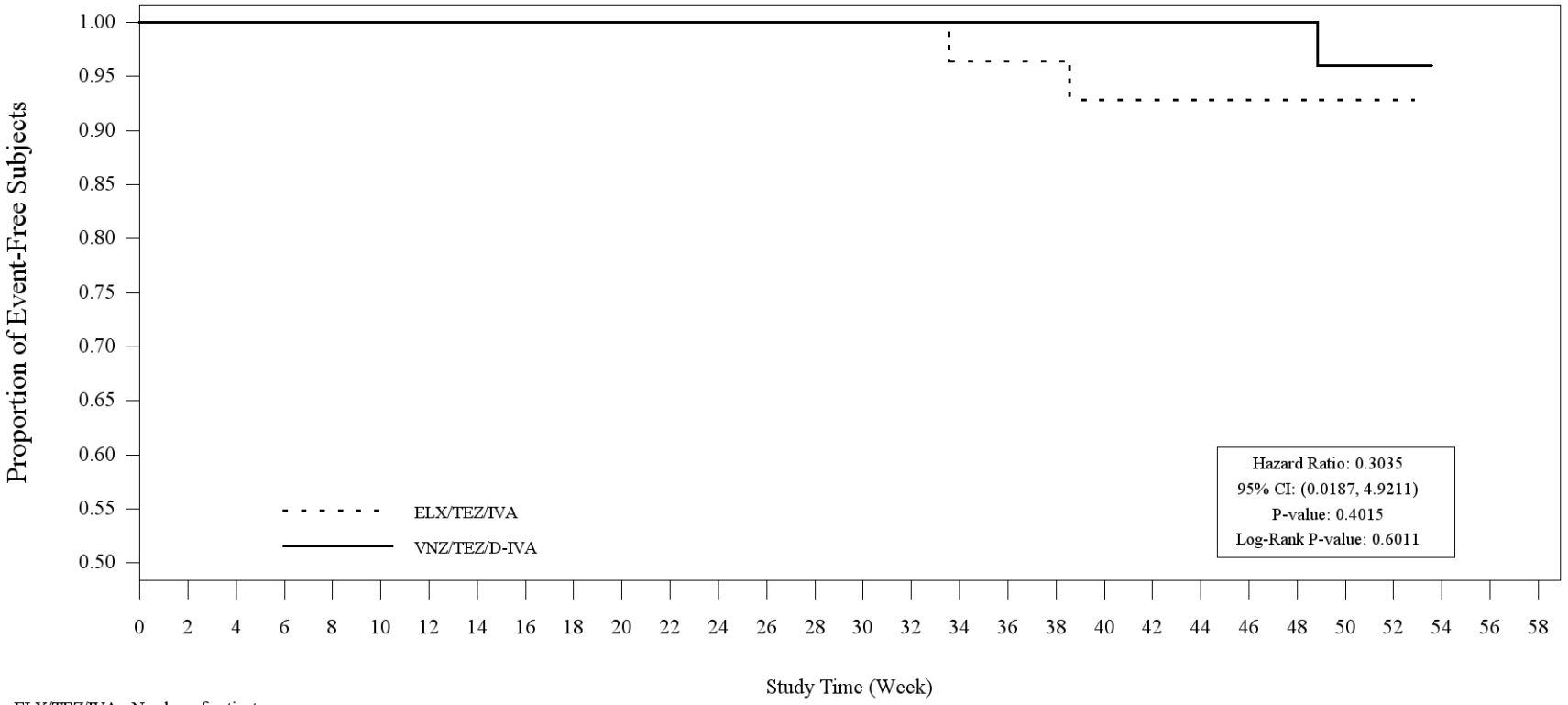
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Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening < 18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	31	29	29	27	25
with event(s)	0	0	0	1	2
censored	0	2	2	3	4
VNZ/TEZ/D-IVA - Number of patients					
at risk	26	26	25	25	25
with event(s)	0	0	0	0	0
censored	0	0	1	1	1

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

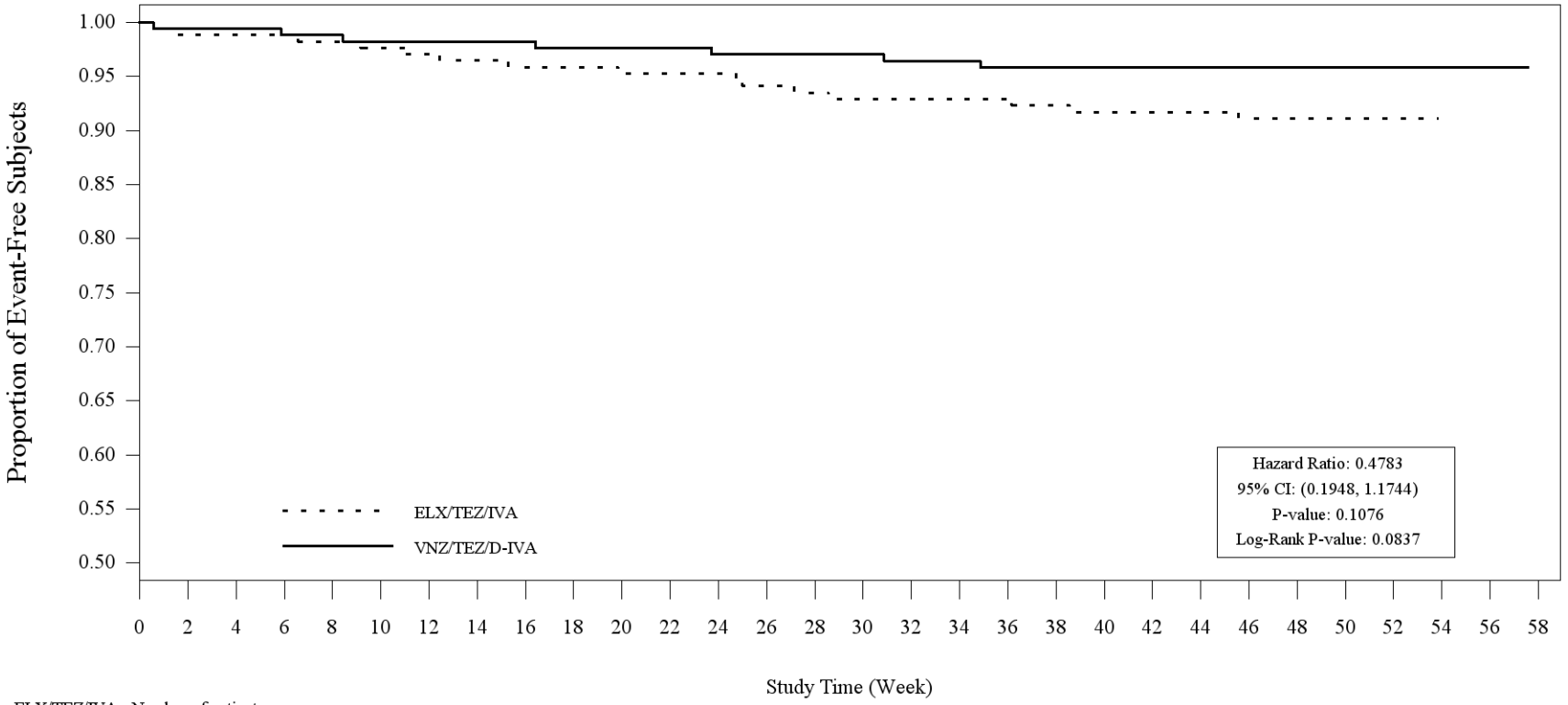
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Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening ≥ 18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	171	164	161	155	150
with event(s)	0	5	8	12	15
censored	0	2	2	4	6
VNZ/TEZ/D-IVA - Number of patients					
at risk	170	166	163	157	156
with event(s)	0	3	5	7	7
censored	0	1	2	6	7

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

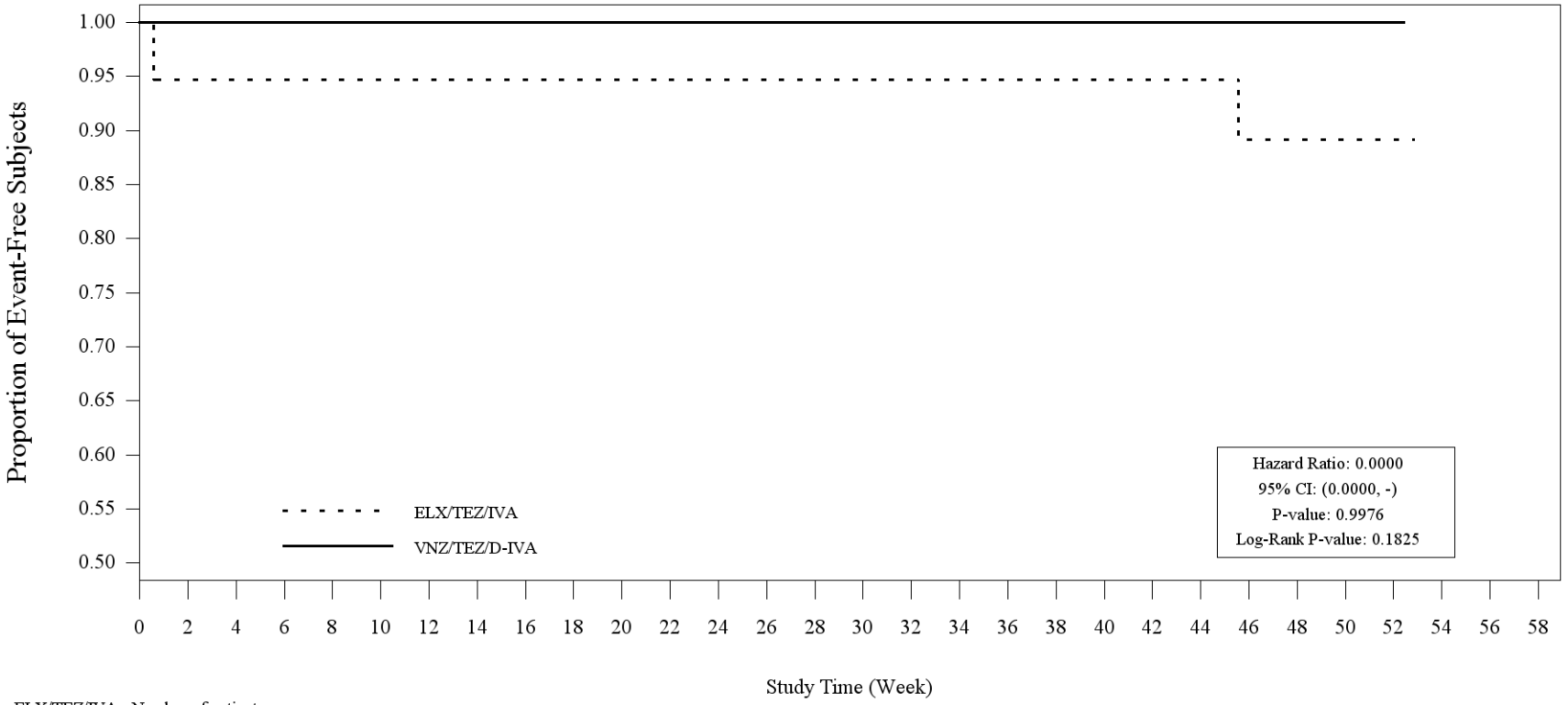
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Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	19	18	18	17	16
with event(s)	0	1	1	1	2
censored	0	0	0	1	1
VNZ/TEZ/D-IVA - Number of patients					
at risk	17	17	17	15	15
with event(s)	0	0	0	0	0
censored	0	0	0	2	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

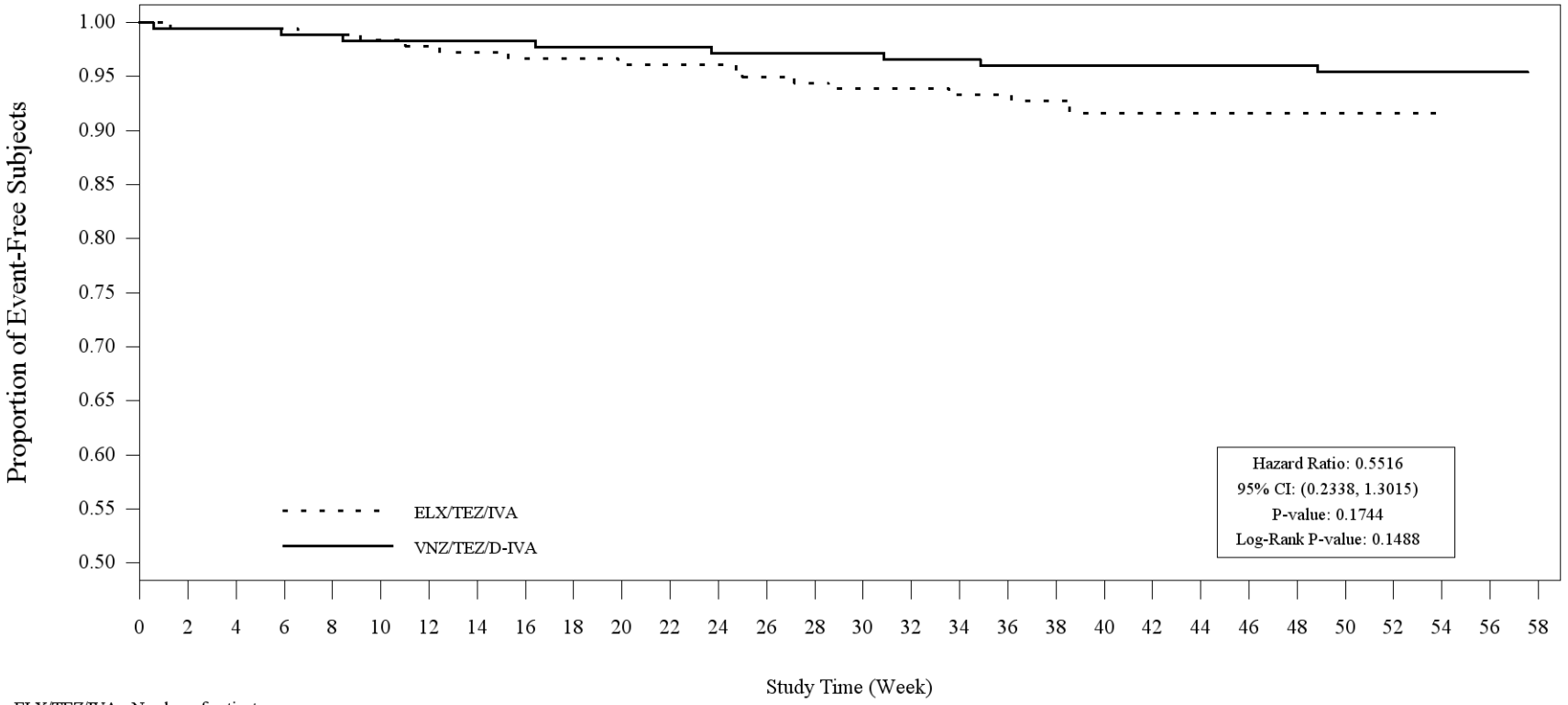
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Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	182	174	171	164	158
with event(s)	0	4	7	12	15
censored	0	4	4	6	9
VNZ/TEZ/D-IVA - Number of patients					
at risk	177	173	169	165	165
with event(s)	0	3	5	7	7
censored	0	1	3	5	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

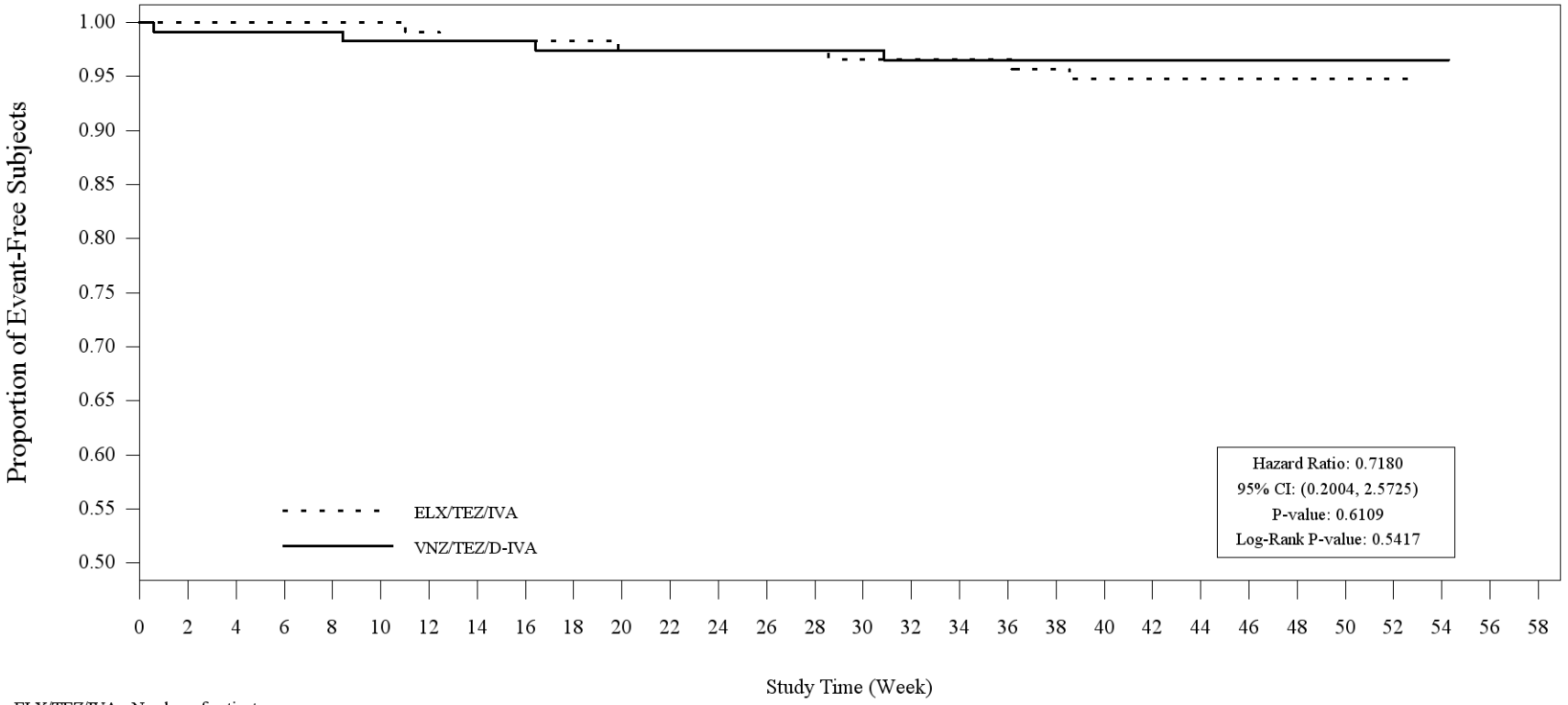
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Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	119	115	113	110	107
with event(s)	0	1	3	4	6
censored	0	3	3	5	6
VNZ/TEZ/D-IVA - Number of patients					
at risk	116	114	112	109	109
with event(s)	0	2	3	4	4
censored	0	0	1	3	3

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

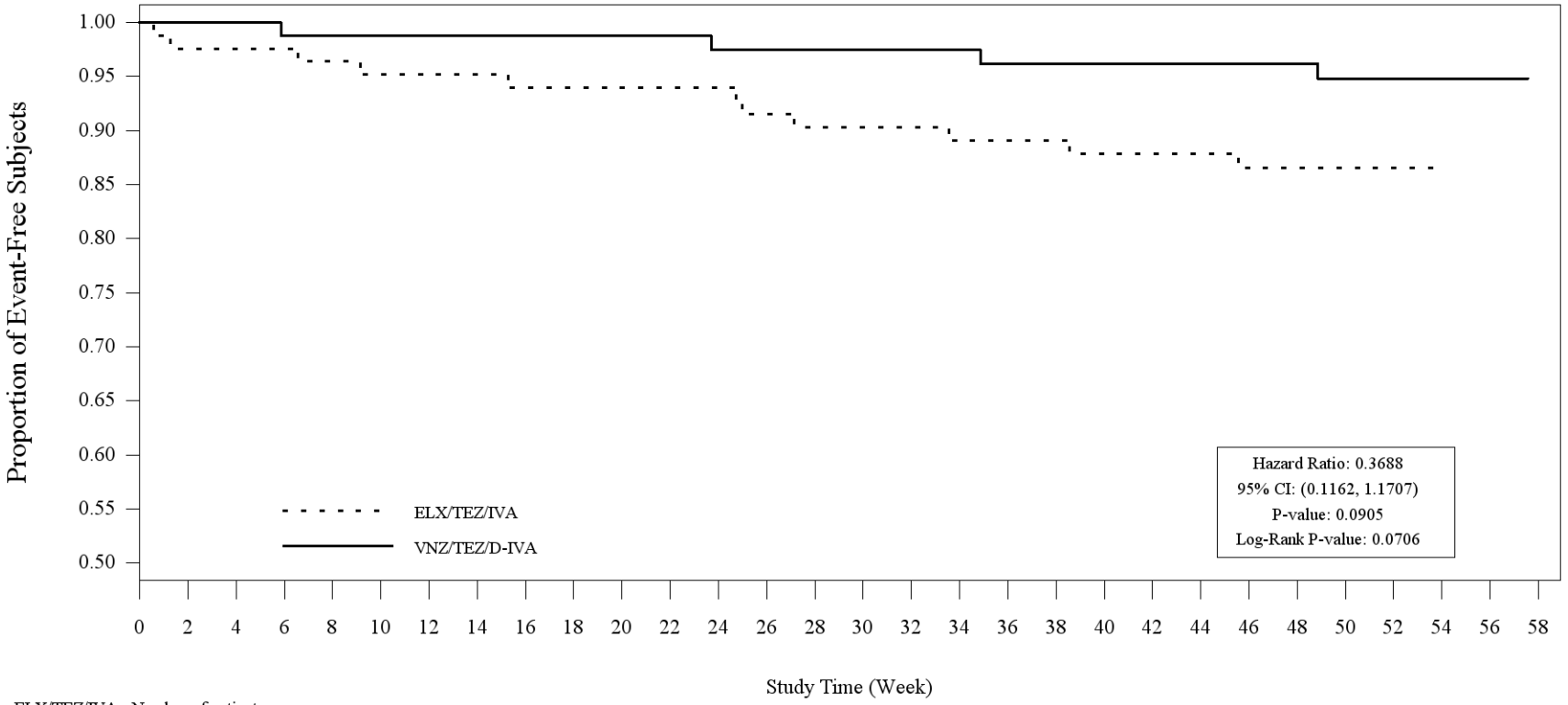
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Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	83	78	77	72	68
with event(s)	0	4	5	9	11
censored	0	1	1	2	4
VNZ/TEZ/D-IVA - Number of patients					
at risk	80	78	76	73	72
with event(s)	0	1	2	3	3
censored	0	1	2	4	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

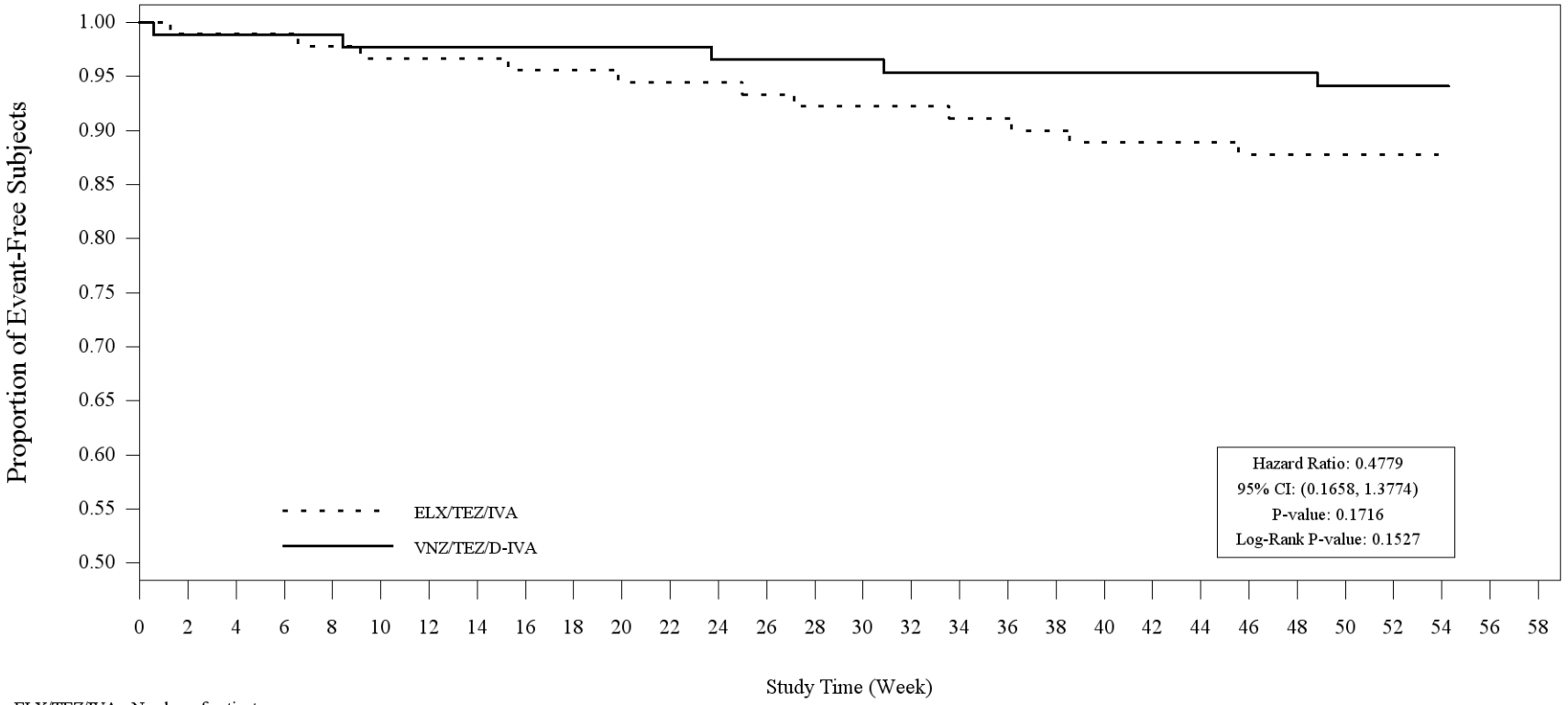
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Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	91	87	85	82	78
with event(s)	0	3	5	8	11
censored	0	1	1	1	2
VNZ/TEZ/D-IVA - Number of patients					
at risk	87	85	83	78	77
with event(s)	0	2	3	4	4
censored	0	0	1	5	6

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

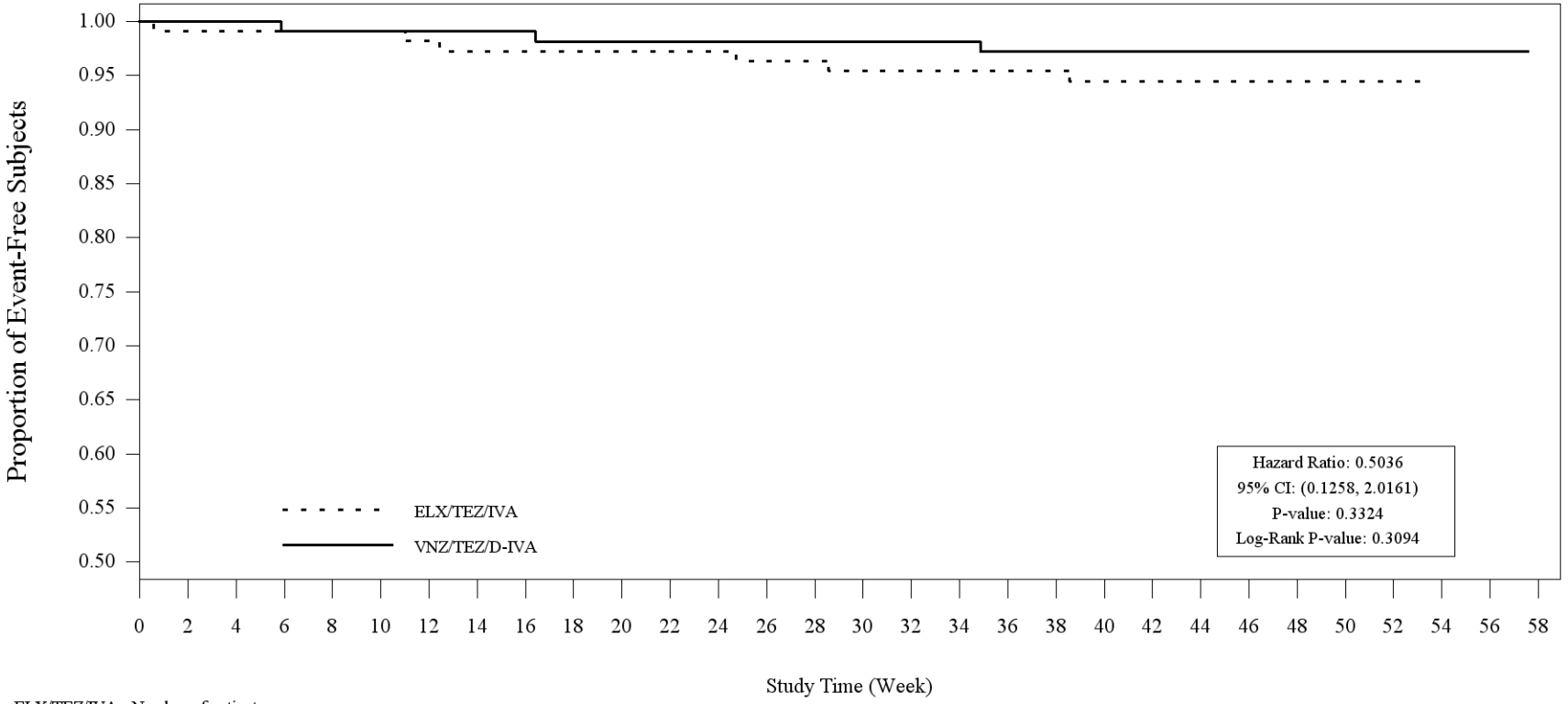
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Figure 1.2.2.7.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = Rest of the World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	111	106	105	100	97
with event(s)	0	2	3	5	6
censored	0	3	3	6	8
VNZ/TEZ/D-IVA - Number of patients					
at risk	109	107	105	104	104
with event(s)	0	1	2	3	3
censored	0	1	2	2	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

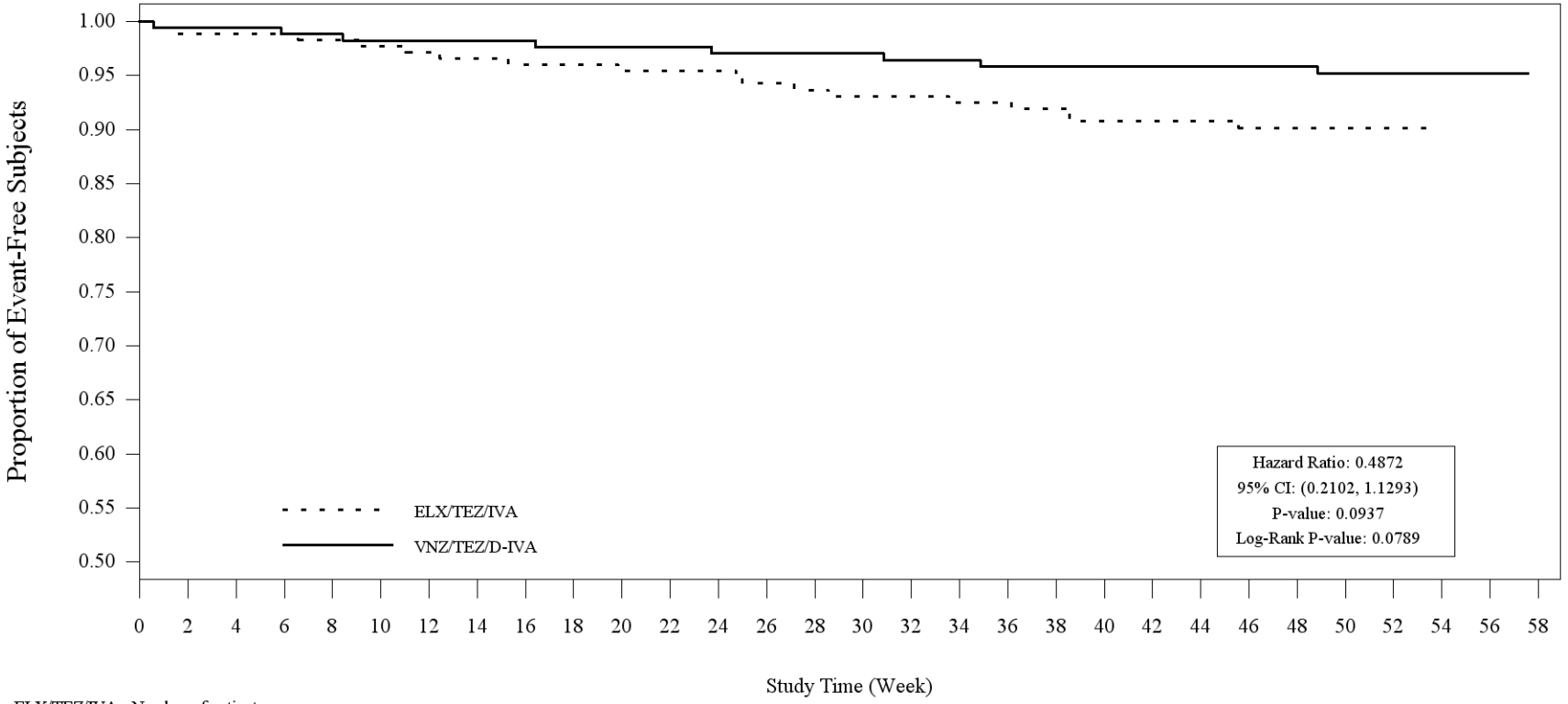
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Figure 1.2.2.7.2.1
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Subgroup: Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	177	168	165	158	152
with event(s)	0	5	8	13	17
censored	0	4	4	6	8
VNZ/TEZ/D-IVA - Number of patients					
at risk	170	166	162	156	155
with event(s)	0	3	5	7	7
censored	0	1	3	7	8

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.

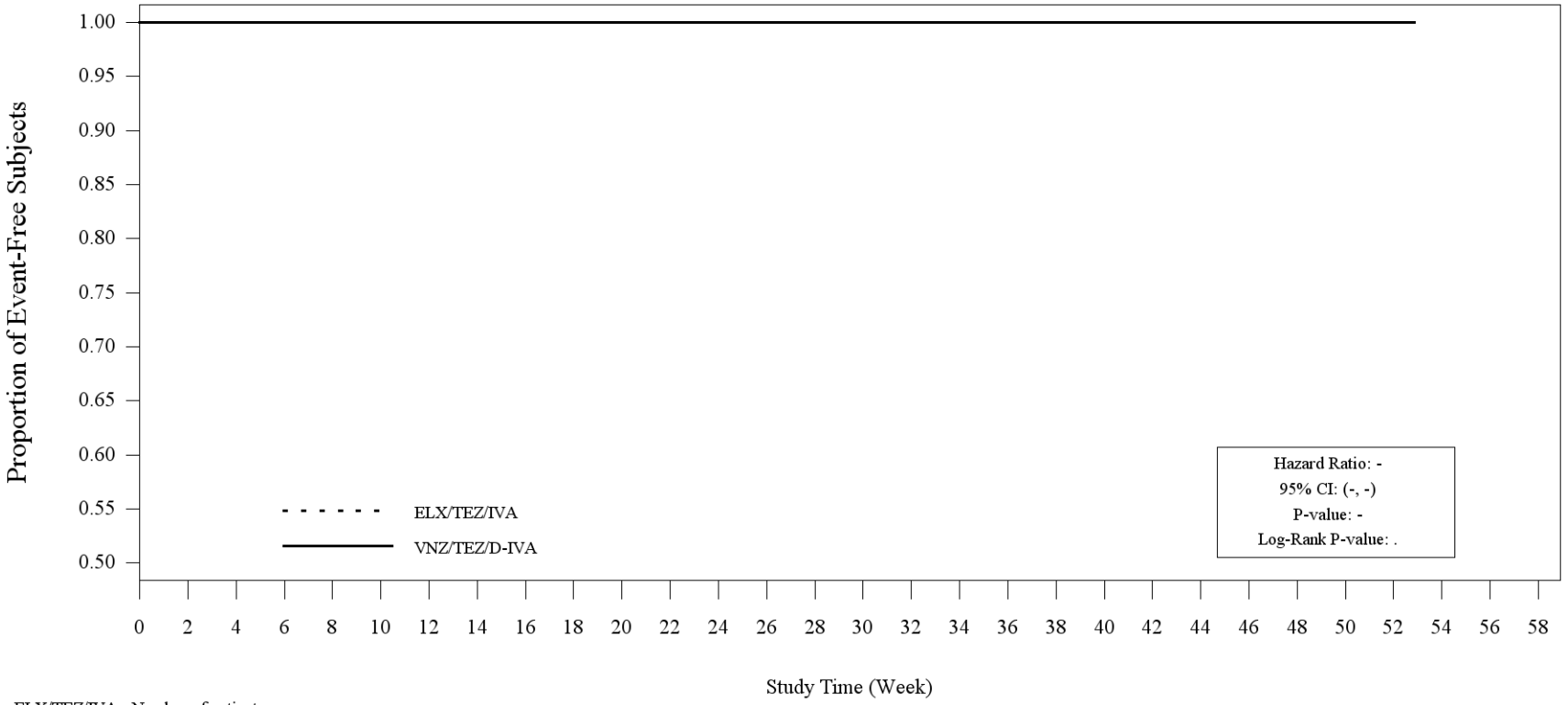
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Figure 1.2.2.7.2.1
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Subgroup: Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	25	25	25	24	23
with event(s)	0	0	0	0	0
censored	0	0	0	1	2
VNZ/TEZ/D-IVA - Number of patients					
at risk	26	26	26	26	26
with event(s)	0	0	0	0	0
censored	0	0	0	0	0

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.

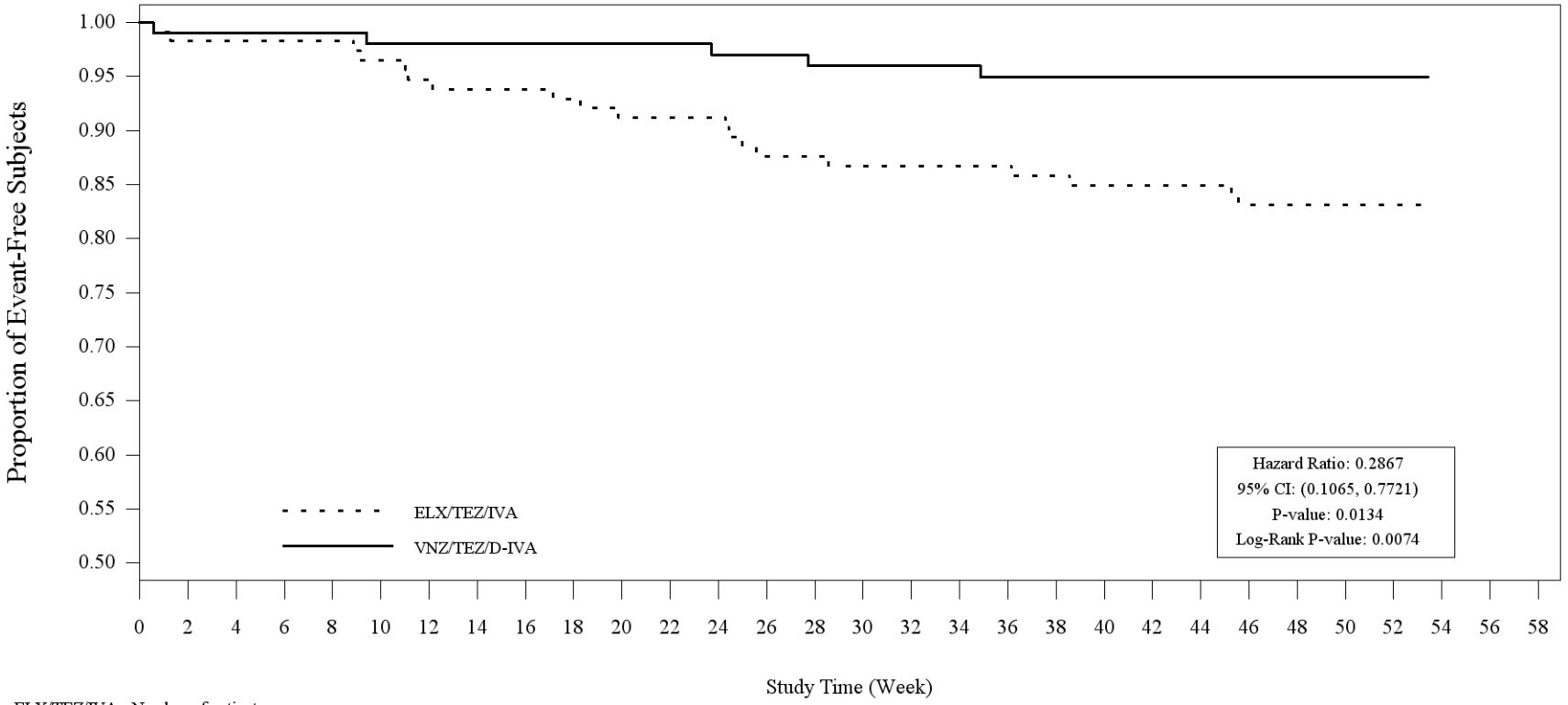
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Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: $ppFEV_1$ at Baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	114	107	103	97	92
with event(s)	0	6	10	15	19
censored	0	1	1	2	3
VNZ/TEZ/D-IVA - Number of patients					
at risk	101	98	97	91	90
with event(s)	0	2	3	5	5
censored	0	1	1	5	6

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

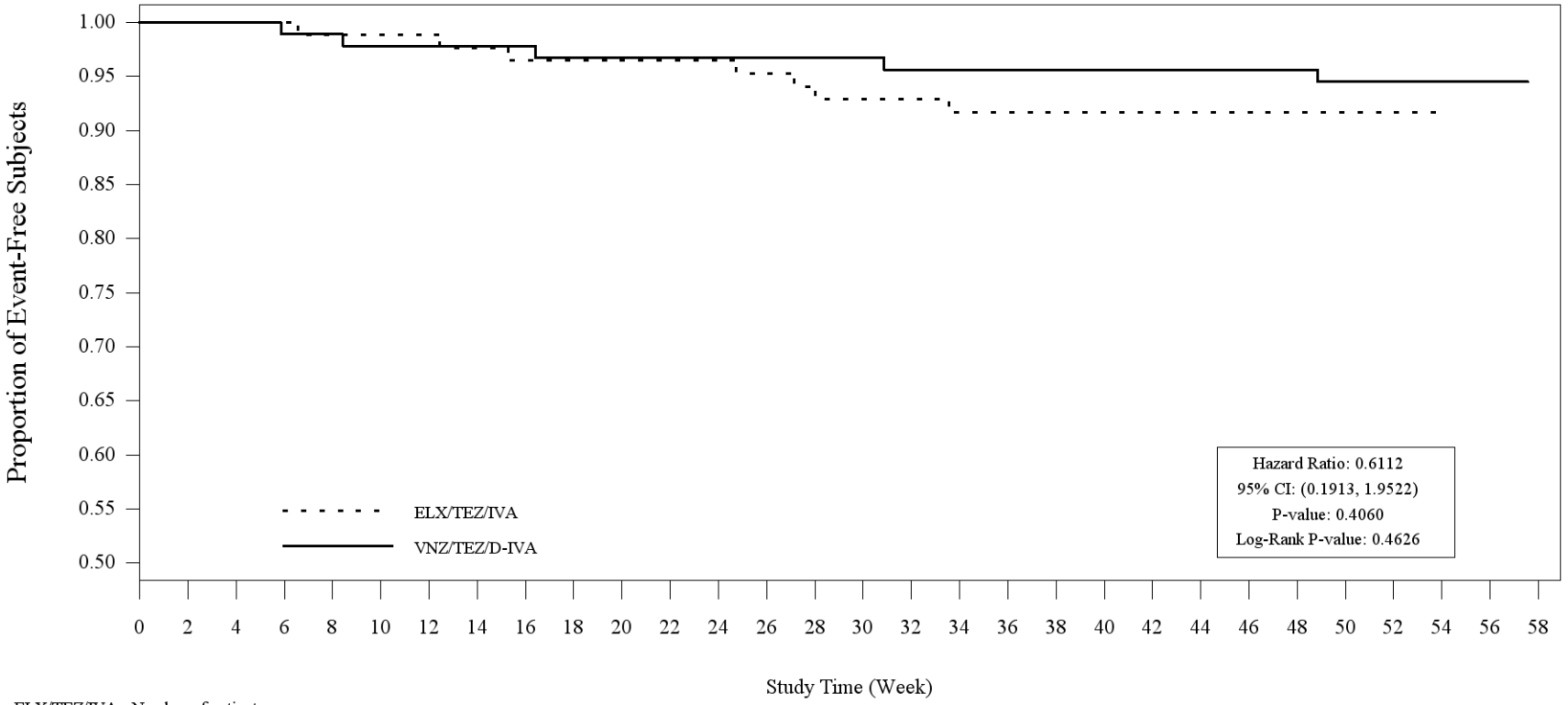
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Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: $ppFEV_1$ at Baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	87	83	81	75	73
with event(s)	0	1	3	7	7
censored	0	3	3	5	7
VNZ/TEZ/D-IVA - Number of patients					
at risk	92	90	87	86	86
with event(s)	0	2	3	4	4
censored	0	0	2	2	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

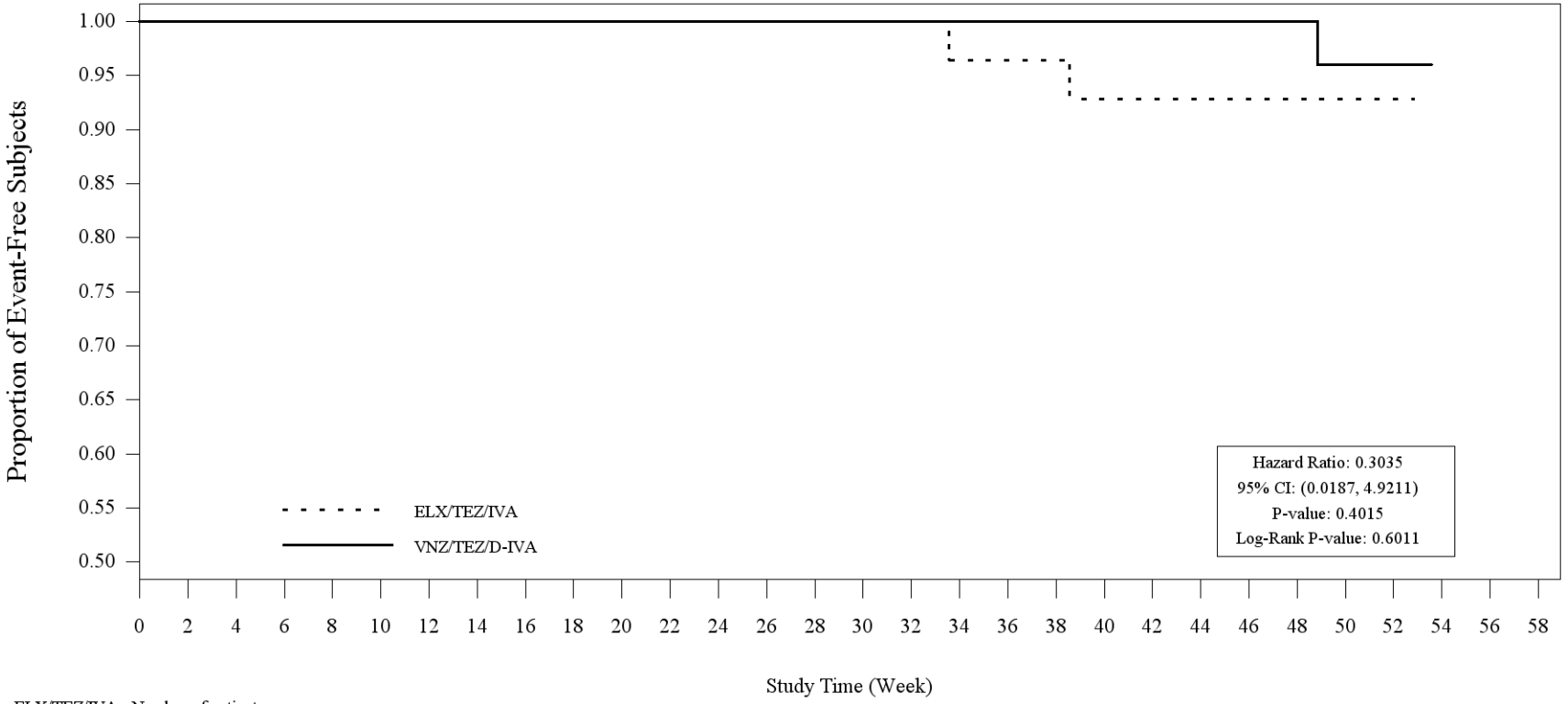
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Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening < 18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	31	29	29	27	25
with event(s)	0	0	0	1	2
censored	0	2	2	3	4
VNZ/TEZ/D-IVA - Number of patients					
at risk	26	26	25	25	25
with event(s)	0	0	0	0	0
censored	0	0	1	1	1

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

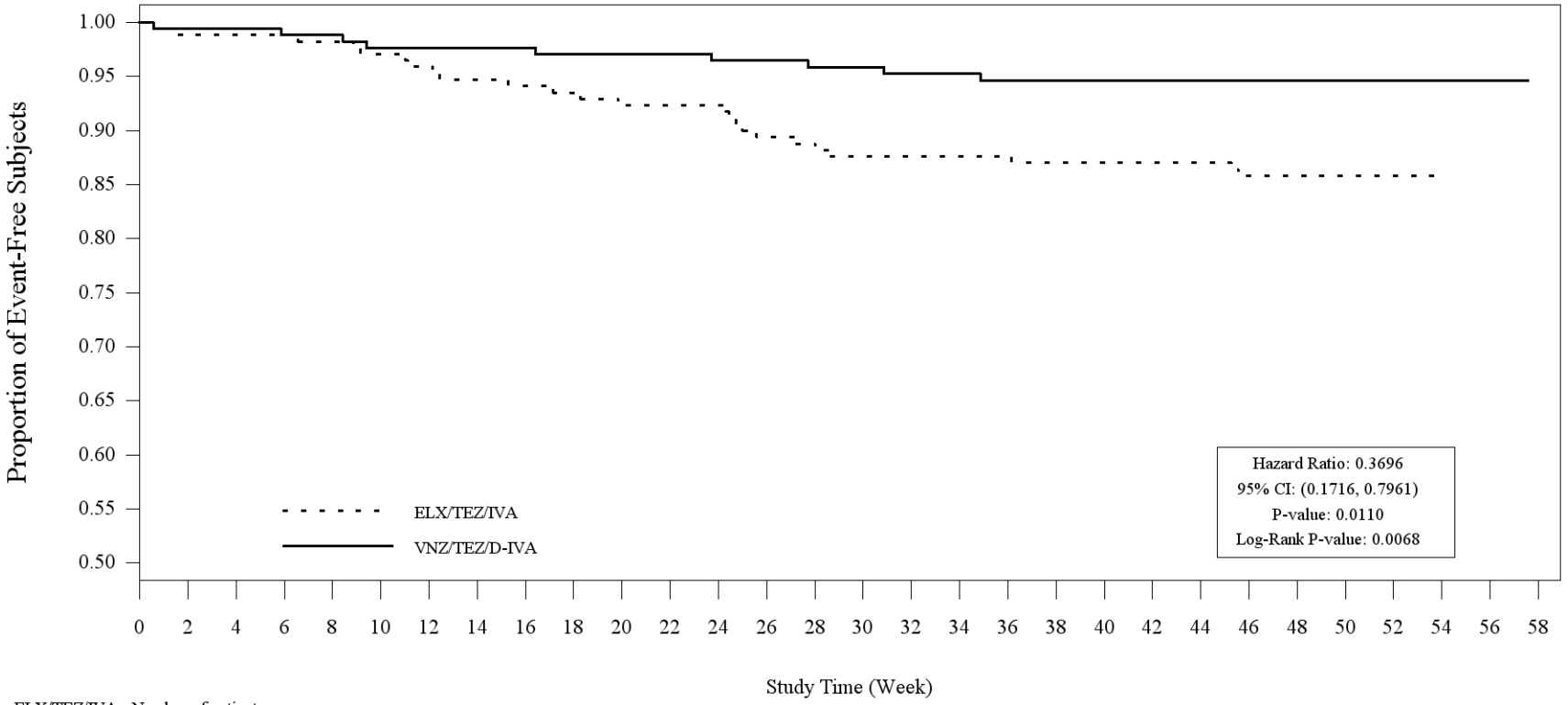
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Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening ≥ 18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	171	162	156	146	141
with event(s)	0	7	13	21	24
censored	0	2	2	4	6
VNZ/TEZ/D-IVA - Number of patients					
at risk	170	165	162	155	154
with event(s)	0	4	6	9	9
censored	0	1	2	6	7

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

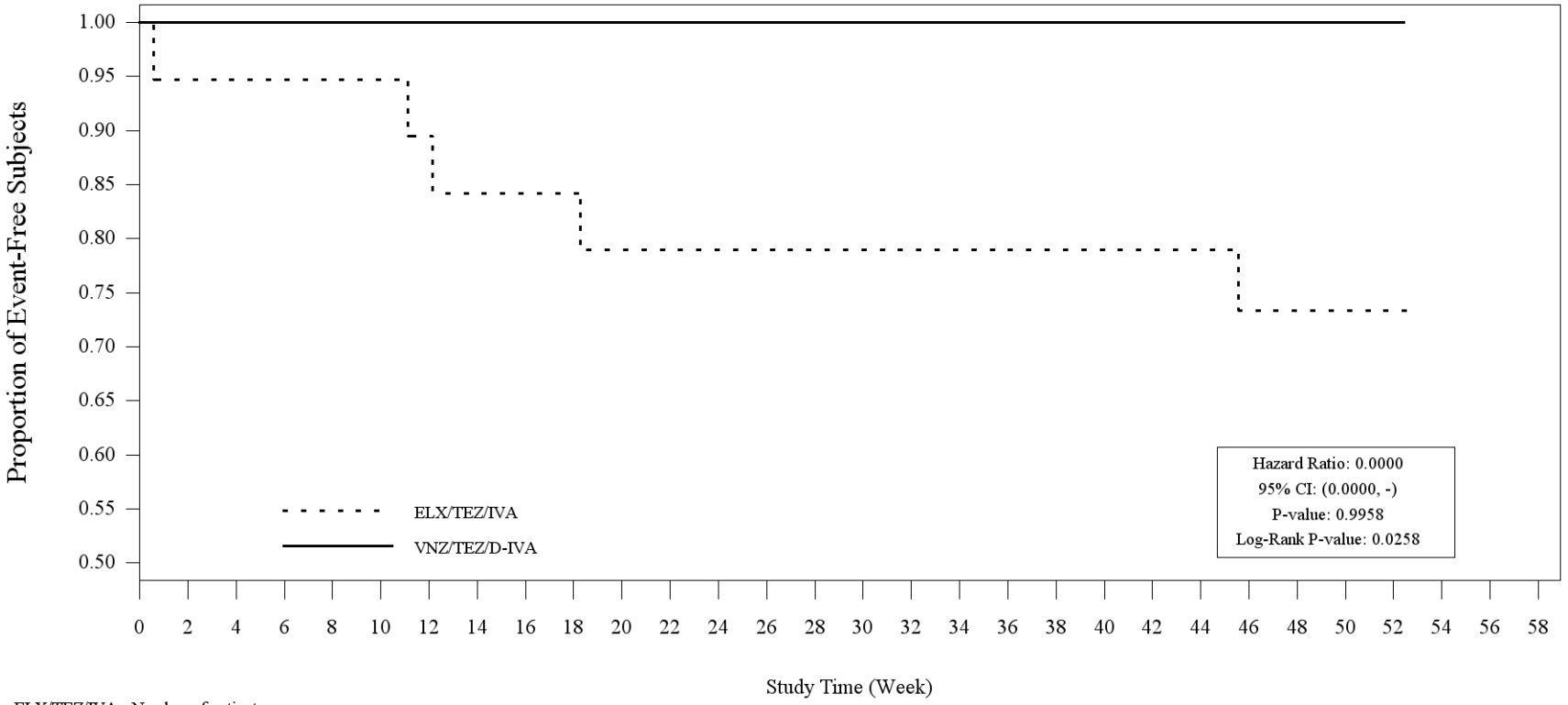
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Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	19	17	15	14	13
with event(s)	0	2	4	4	5
censored	0	0	0	1	1
VNZ/TEZ/D-IVA - Number of patients					
at risk	17	17	17	15	15
with event(s)	0	0	0	0	0
censored	0	0	0	2	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

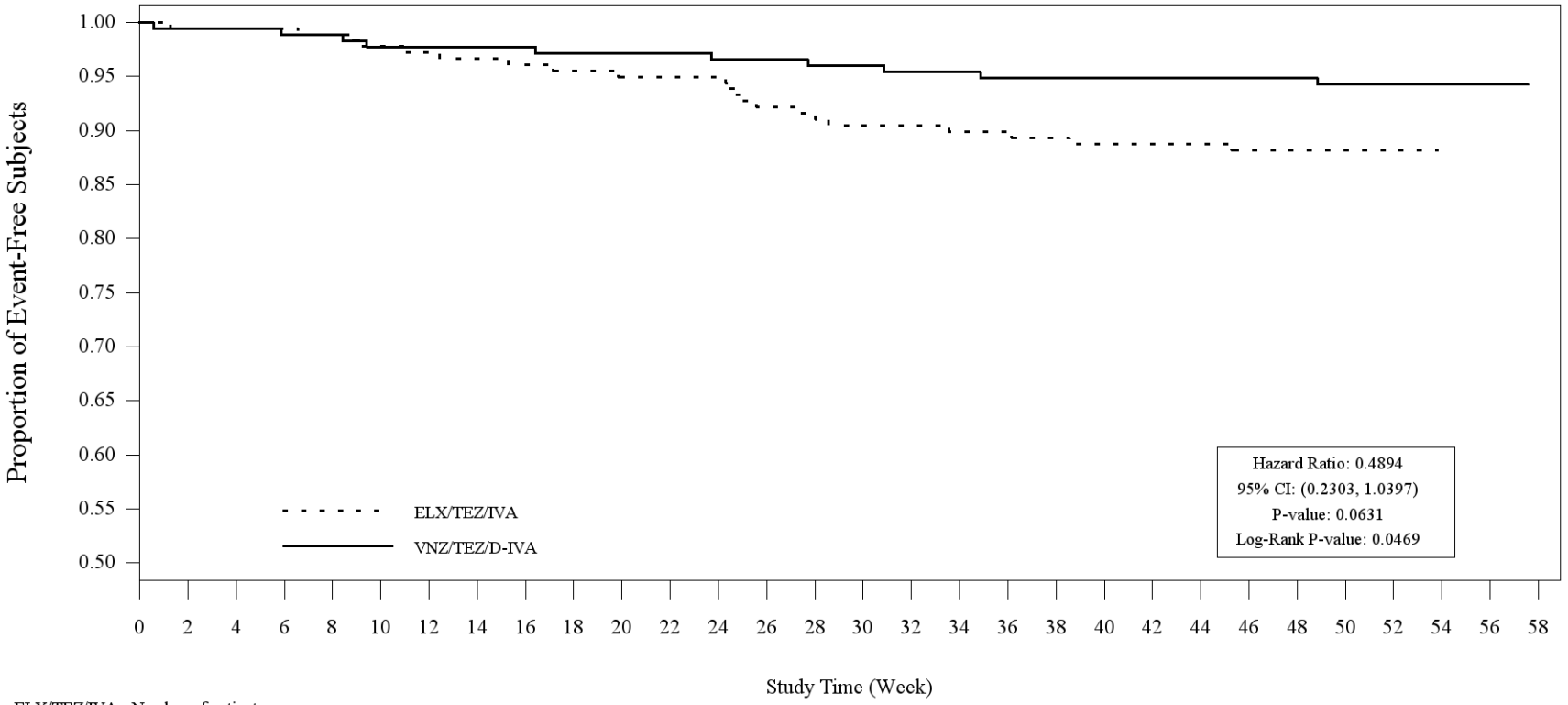
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Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	182	173	169	158	152
with event(s)	0	5	9	18	21
censored	0	4	4	6	9
VNZ/TEZ/D-IVA - Number of patients					
at risk	177	172	168	163	163
with event(s)	0	4	6	9	9
censored	0	1	3	5	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

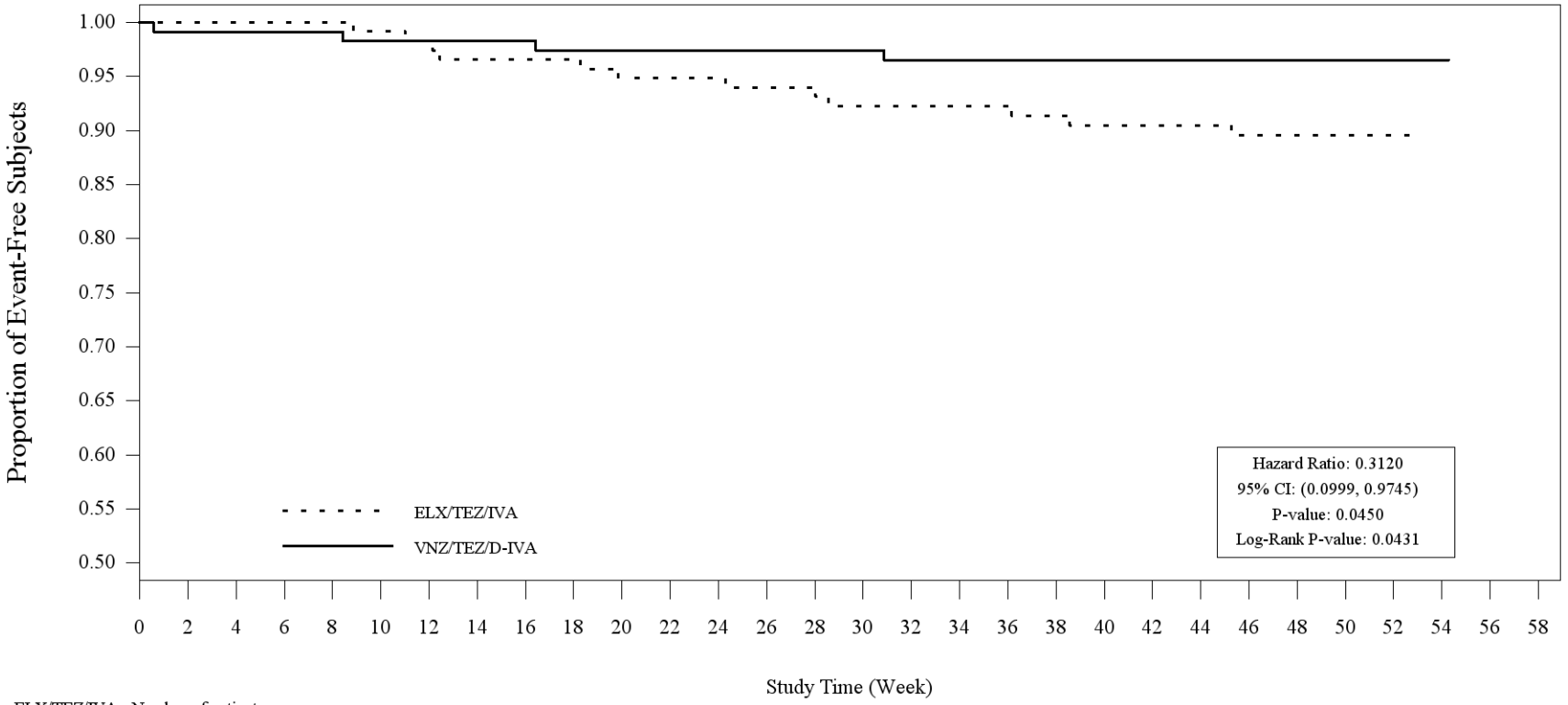
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Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	119	114	110	105	101
with event(s)	0	2	6	9	12
censored	0	3	3	5	6
VNZ/TEZ/D-IVA - Number of patients					
at risk	116	114	112	109	109
with event(s)	0	2	3	4	4
censored	0	0	1	3	3

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

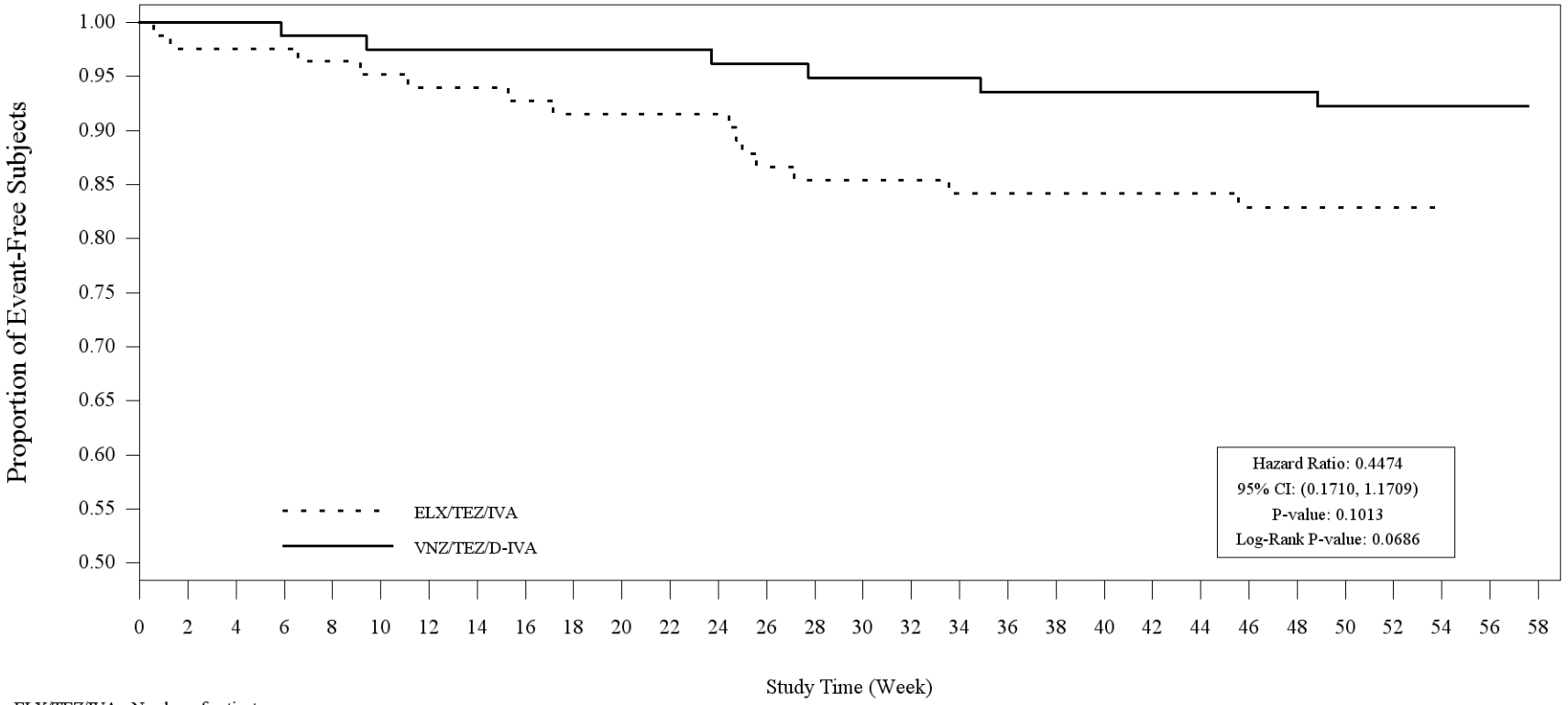
Program: GMA\VX121\global\clinstat_prod\20251216\f-ce-pe-iv-km-52wks-sub-102.sas Creation: 18FEB2026 15:41

Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	83	77	75	68	65
with event(s)	0	5	7	13	14
censored	0	1	1	2	4
VNZ/TEZ/D-IVA - Number of patients					
at risk	80	77	75	71	70
with event(s)	0	2	3	5	5
censored	0	1	2	4	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

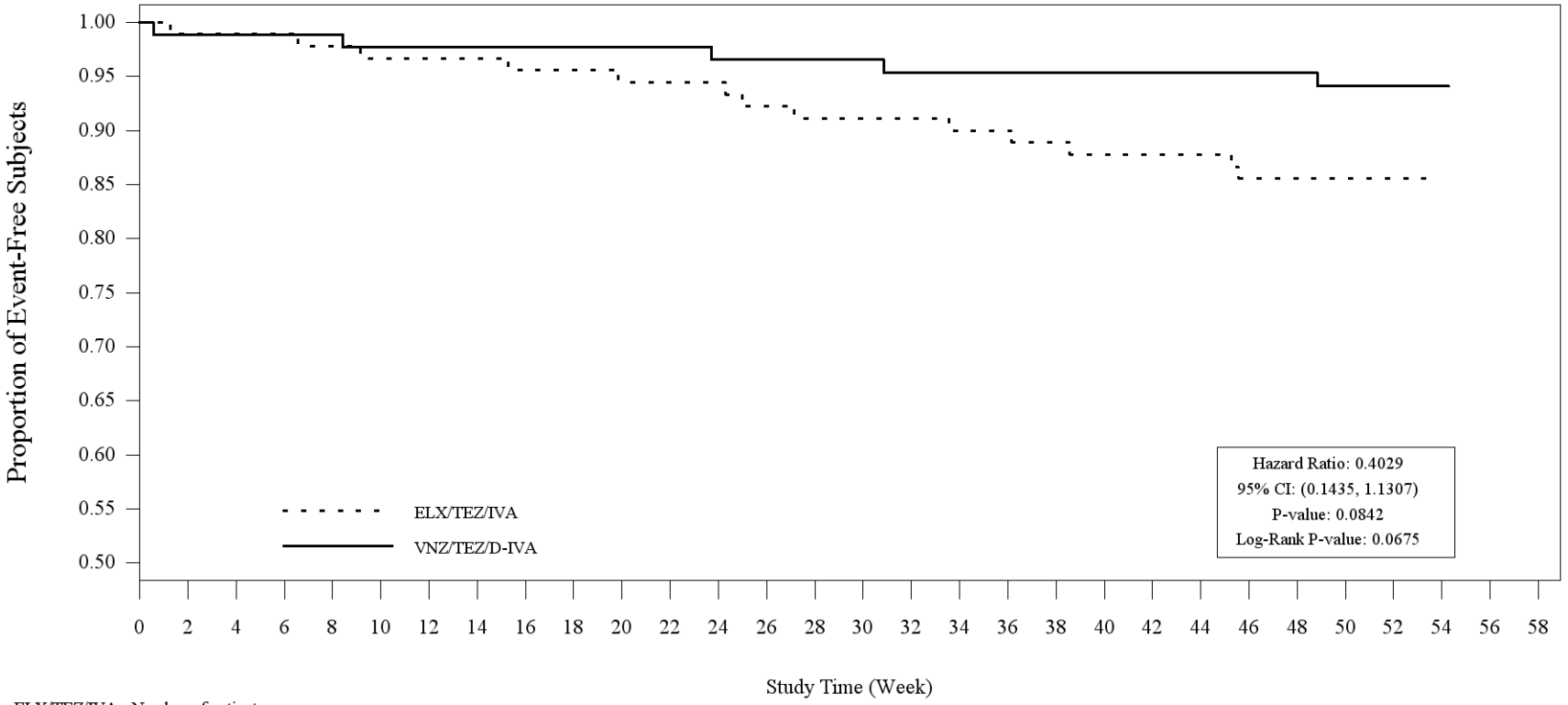
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Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	91	87	85	81	76
with event(s)	0	3	5	9	13
censored	0	1	1	1	2
VNZ/TEZ/D-IVA - Number of patients					
at risk	87	85	83	78	77
with event(s)	0	2	3	4	4
censored	0	0	1	5	6

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

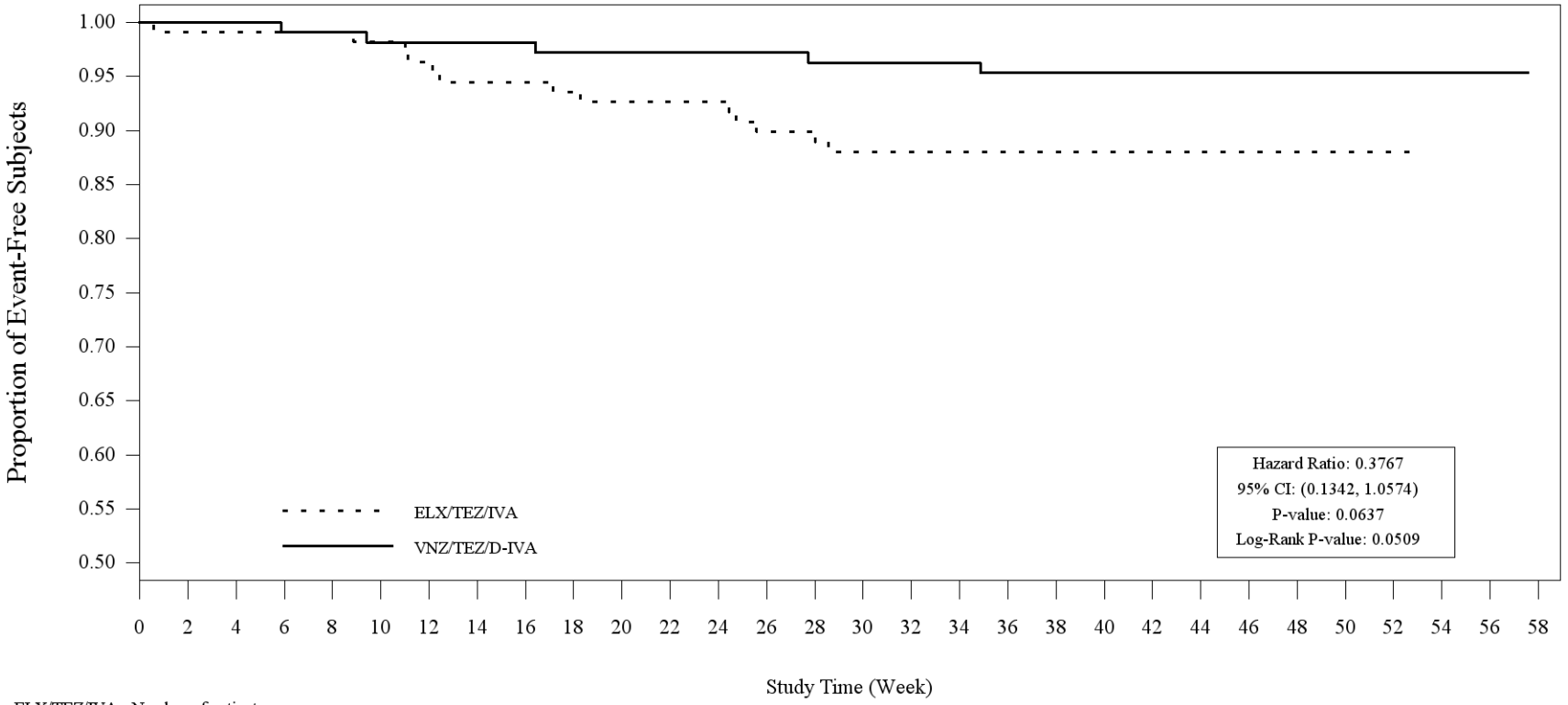
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Figure 1.2.2.8.2
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = Rest of the World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	111	104	100	92	90
with event(s)	0	4	8	13	13
censored	0	3	3	6	8
VNZ/TEZ/D-IVA - Number of patients					
at risk	109	106	104	102	102
with event(s)	0	2	3	5	5
censored	0	1	2	2	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

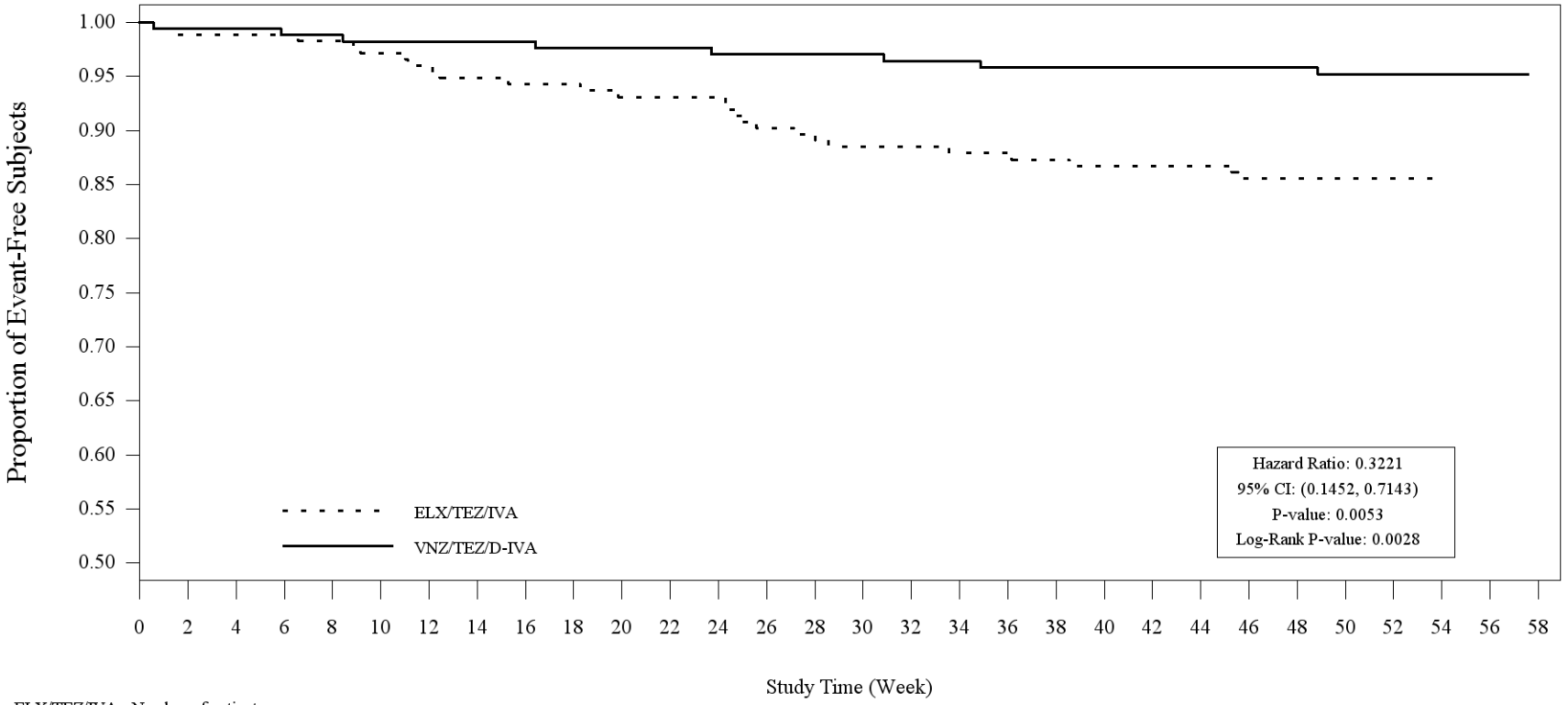
Program: GMA\VX121\global\clinstat_prod\20251216\f-ce-pe-iv-km-52wks-sub-102.sas Creation: 18FEB2026 15:41

Figure 1.2.2.8.2.1
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Subgroup: Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.

Zusatzanalysen zur Studie VX20-121-102



ELX/TEZ/IVA - Number of patients					
at risk	177	166	161	150	144
with event(s)	0	7	12	21	25
censored	0	4	4	6	8
VNZ/TEZ/D-IVA - Number of patients					
at risk	170	166	162	156	155
with event(s)	0	3	5	7	7
censored	0	1	3	7	8

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.

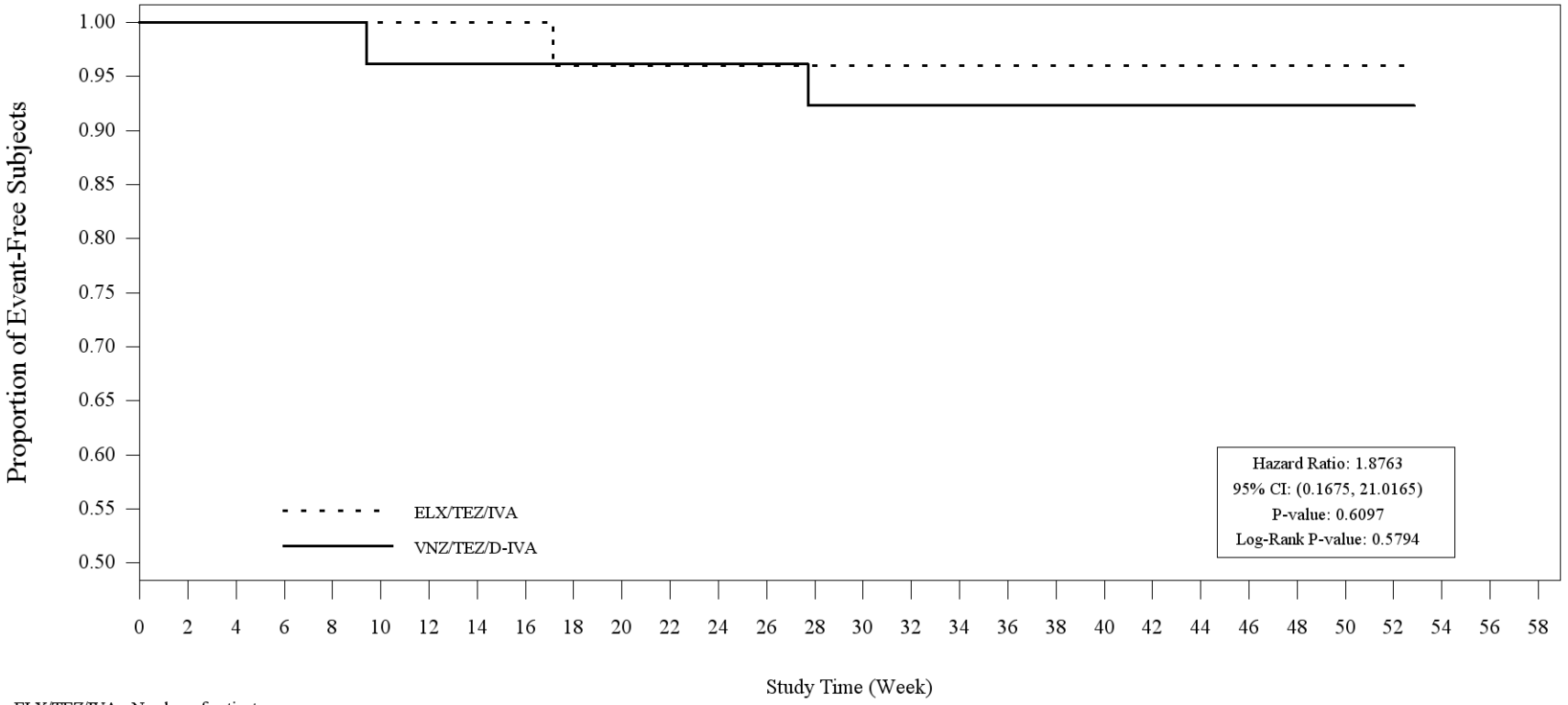
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Figure 1.2.2.8.2.1
Study VX20-121-102: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

Subgroup: Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.

Zusatzanalysen zur Studie VX20-121-102



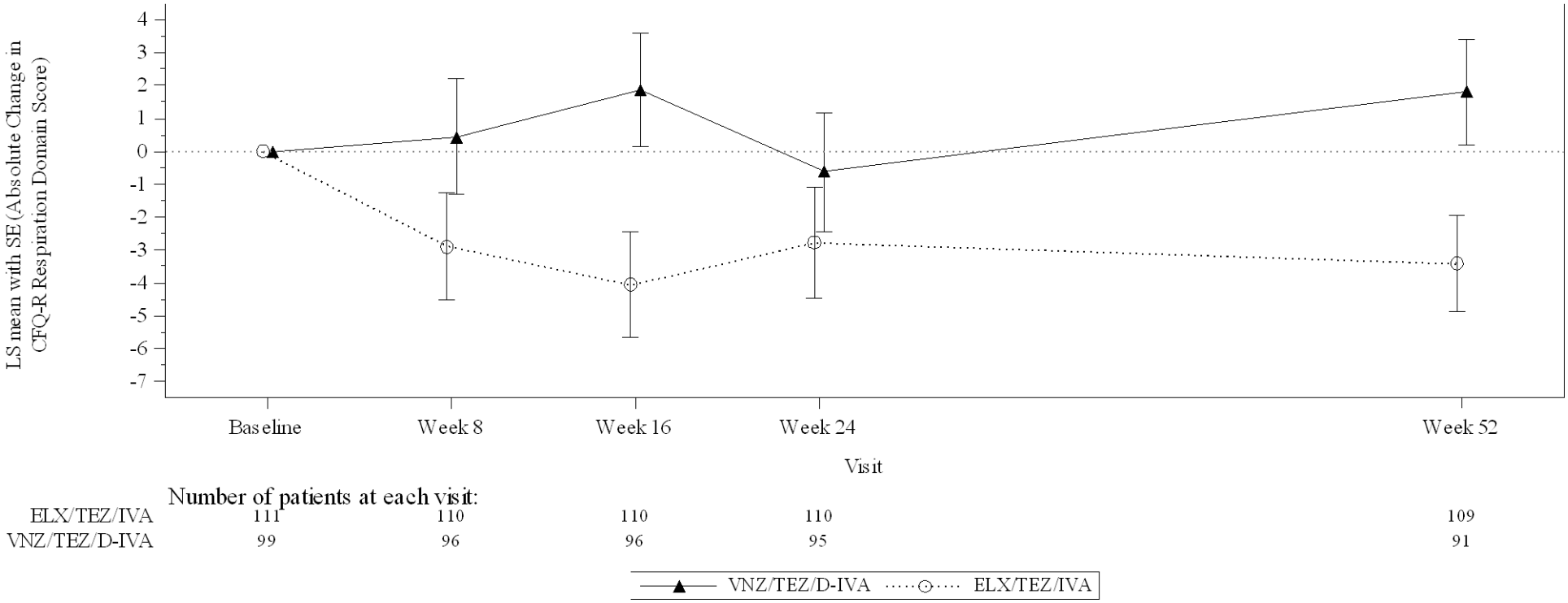
ELX/TEZ/IVA - Number of patients					
at risk	25	25	24	23	22
with event(s)	0	0	1	1	1
censored	0	0	0	1	2
VNZ/TEZ/D-IVA - Number of patients					
at risk	26	25	25	24	24
with event(s)	0	1	1	2	2
censored	0	0	0	0	0

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.

Program: GMA\VX121\global\clinstat_prod\20251216\f-ce-pe-iv-km-52wks-sub2-102.sas Creation: 18FEB2026 16:00

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

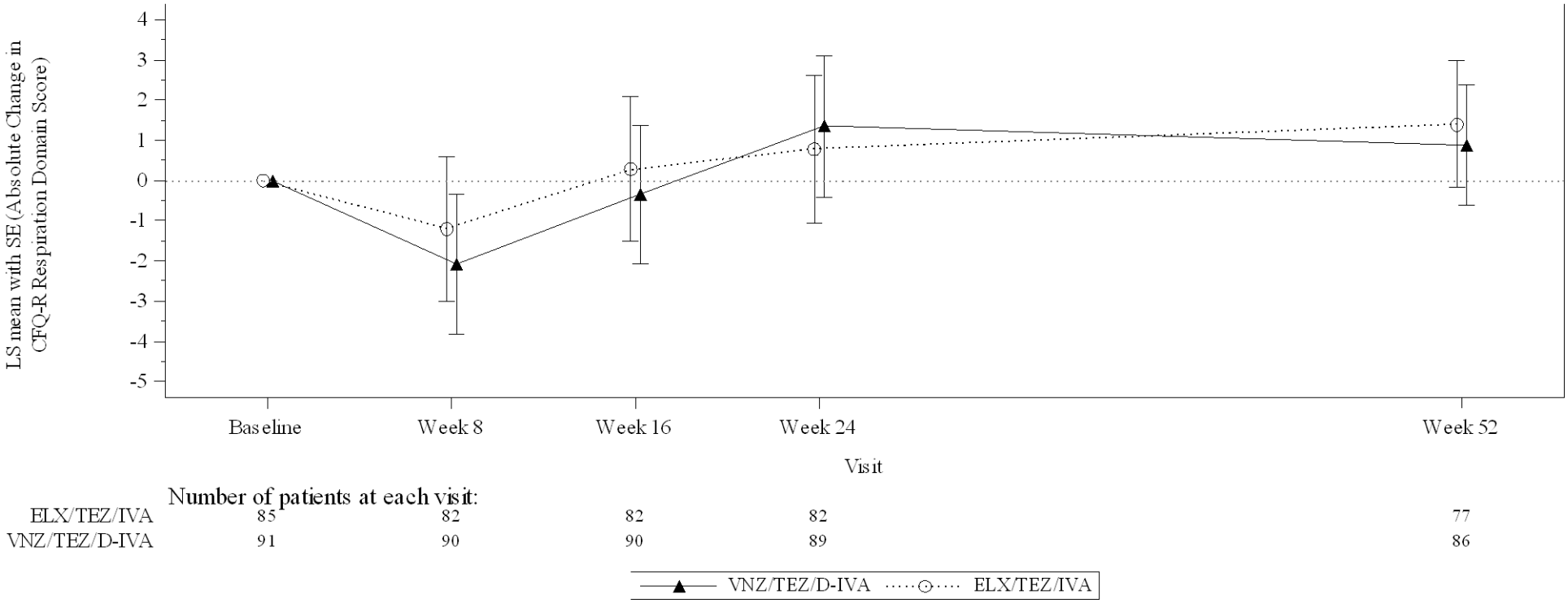
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
ppFEV$_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

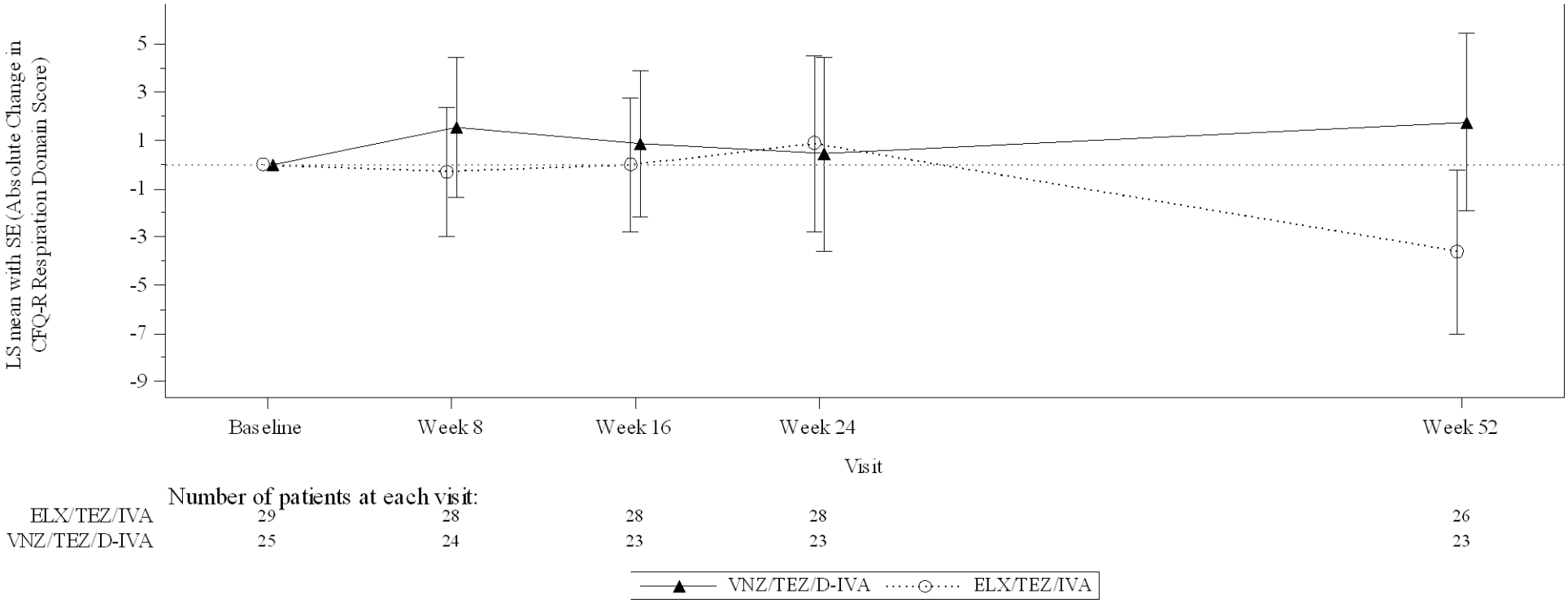
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
$ppFEV_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

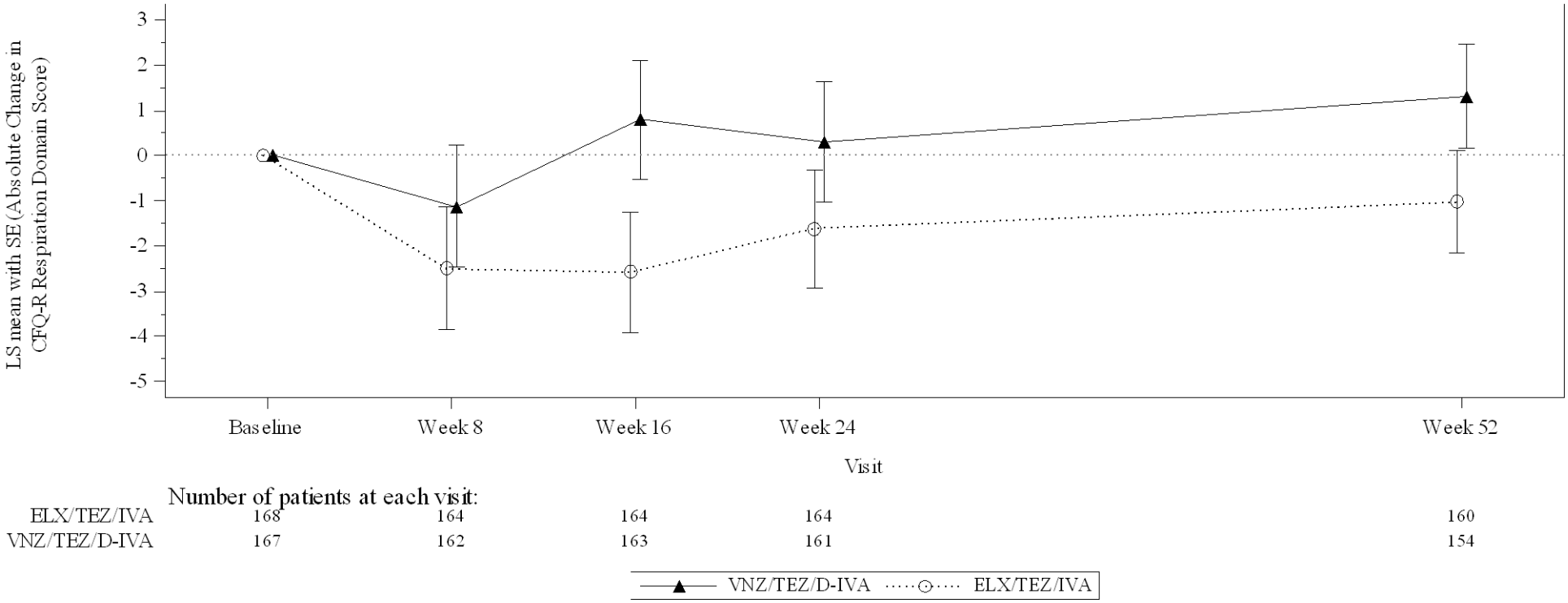
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Age at screening <18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

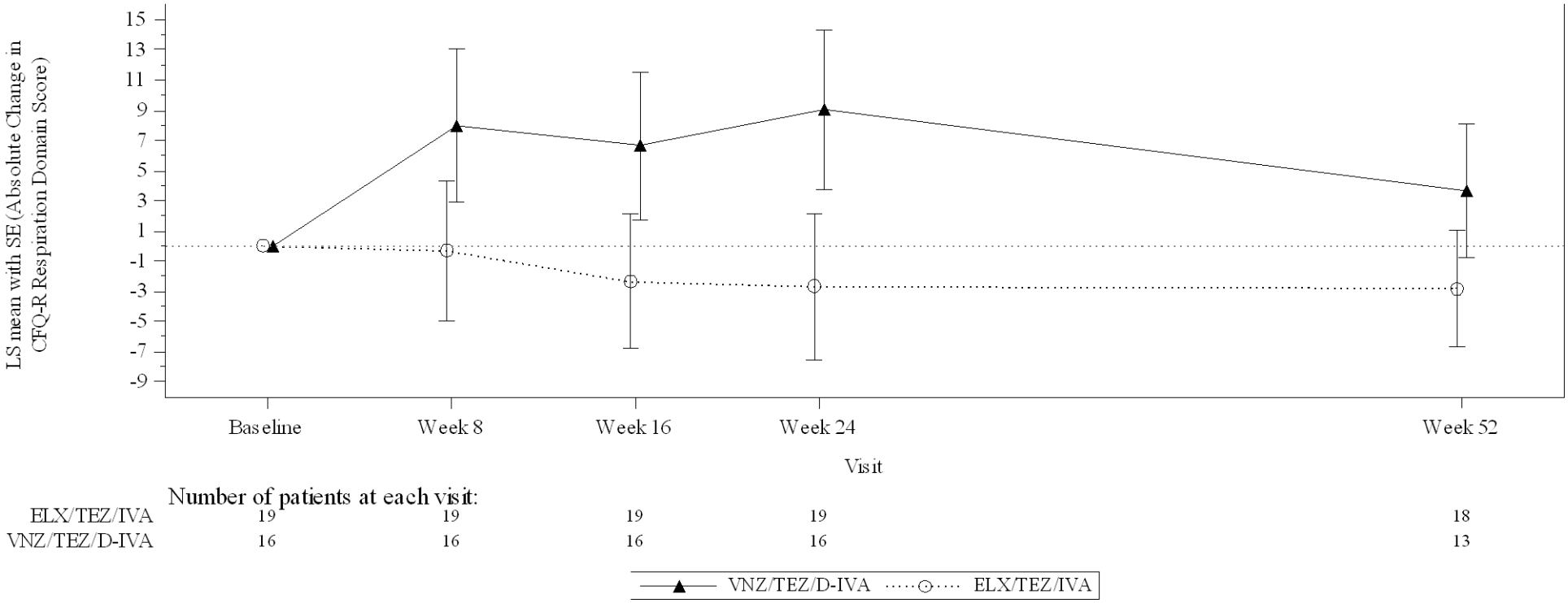
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Age at screening ≥18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

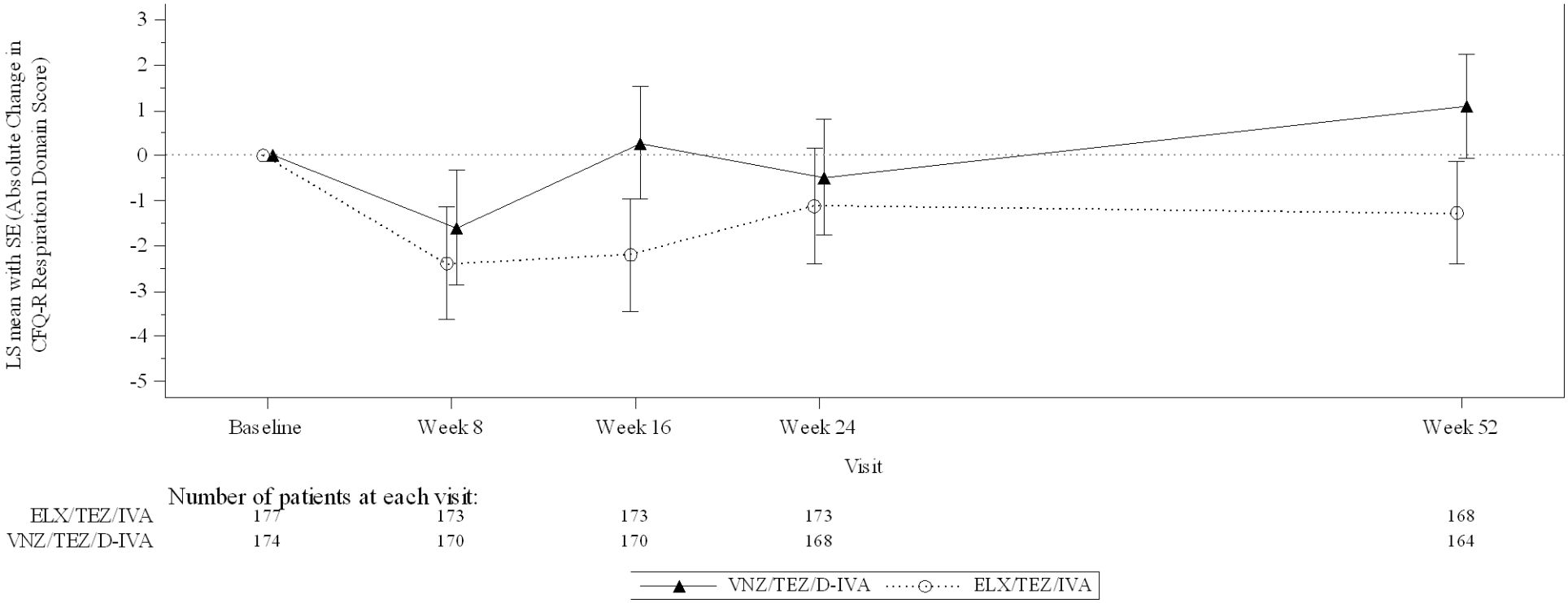
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
SwCl at baseline ≥30 mmol/L



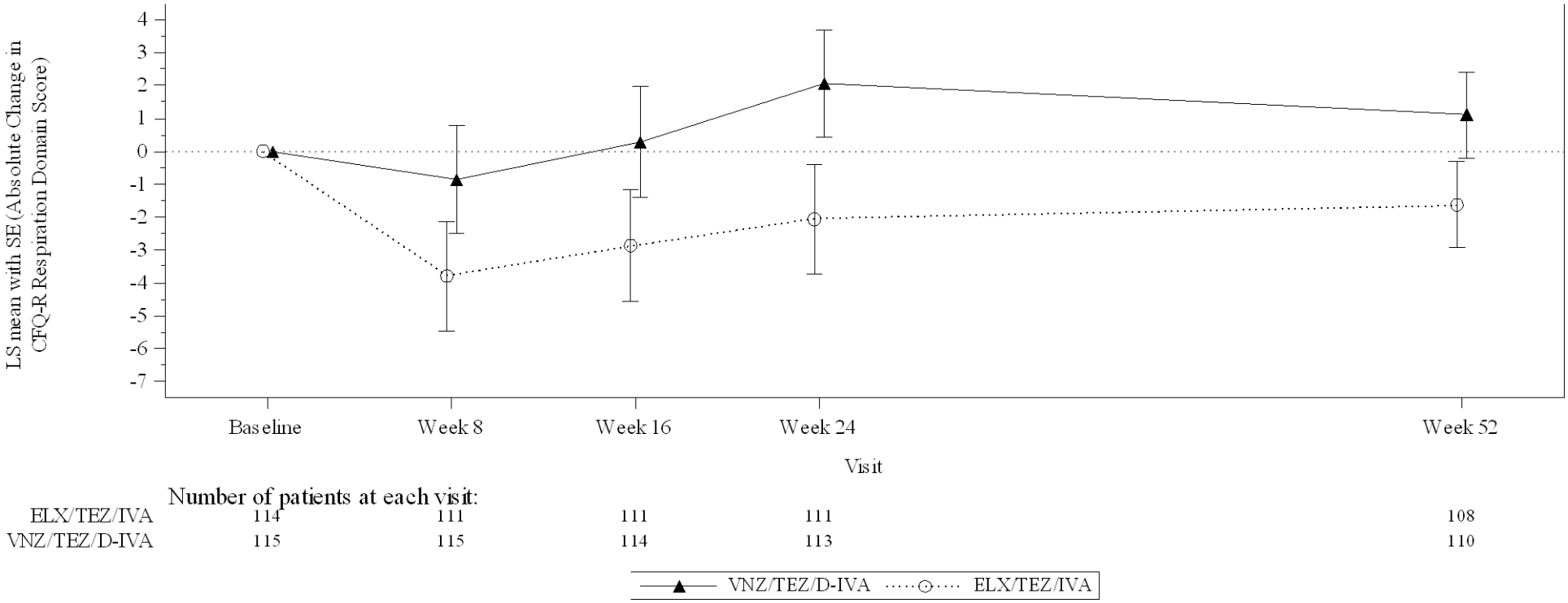
Number of patients at each visit:

ELX/TEZ/IVA	177	173	173	173	168
VNZ/TEZ/D-IVA	174	170	170	168	164

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

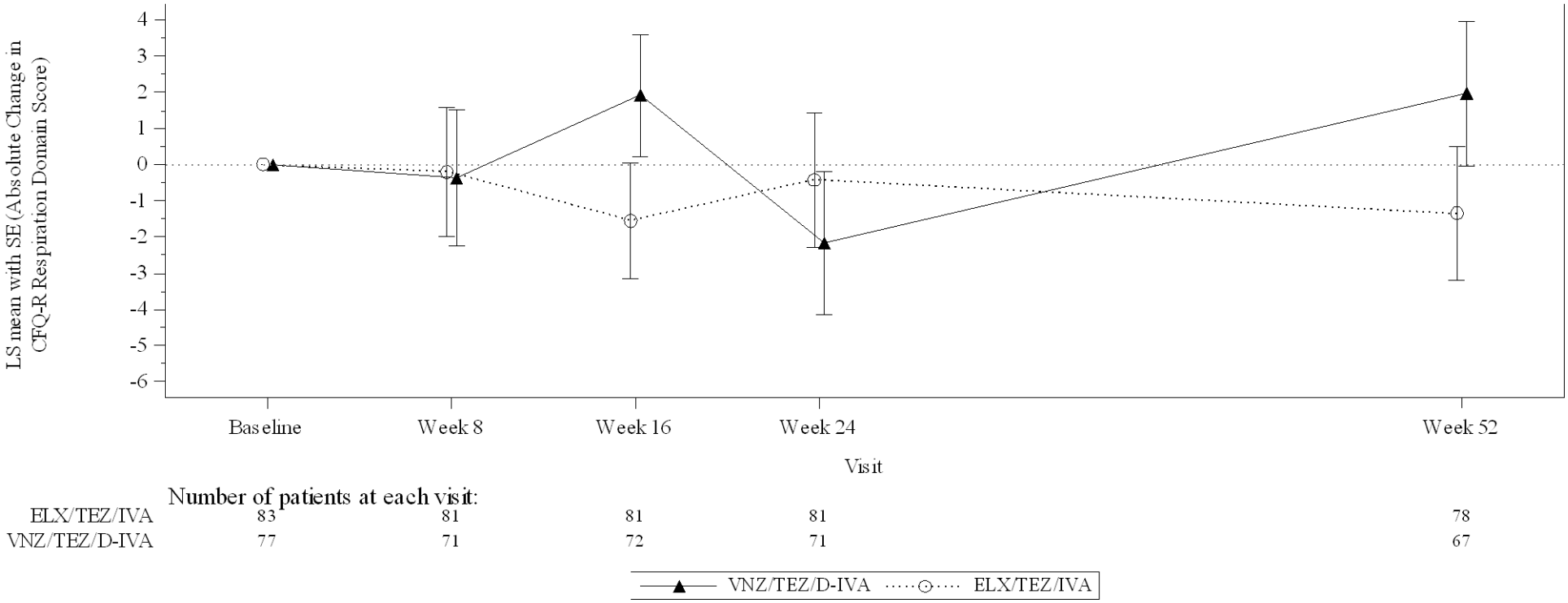
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Sex = Male



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Figure 1.2.2.9.5
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Full Analysis Set

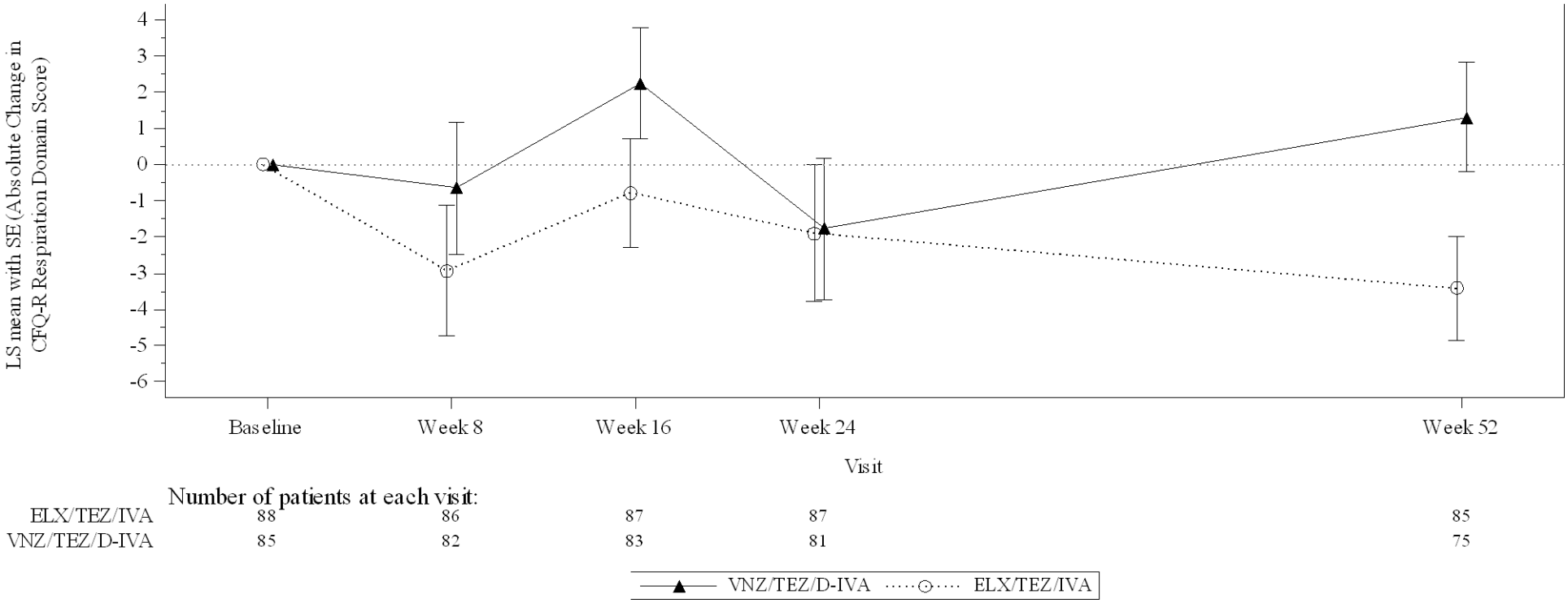
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
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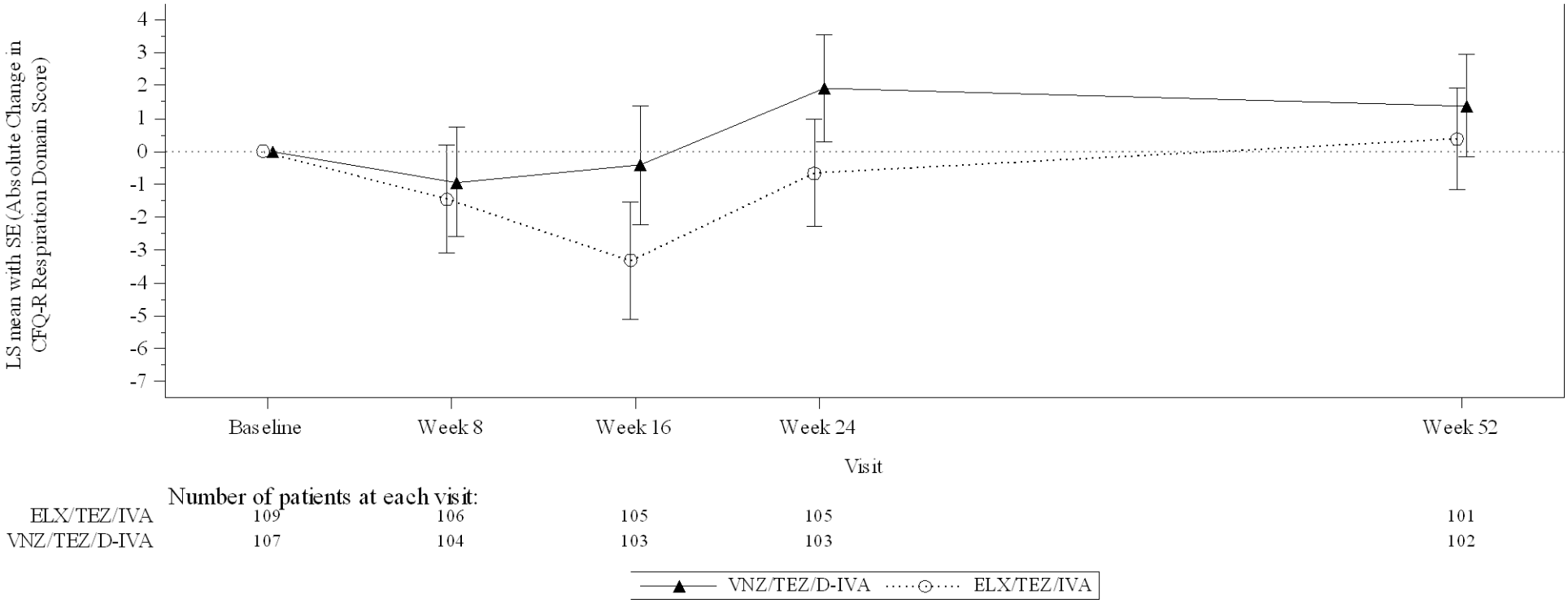
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Region = North America



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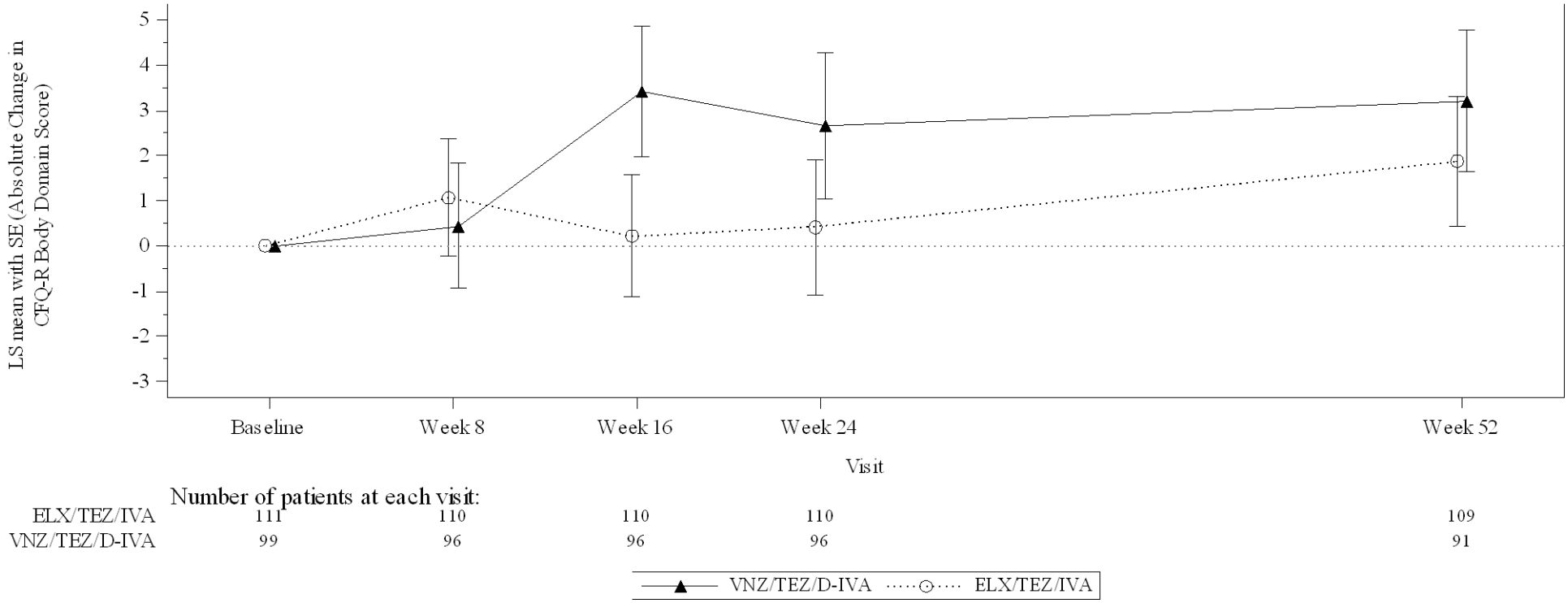
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Region = Rest of World



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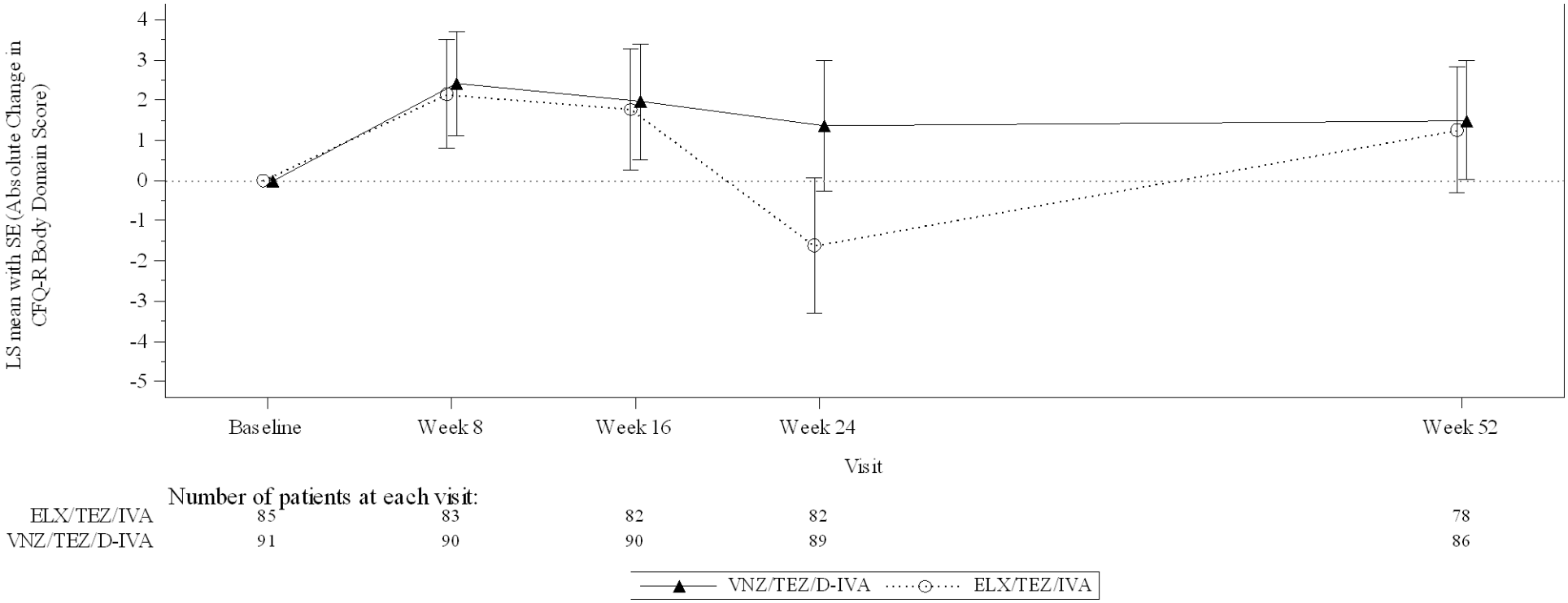
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %



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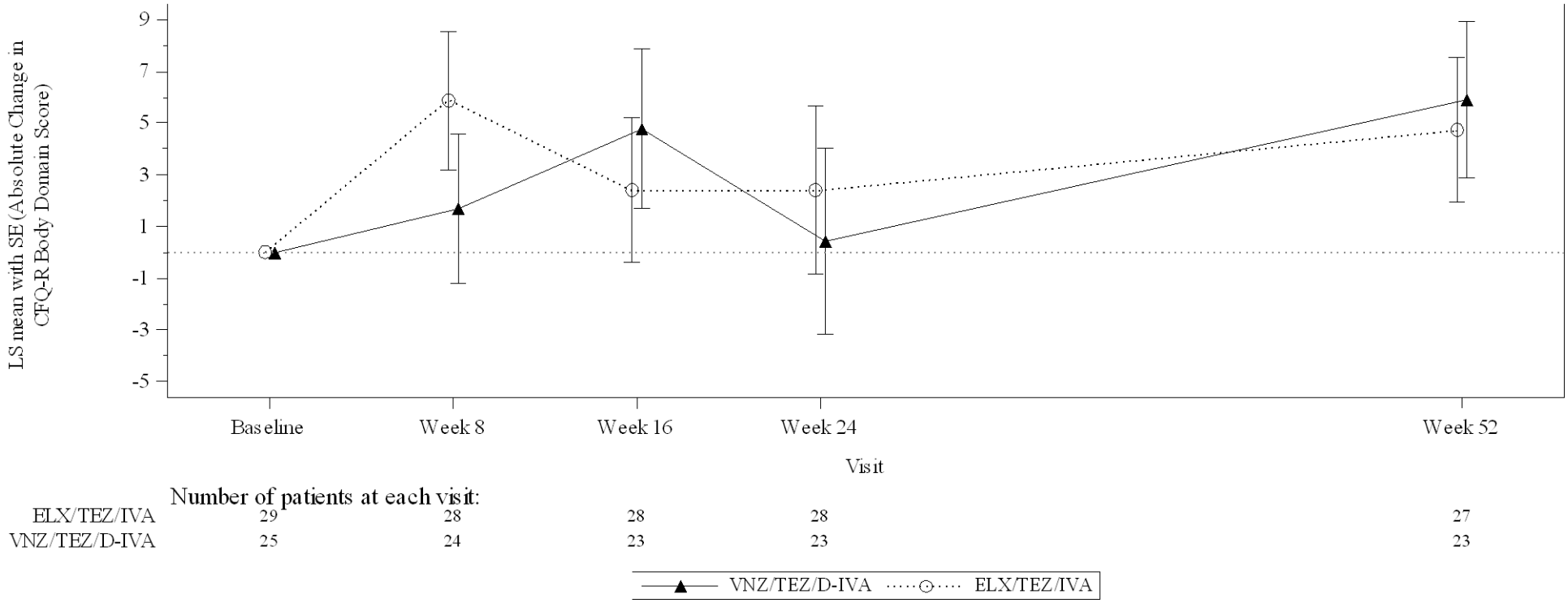
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %



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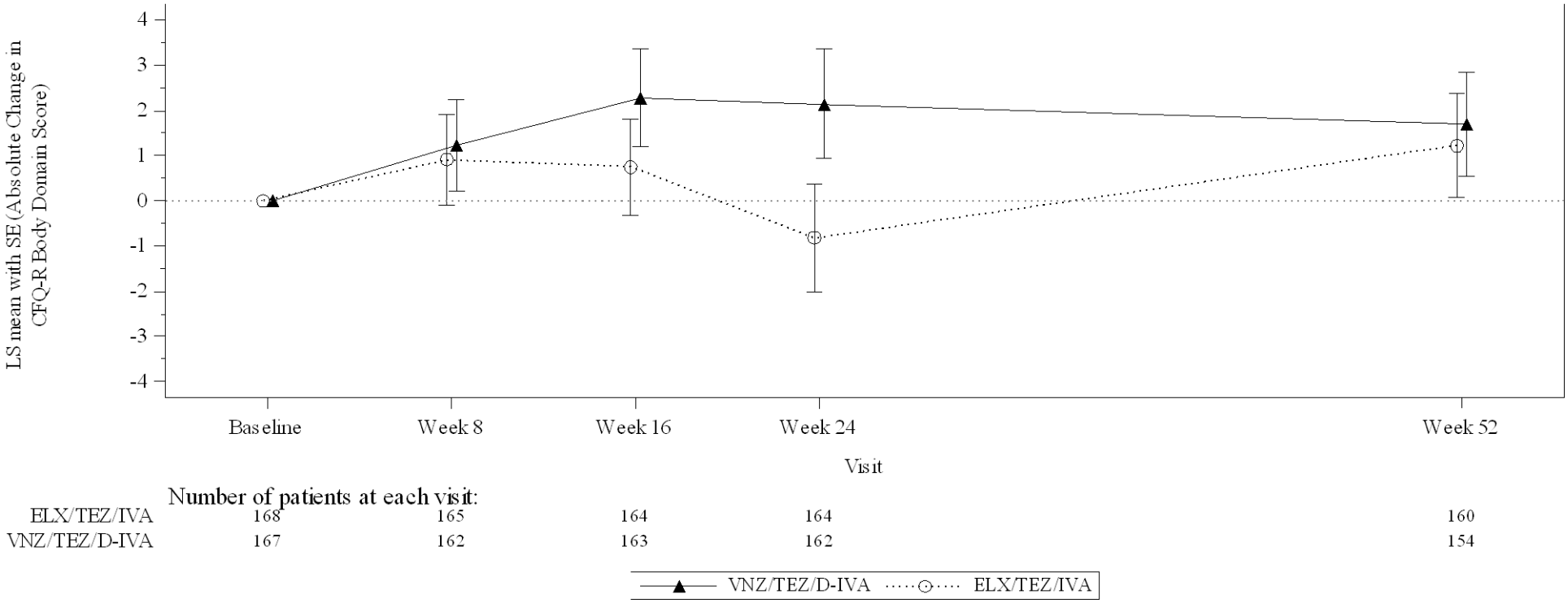
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years



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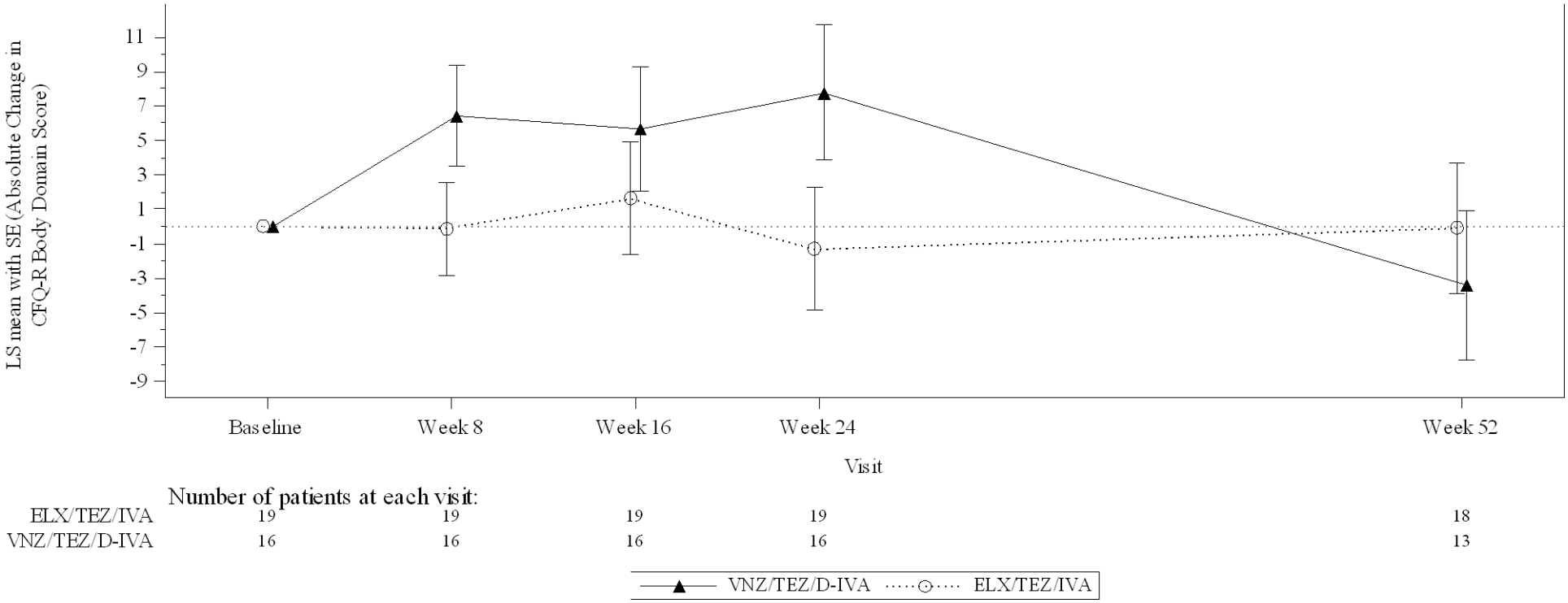
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years



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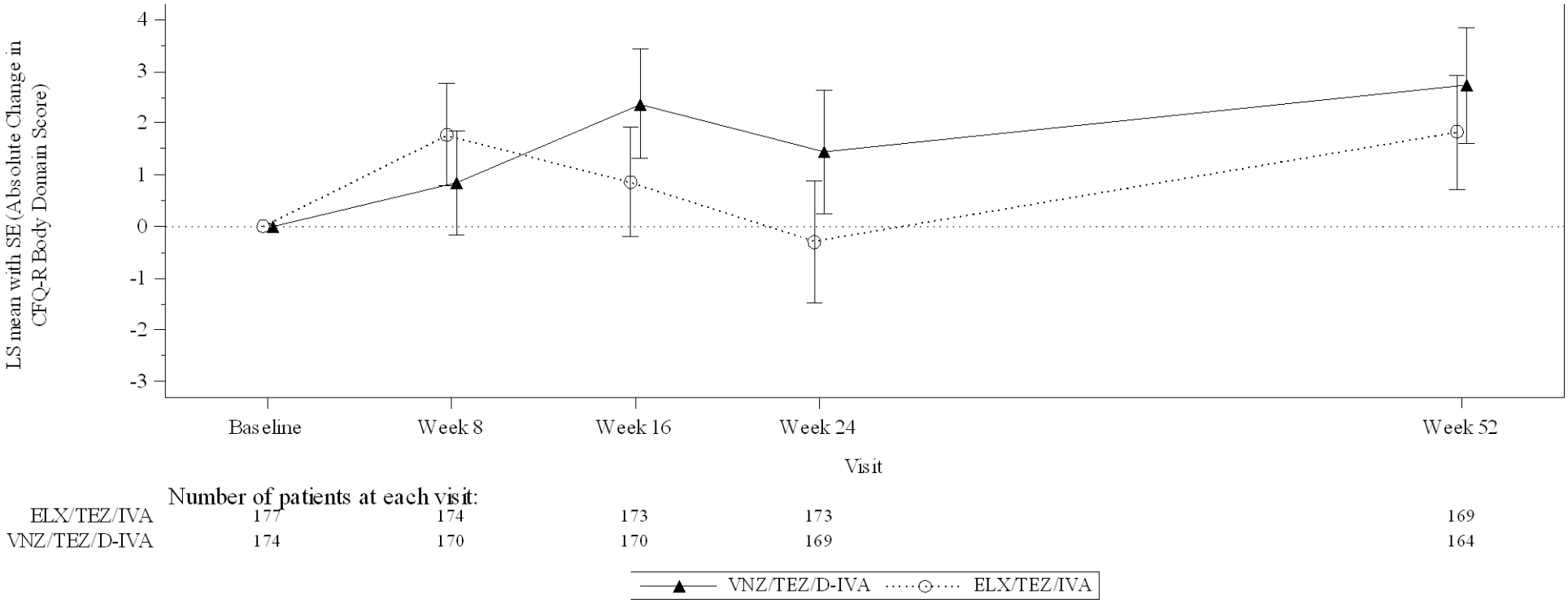
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L



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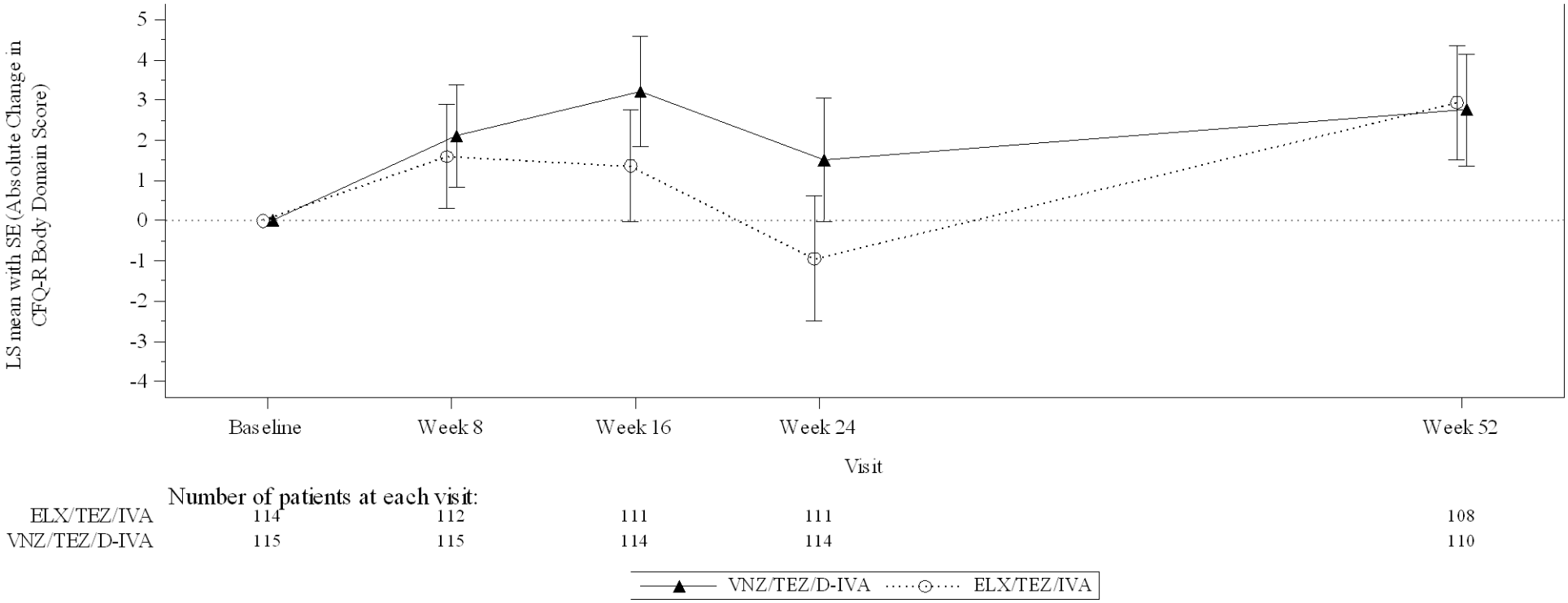
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L



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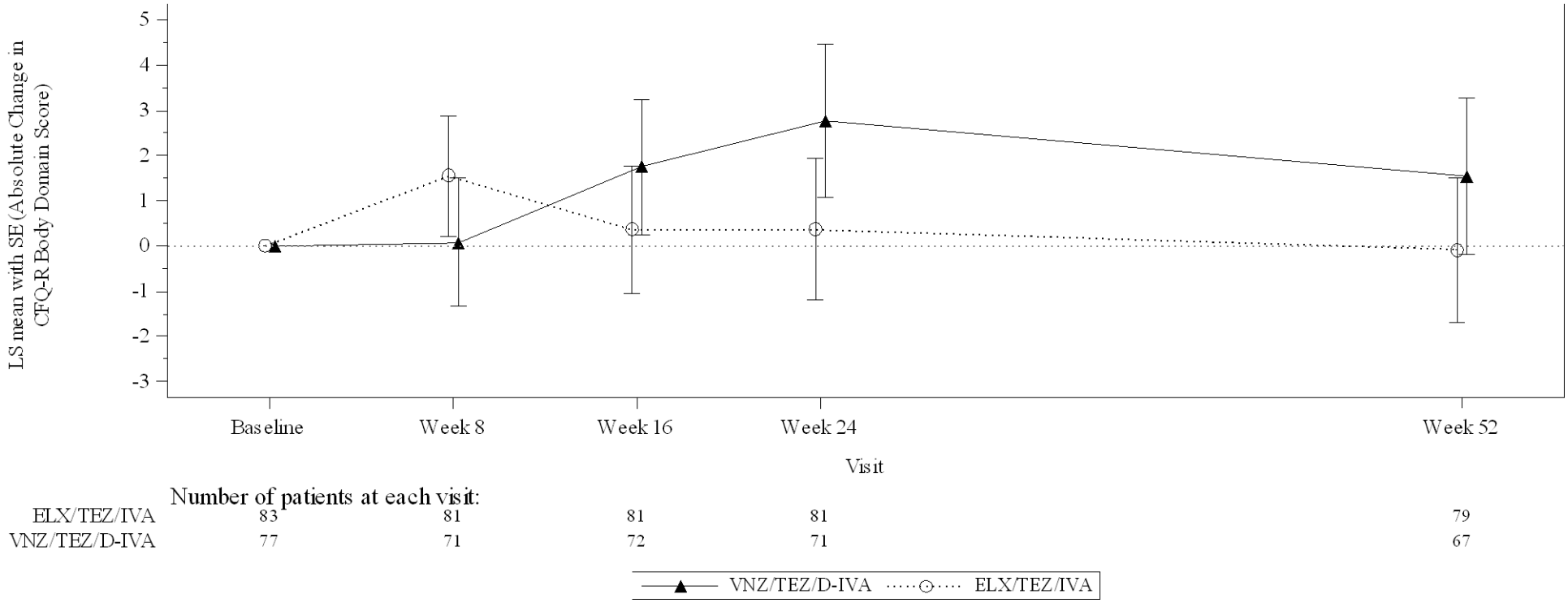
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Sex = Male



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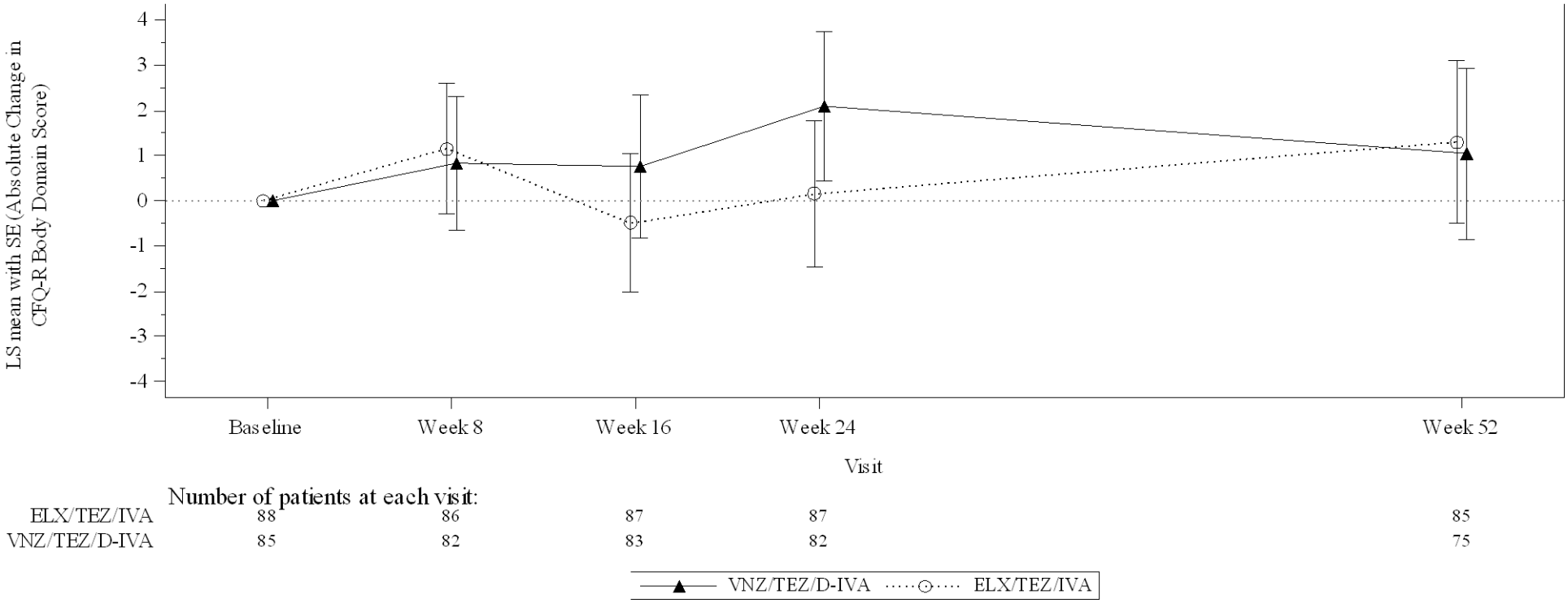
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
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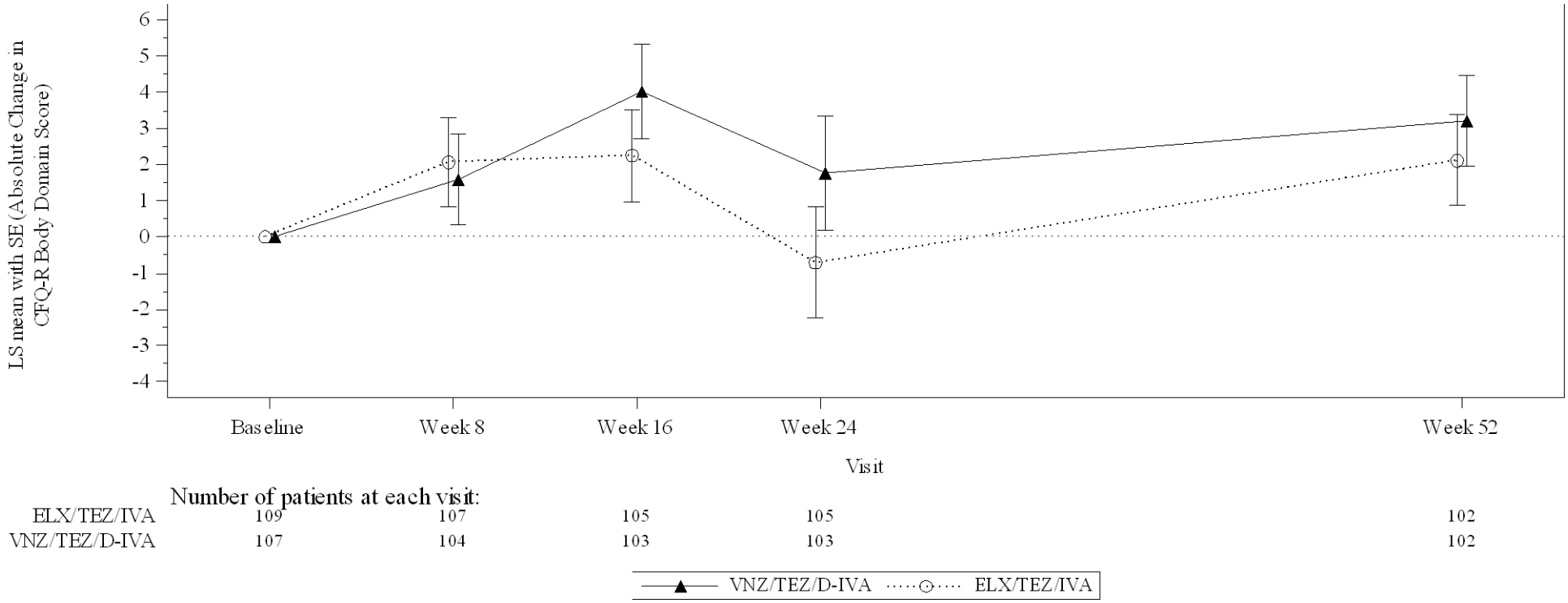
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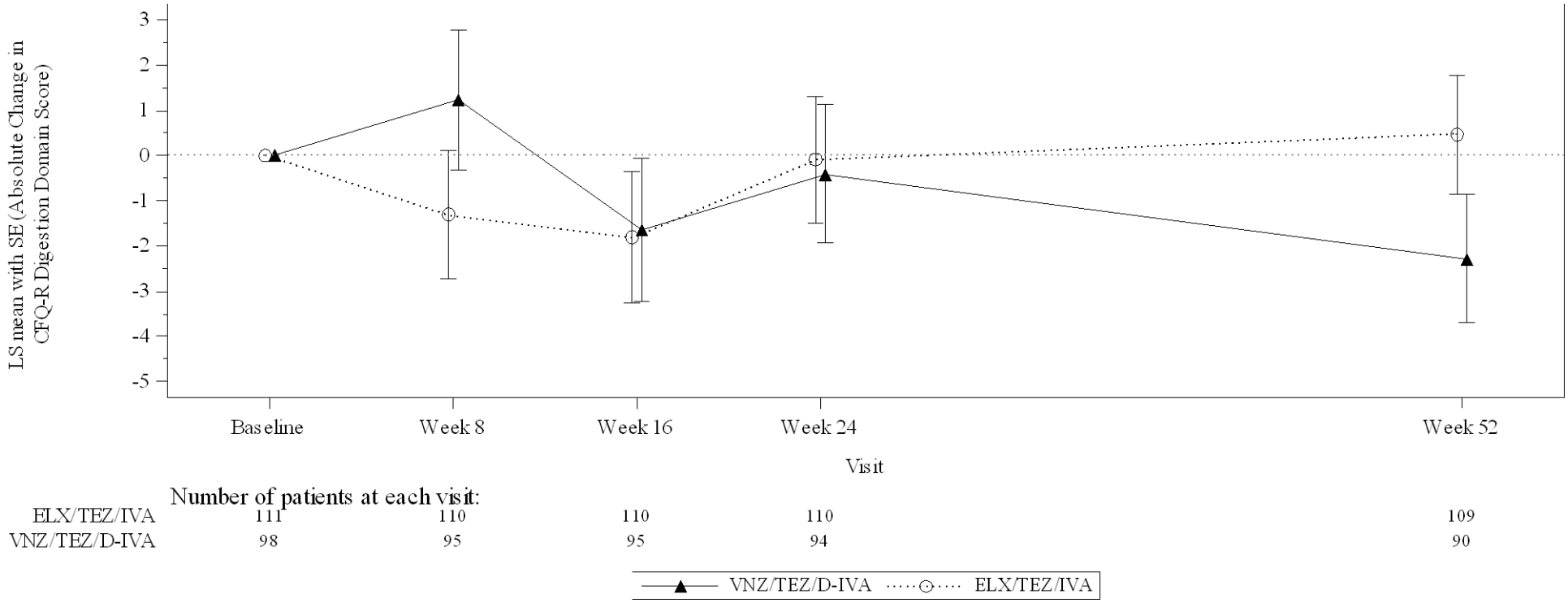
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Region = Rest of World



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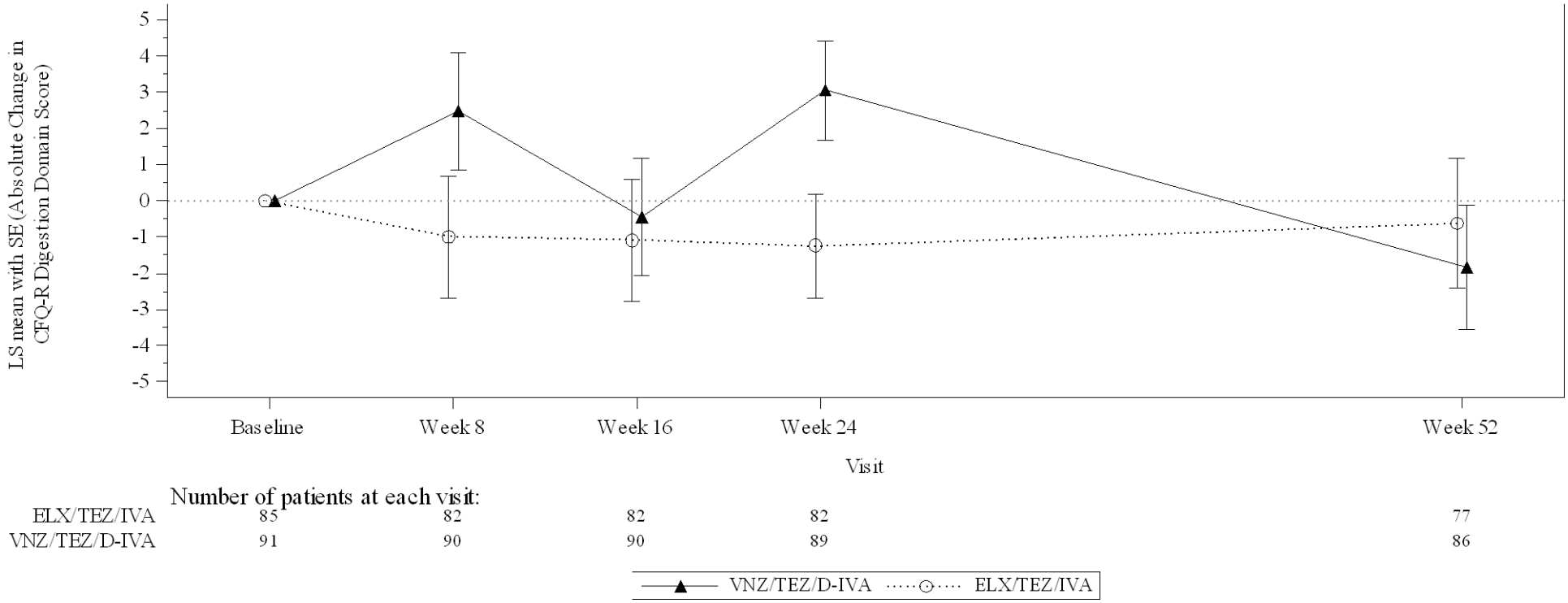
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
ppFEV$_1$ at baseline <70 %



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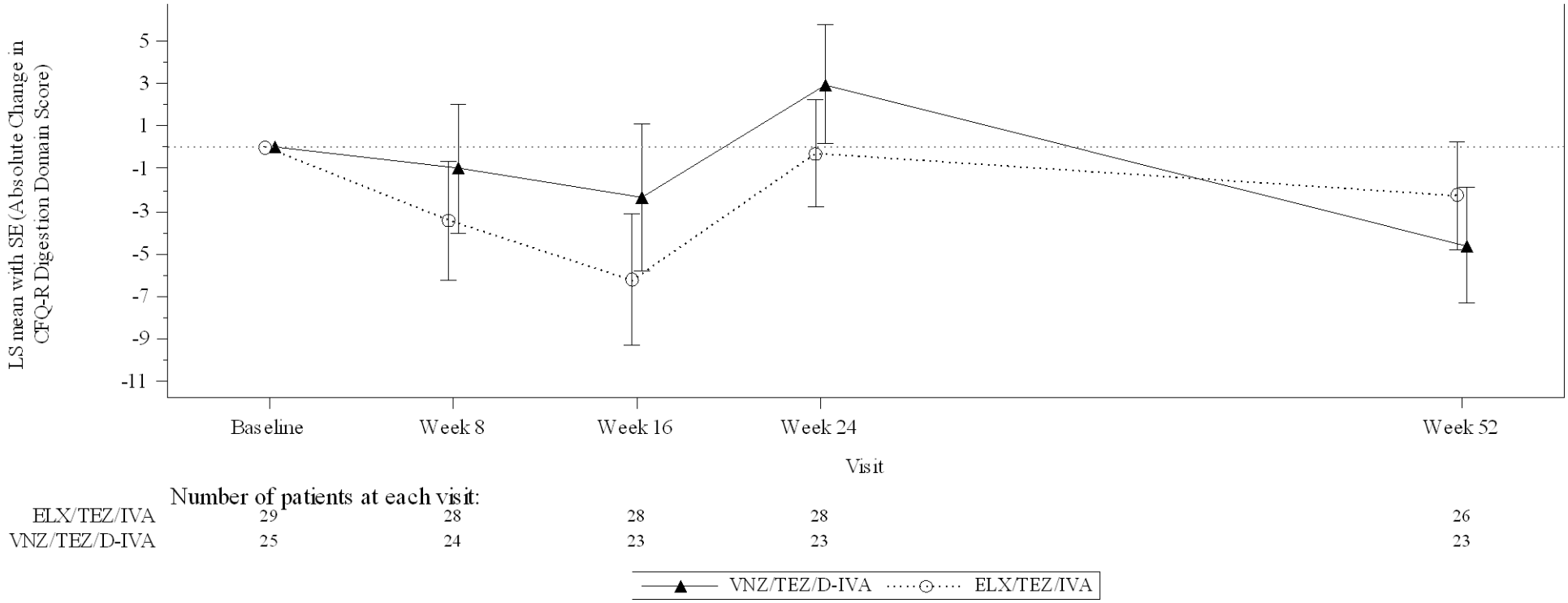
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
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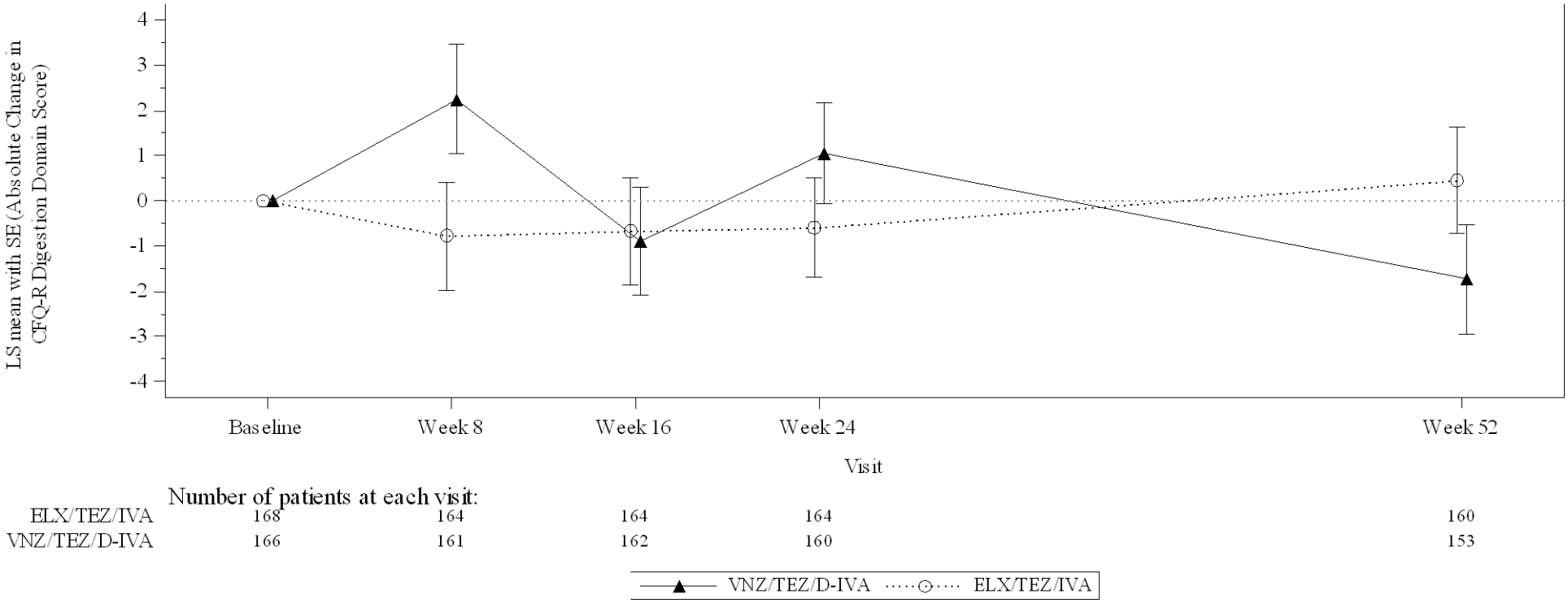
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years



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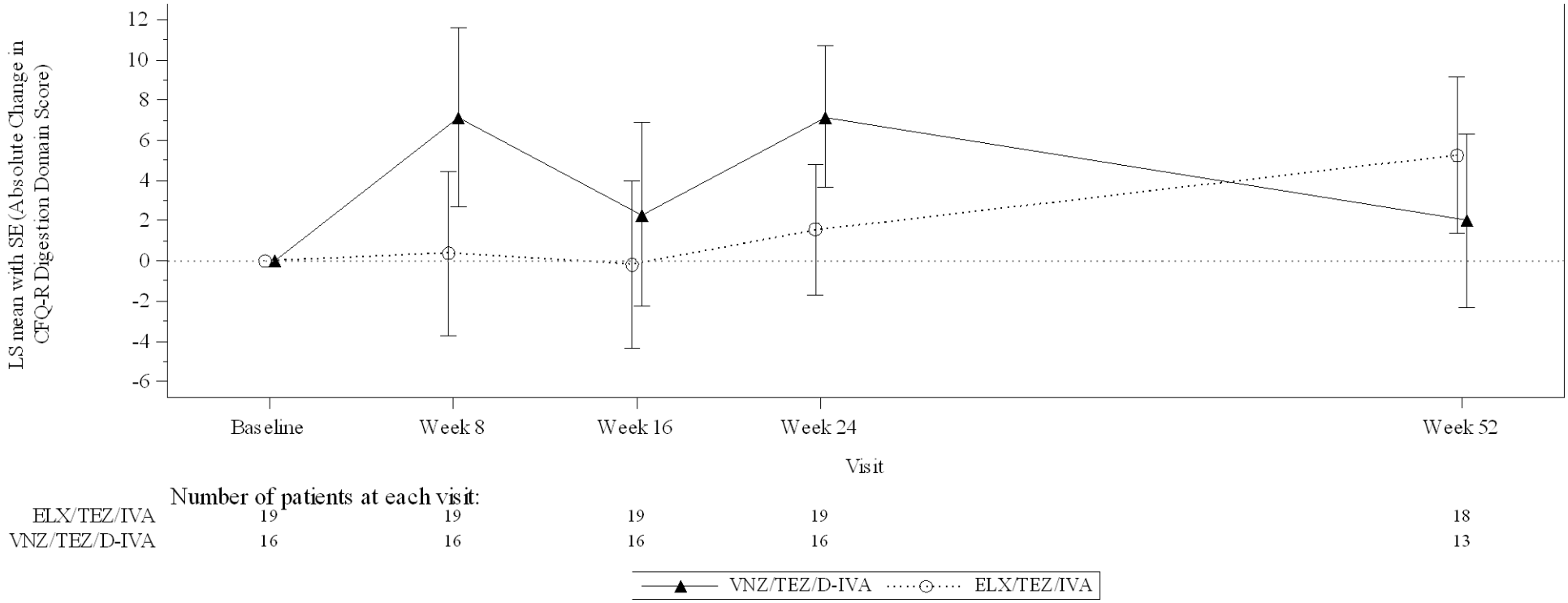
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years



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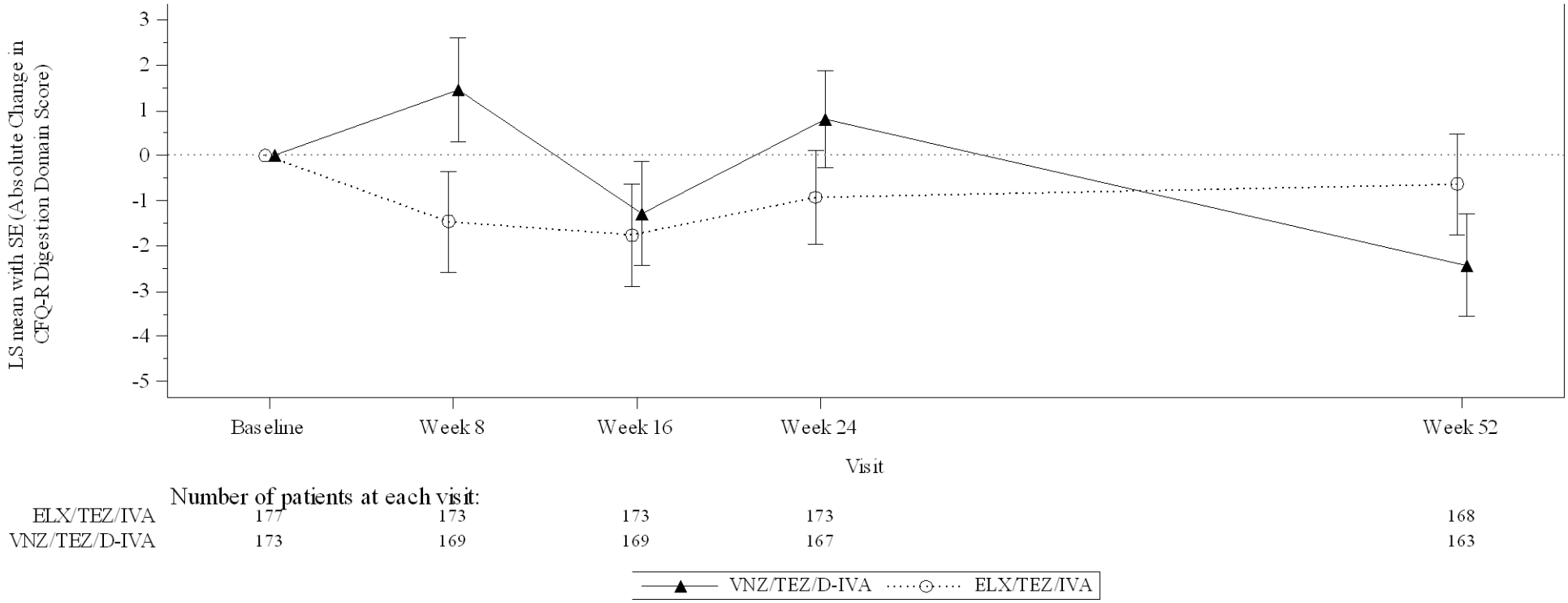
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Domain: Digestion
SwCl at baseline <30 mmol/L



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Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L



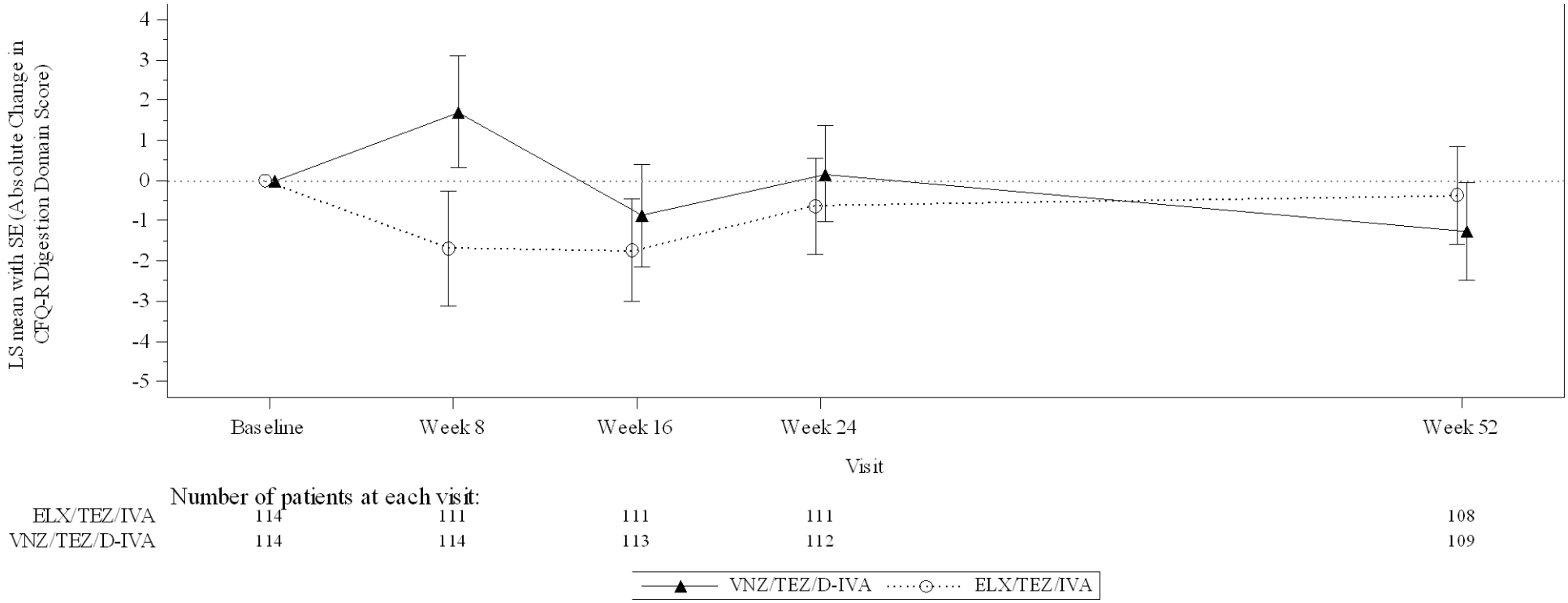
Number of patients at each visit:

ELX/TEZ/IVA	177	173	173	173	168
VNZ/TEZ/D-IVA	173	169	169	167	163

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

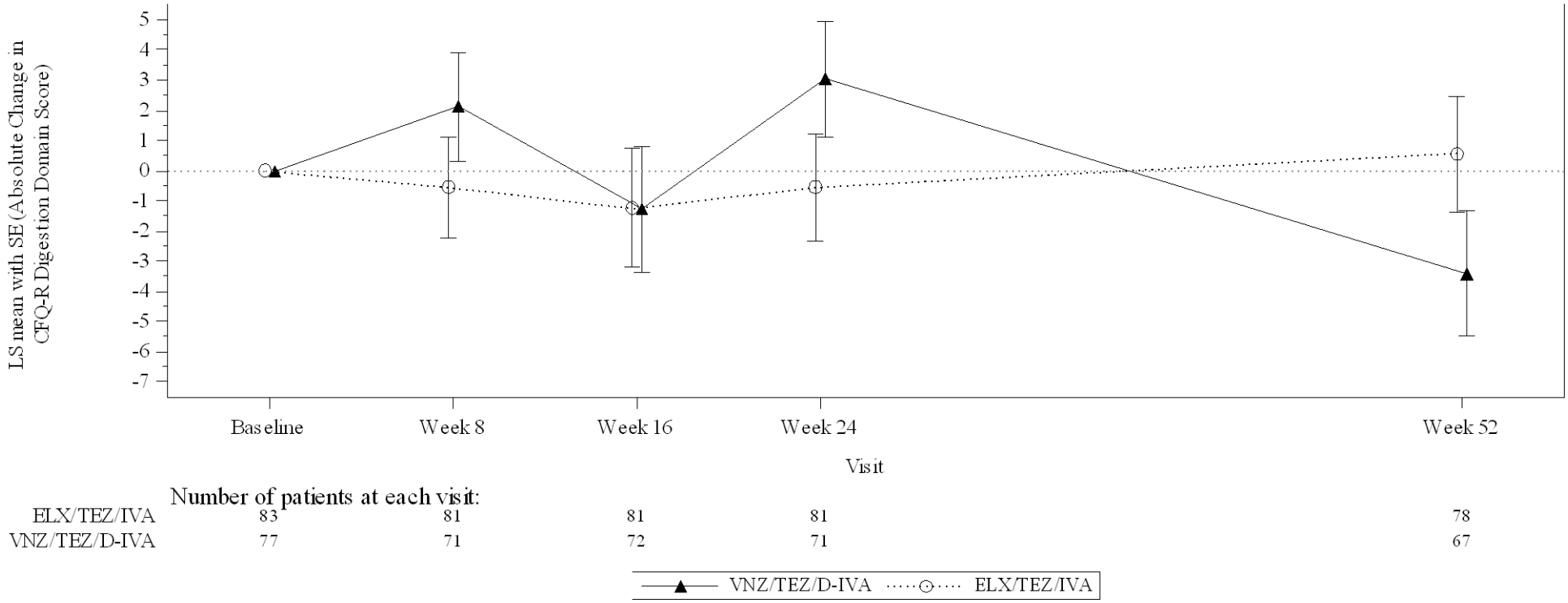
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male



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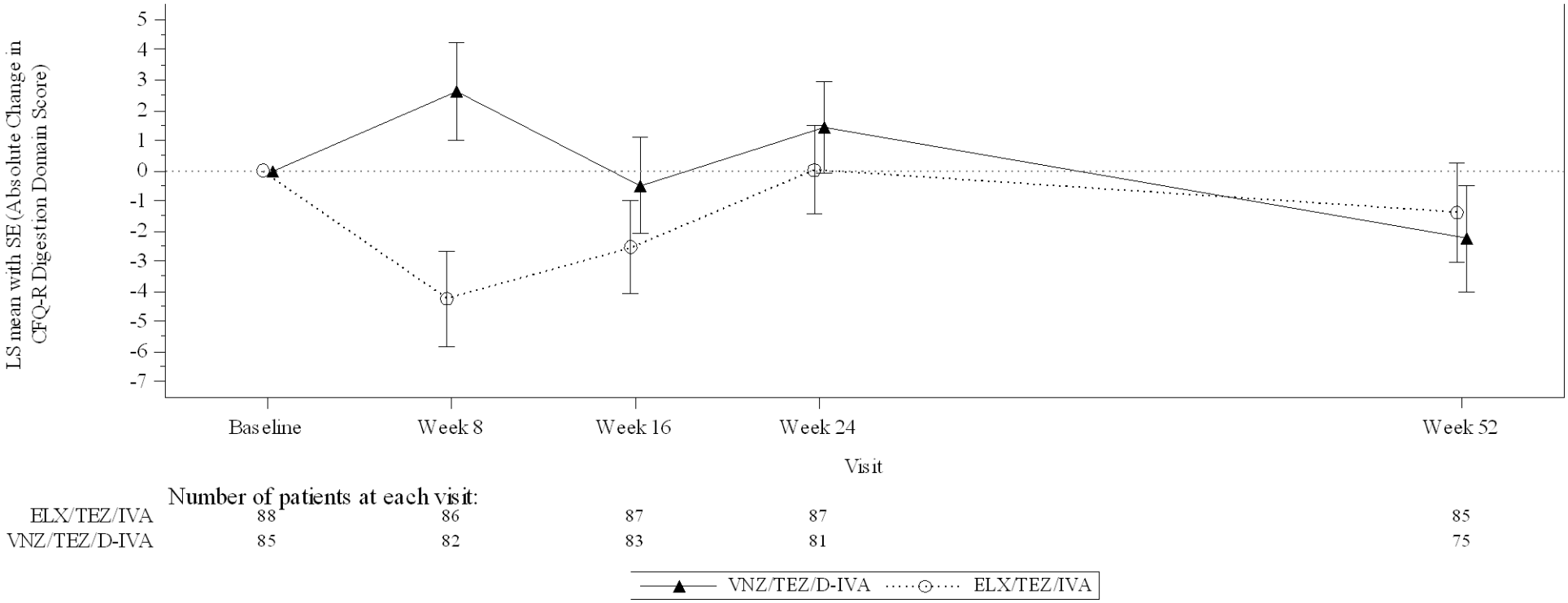
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female



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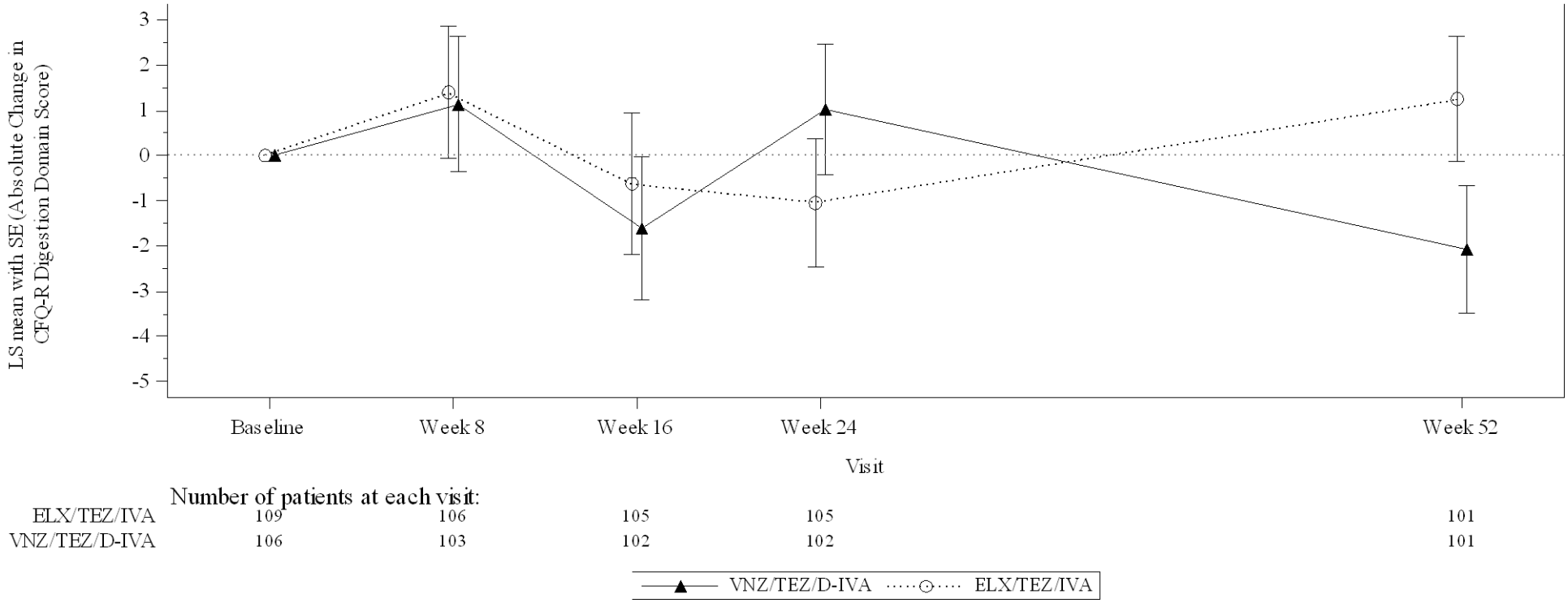
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America



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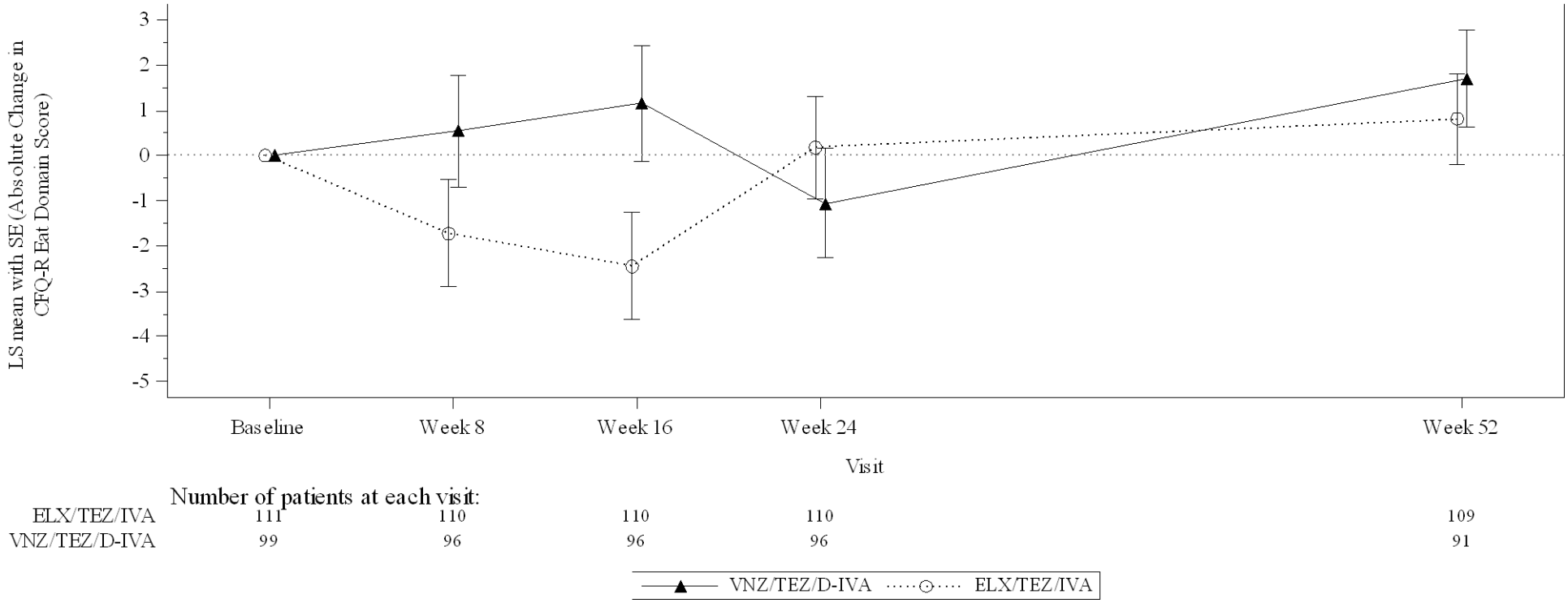
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World



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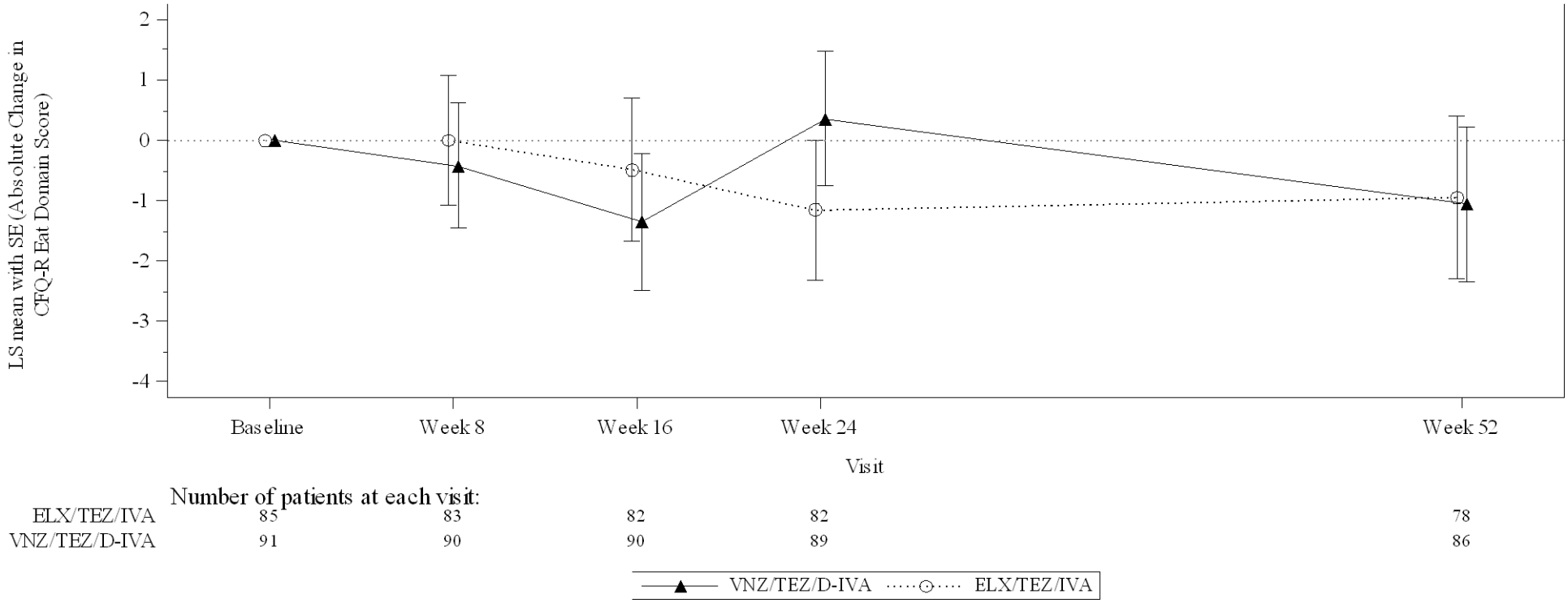
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %



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Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
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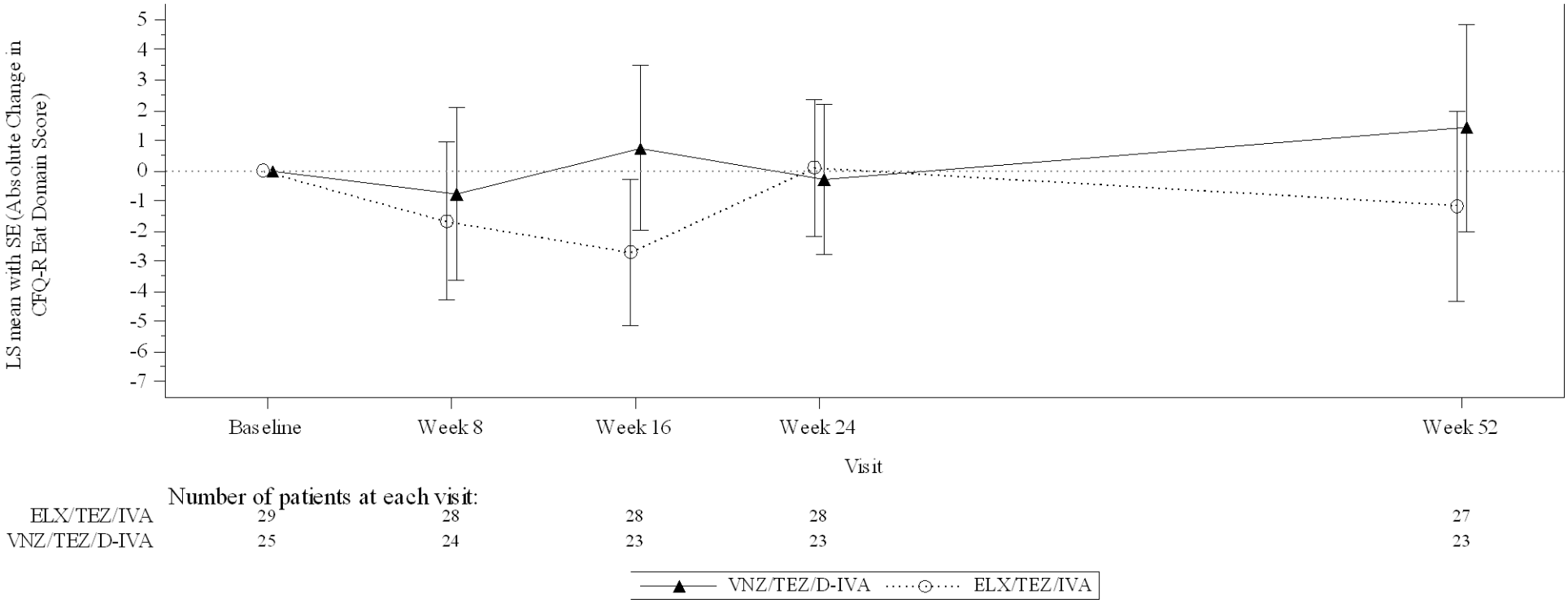
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %



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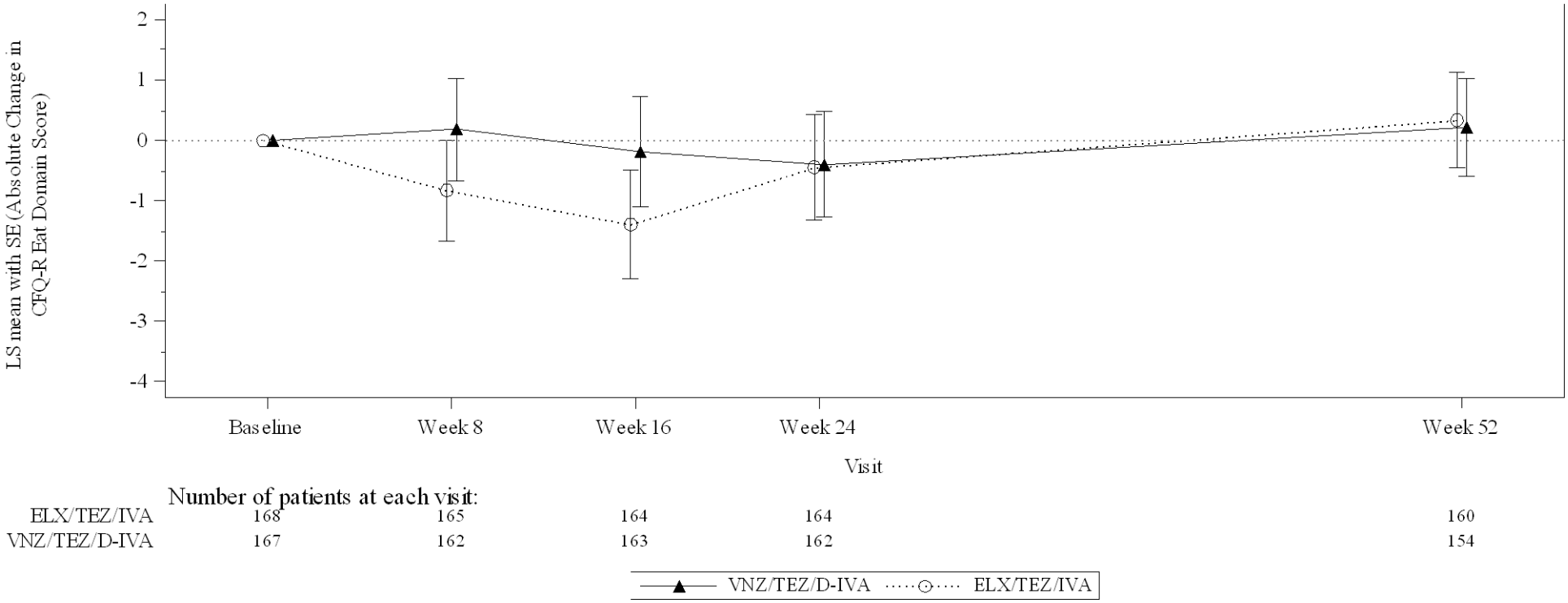
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years



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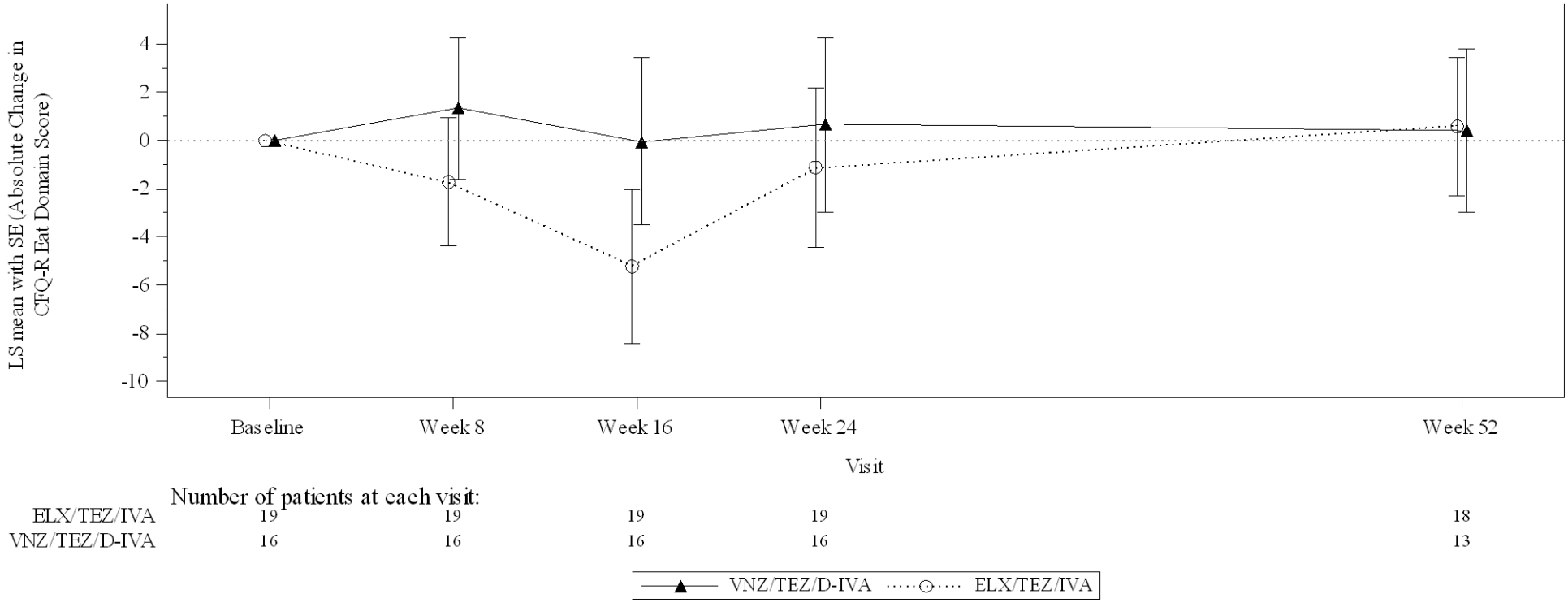
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years



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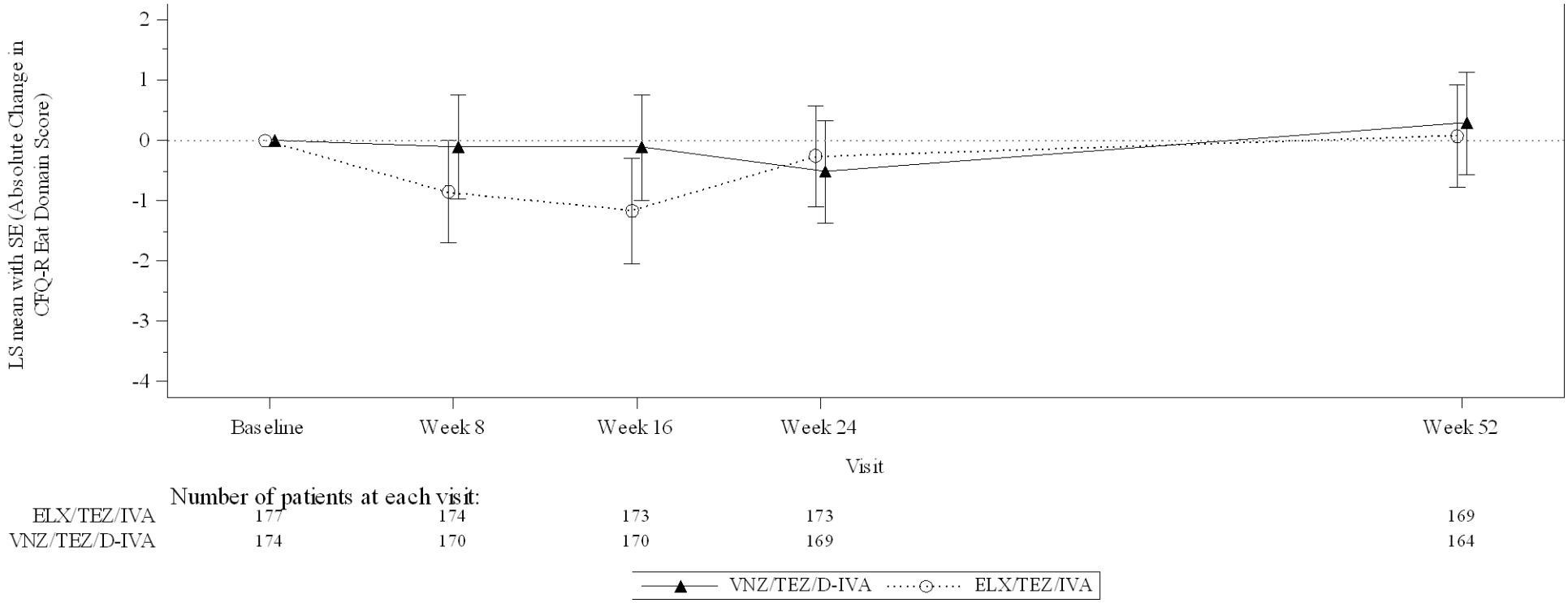
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L



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Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L



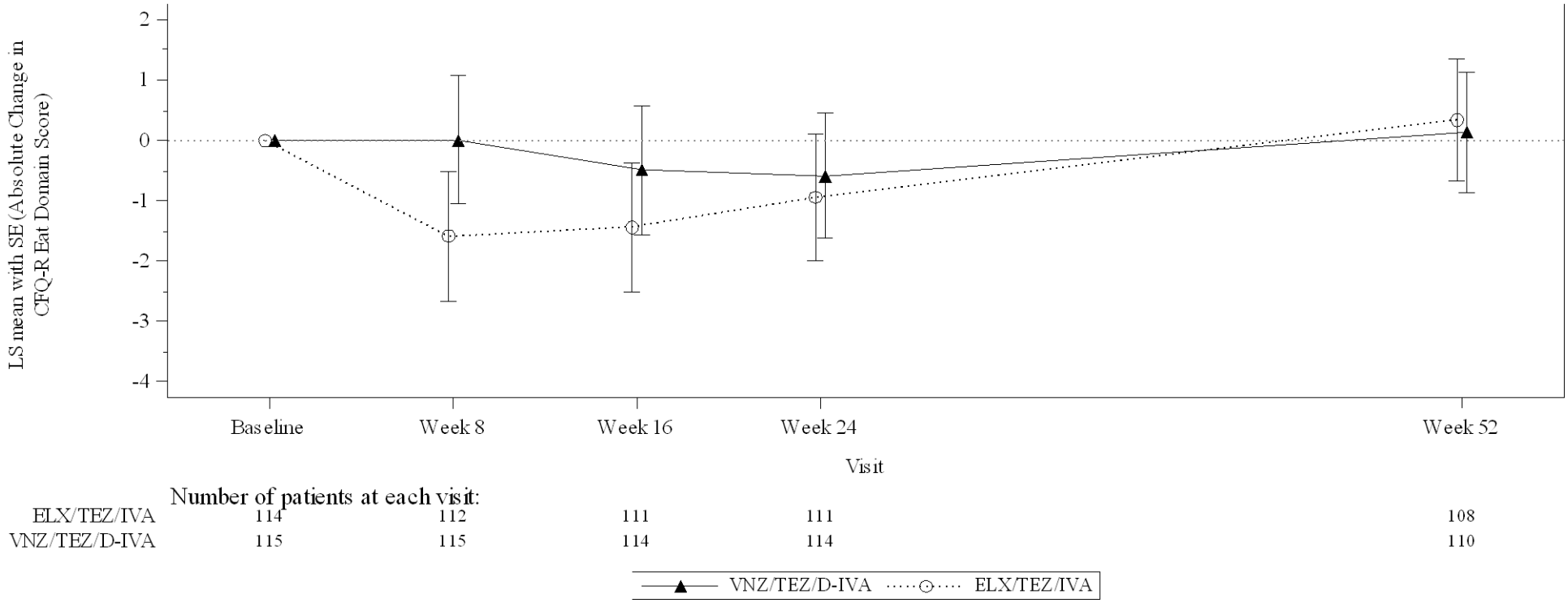
Number of patients at each visit:

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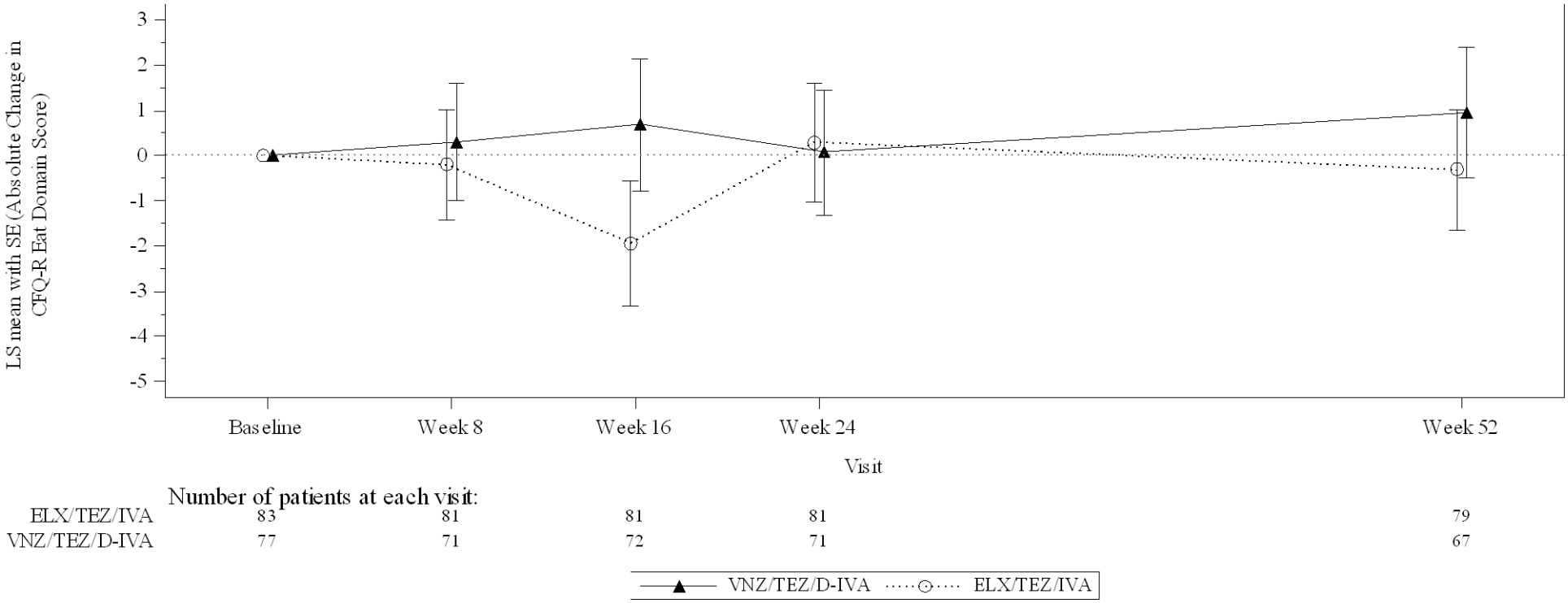
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male



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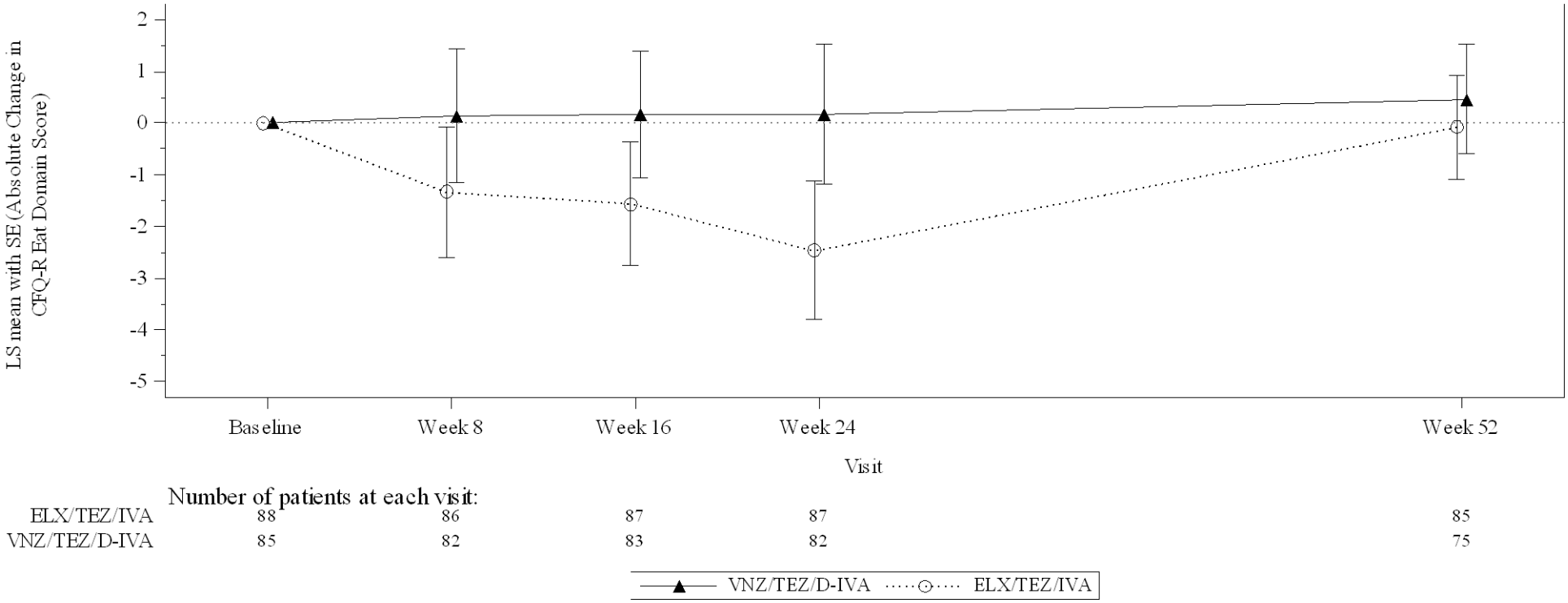
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female



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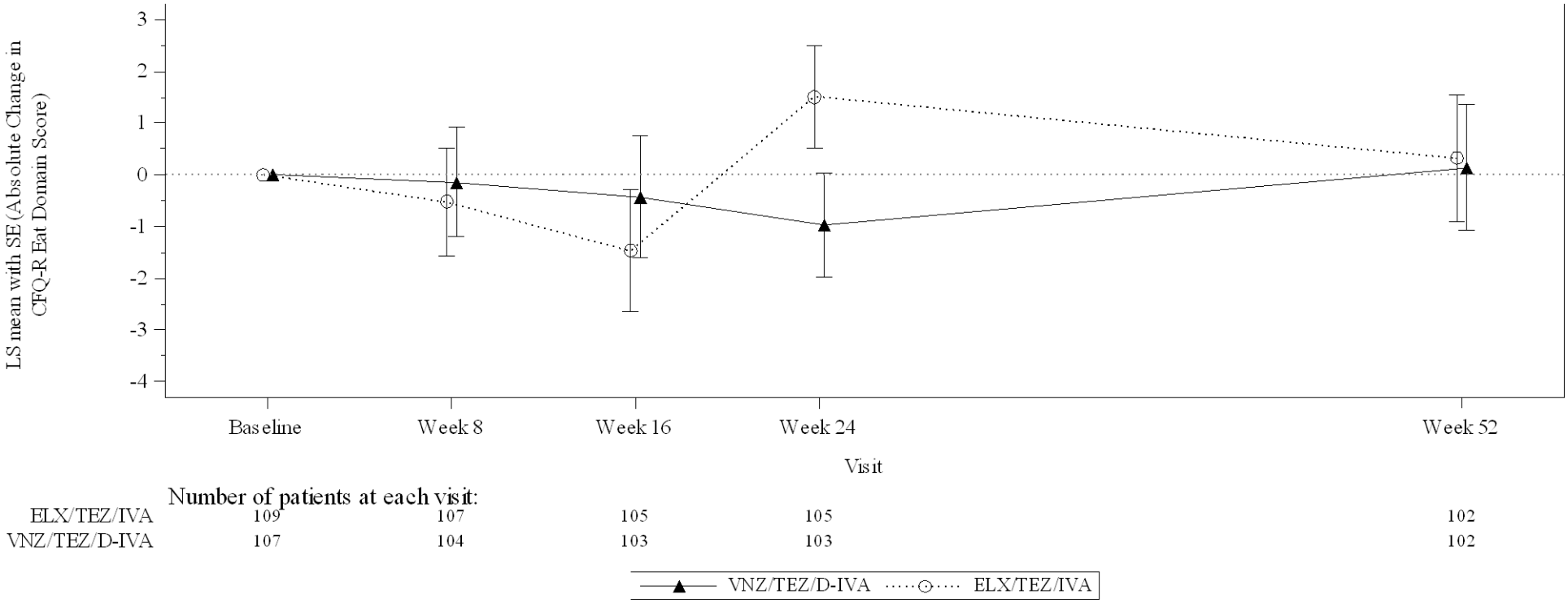
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America



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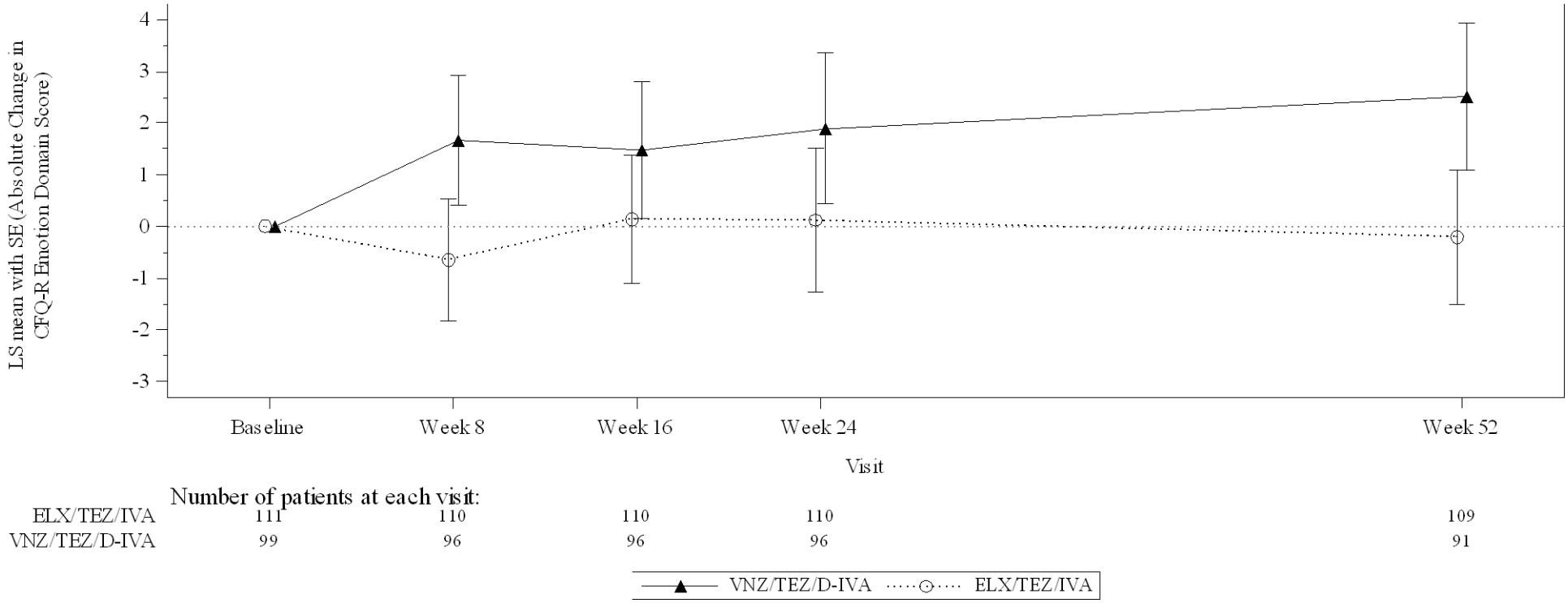
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
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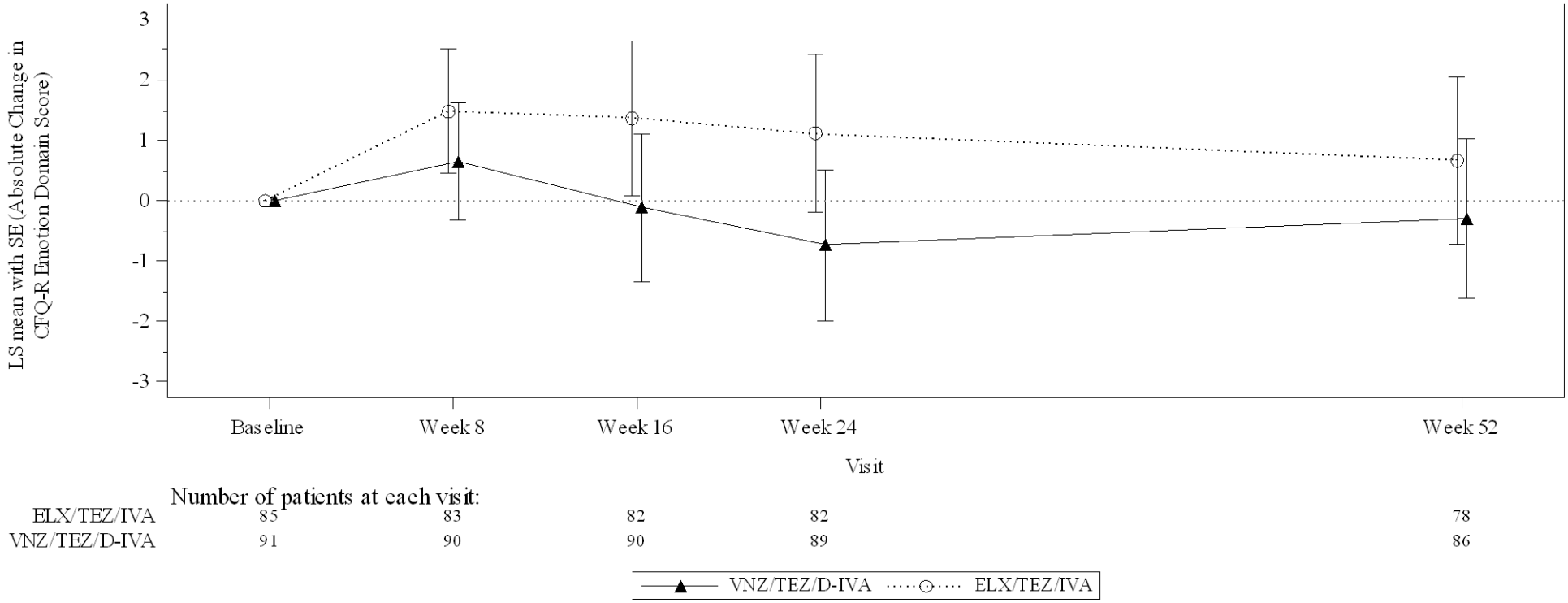
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %



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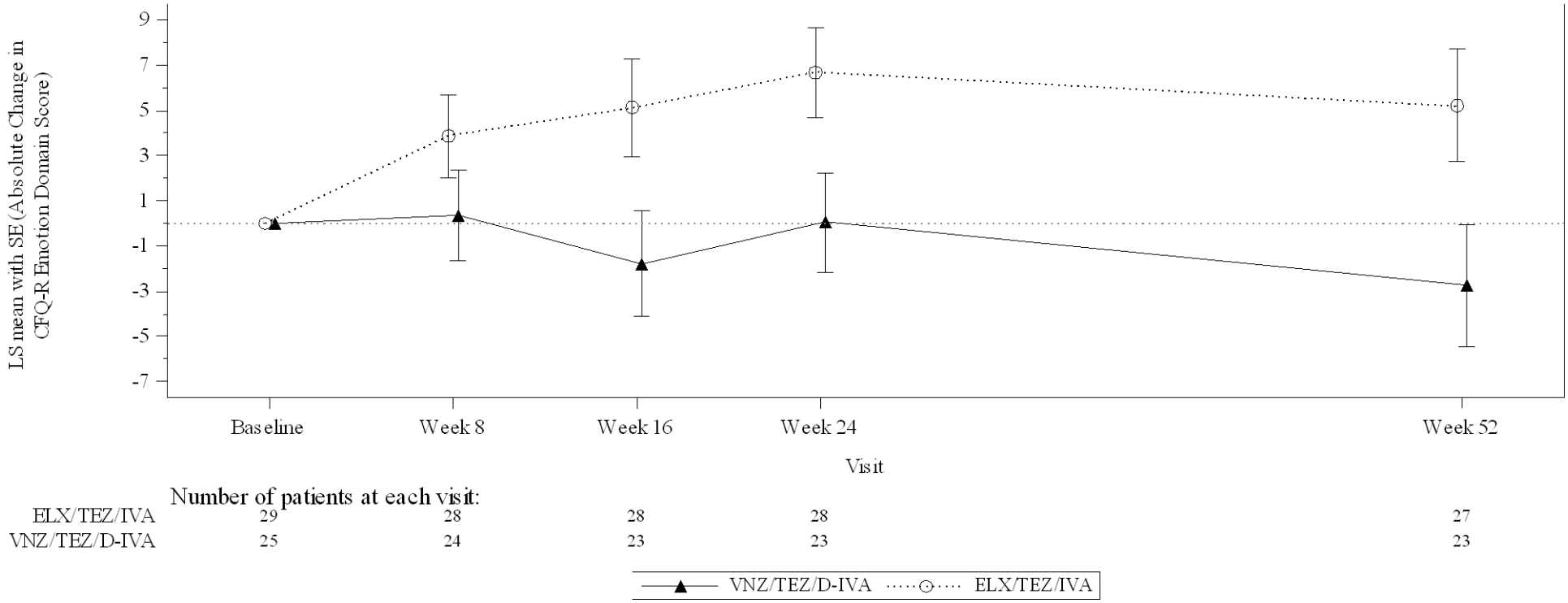
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %



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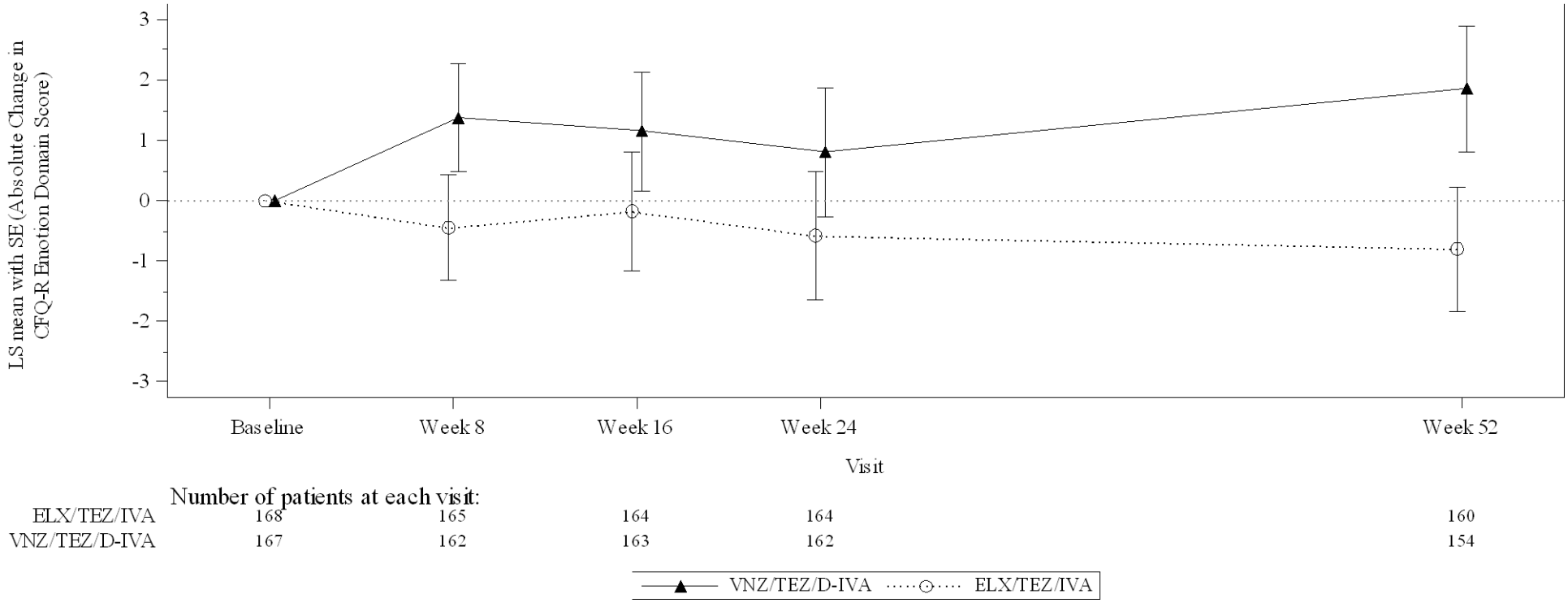
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years



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Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years



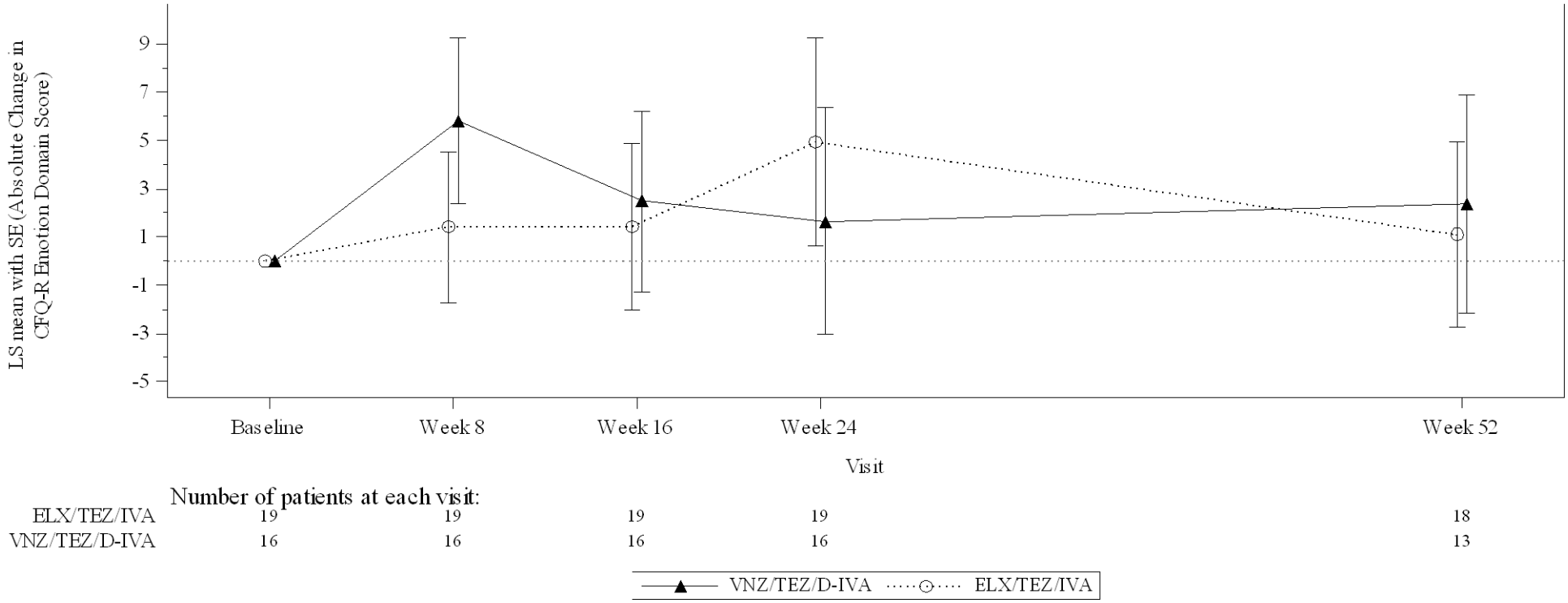
Number of patients at each visit:

	Baseline	Week 8	Week 16	Week 24	Week 52
ELX/TEZ/IVA	168	165	164	164	160
VNZ/TEZ/D-IVA	167	162	163	162	154

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

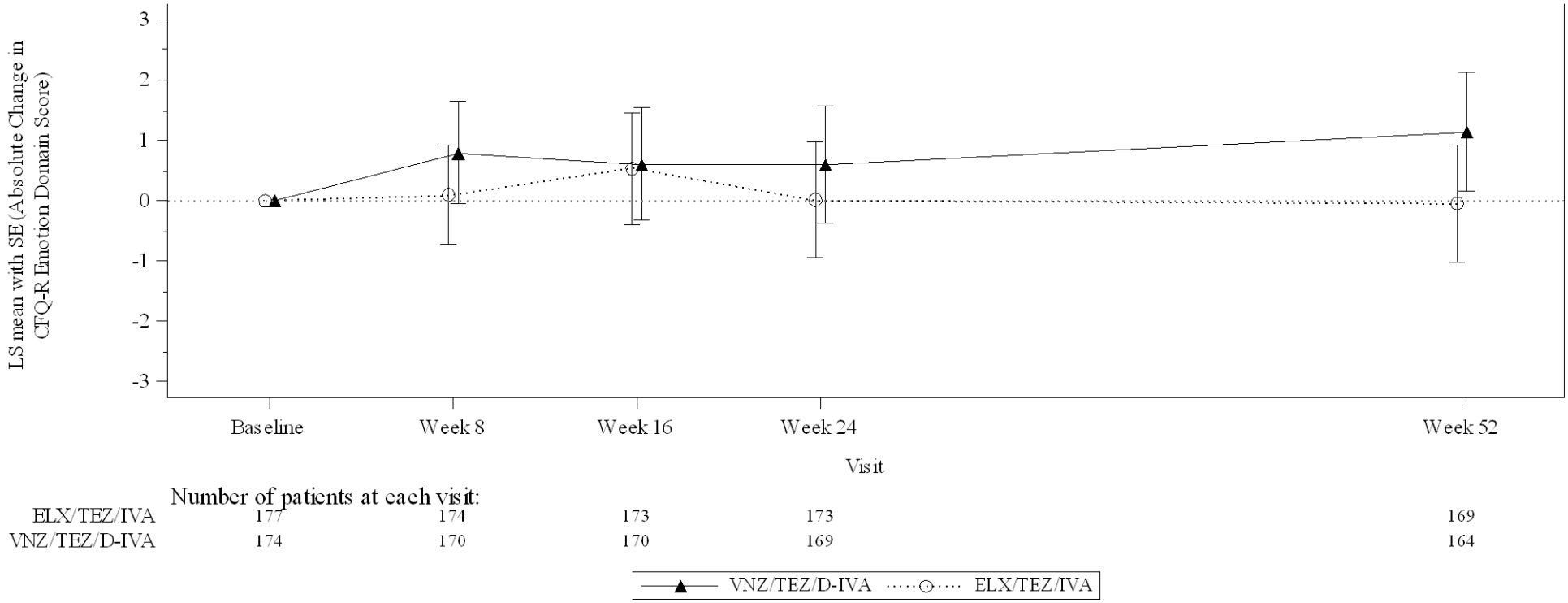
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L



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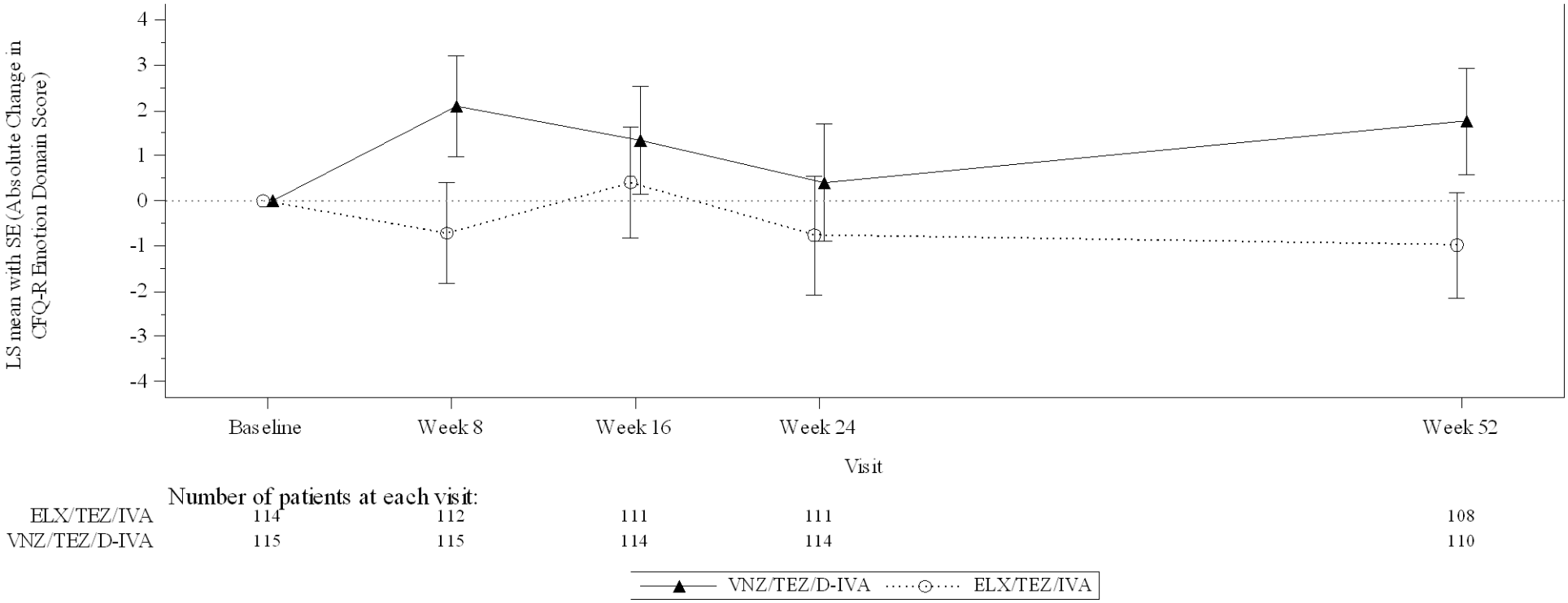
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L



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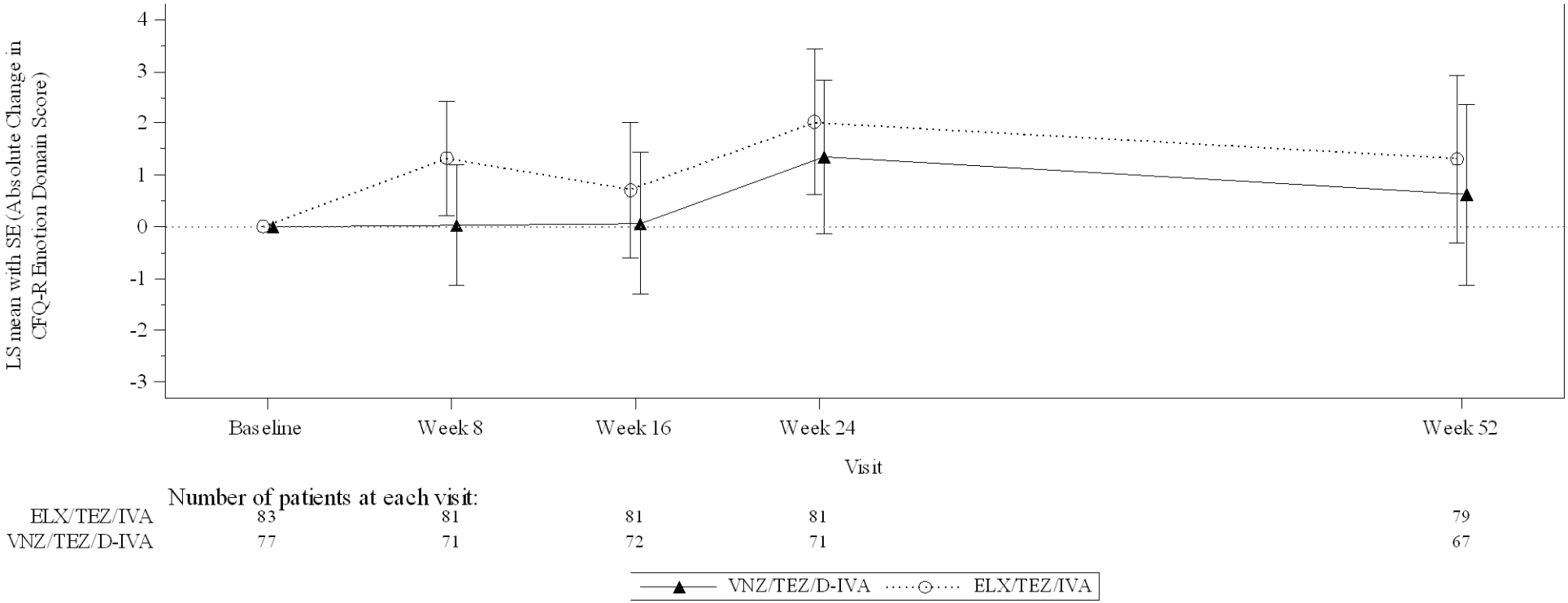
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male



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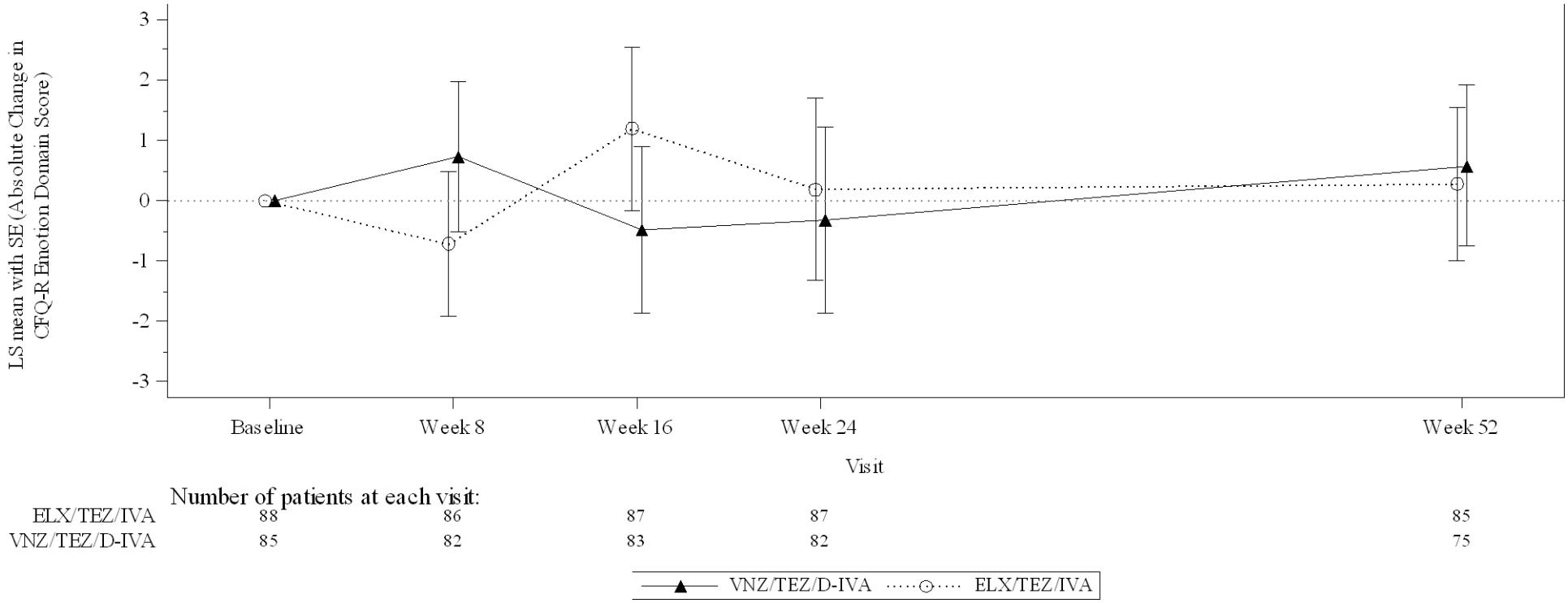
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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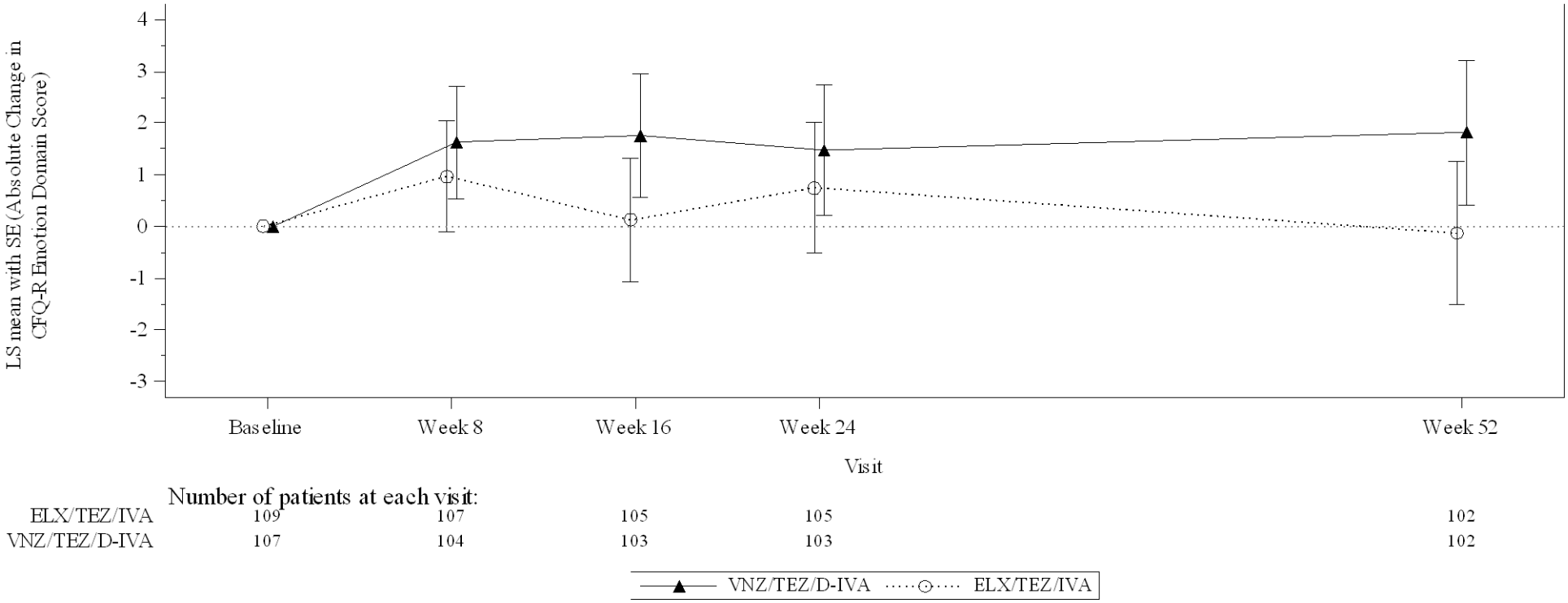
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America



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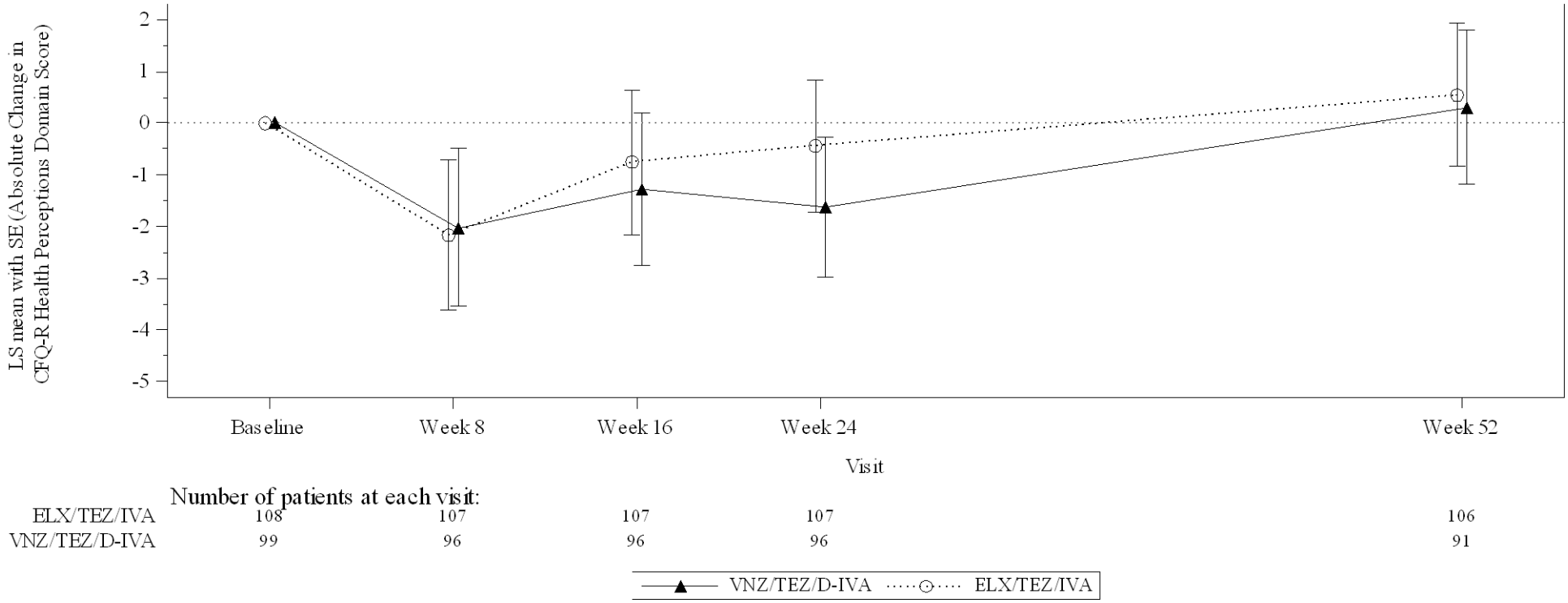
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World



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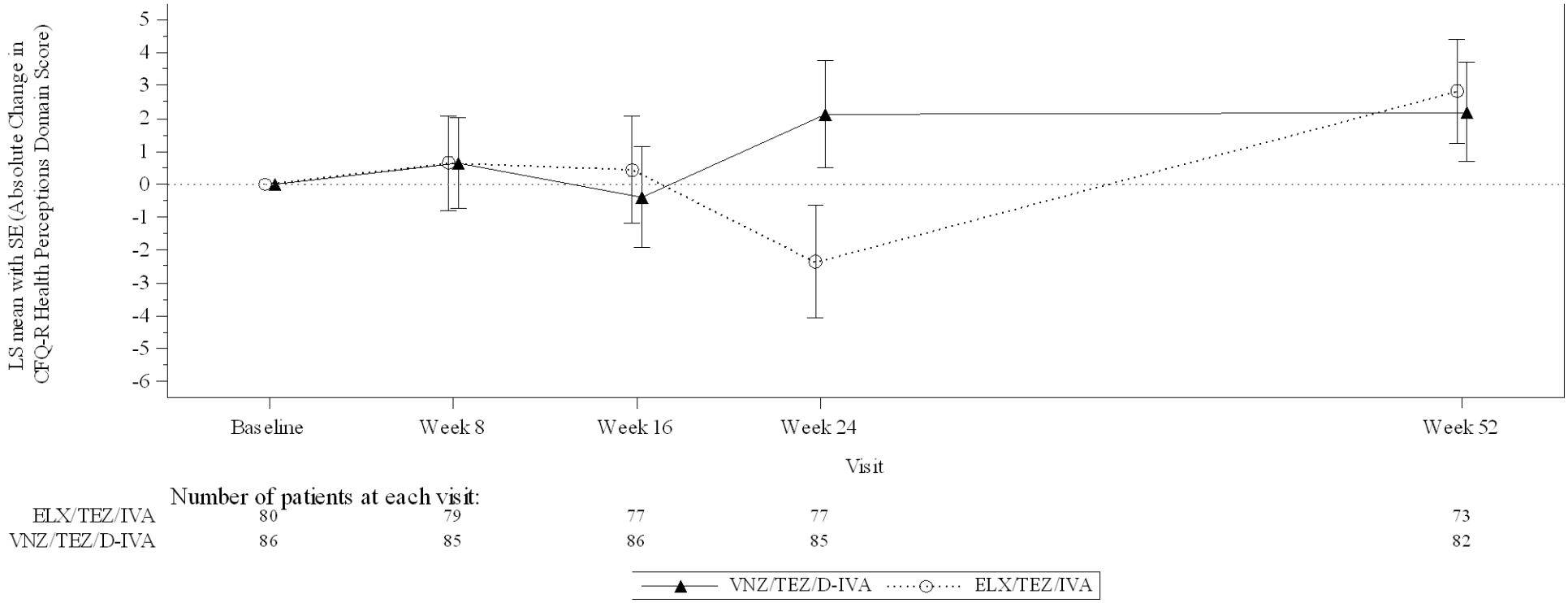
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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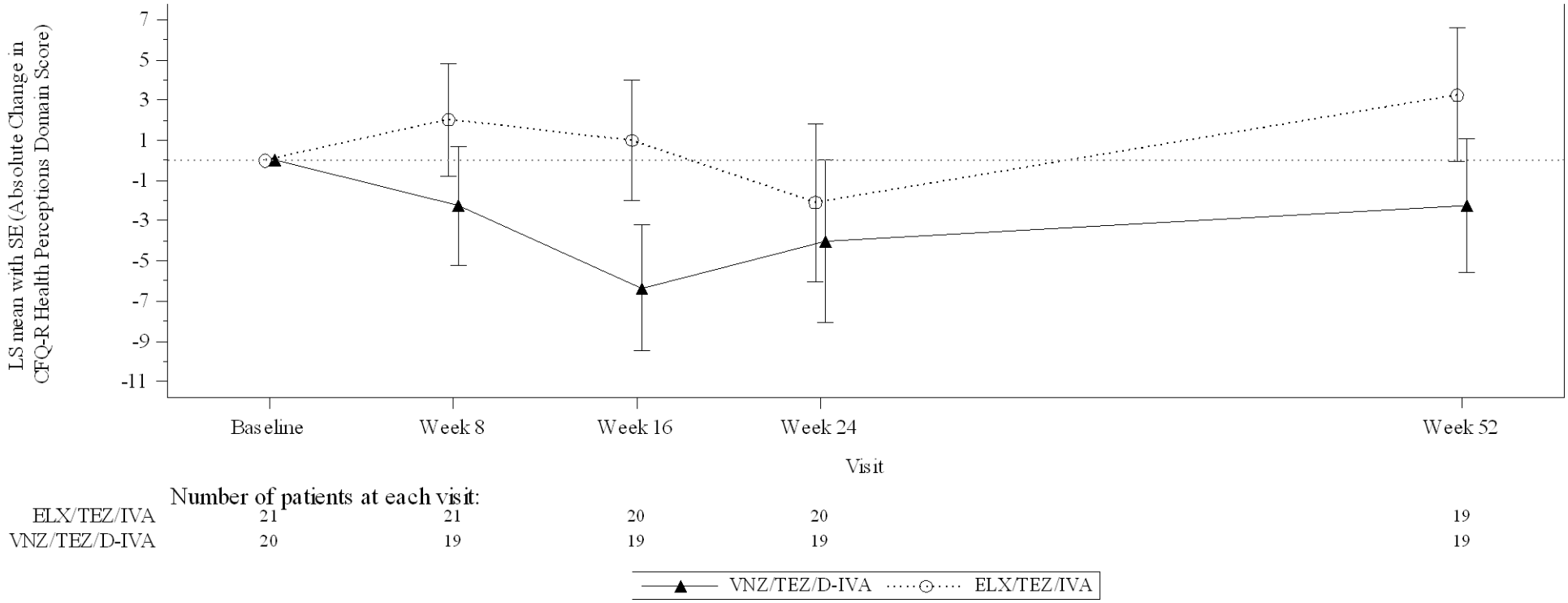
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %



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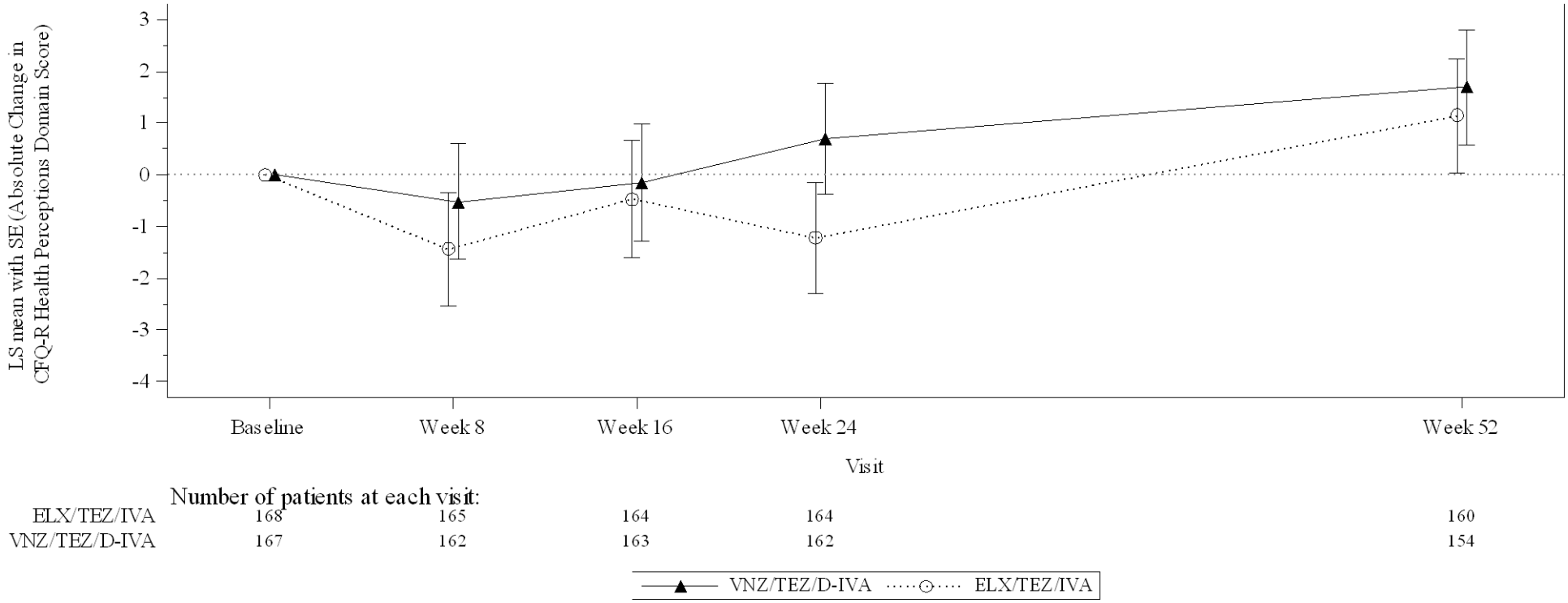
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years



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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years



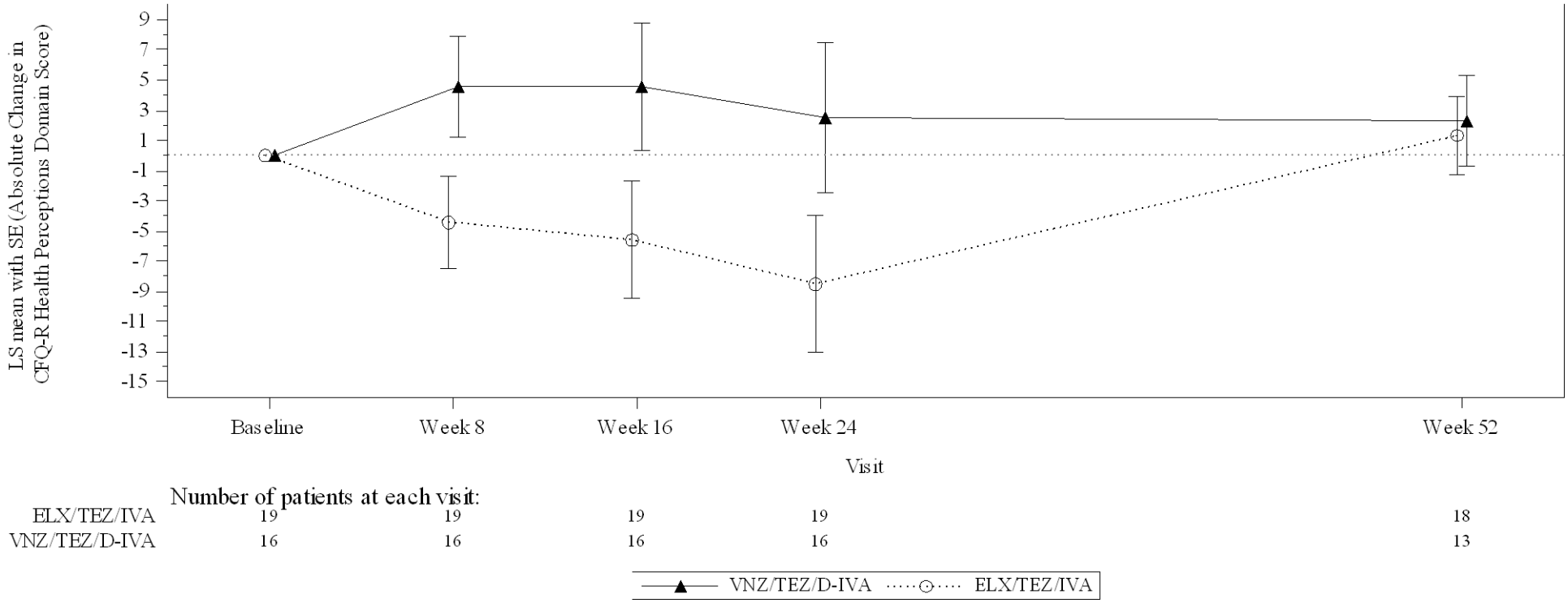
Number of patients at each visit:

	Baseline	Week 8	Week 16	Week 24	Week 52
ELX/TEZ/IVA	168	165	164	164	160
VNZ/TEZ/D-IVA	167	162	163	162	154

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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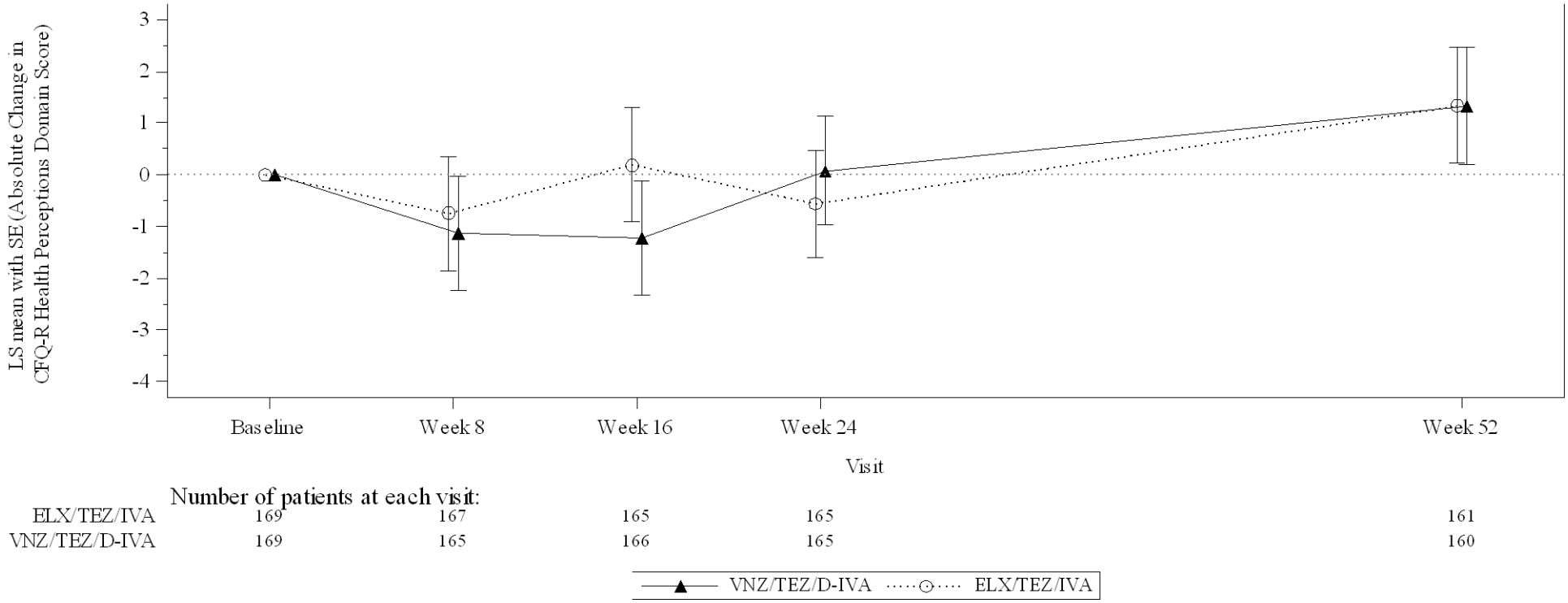
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L



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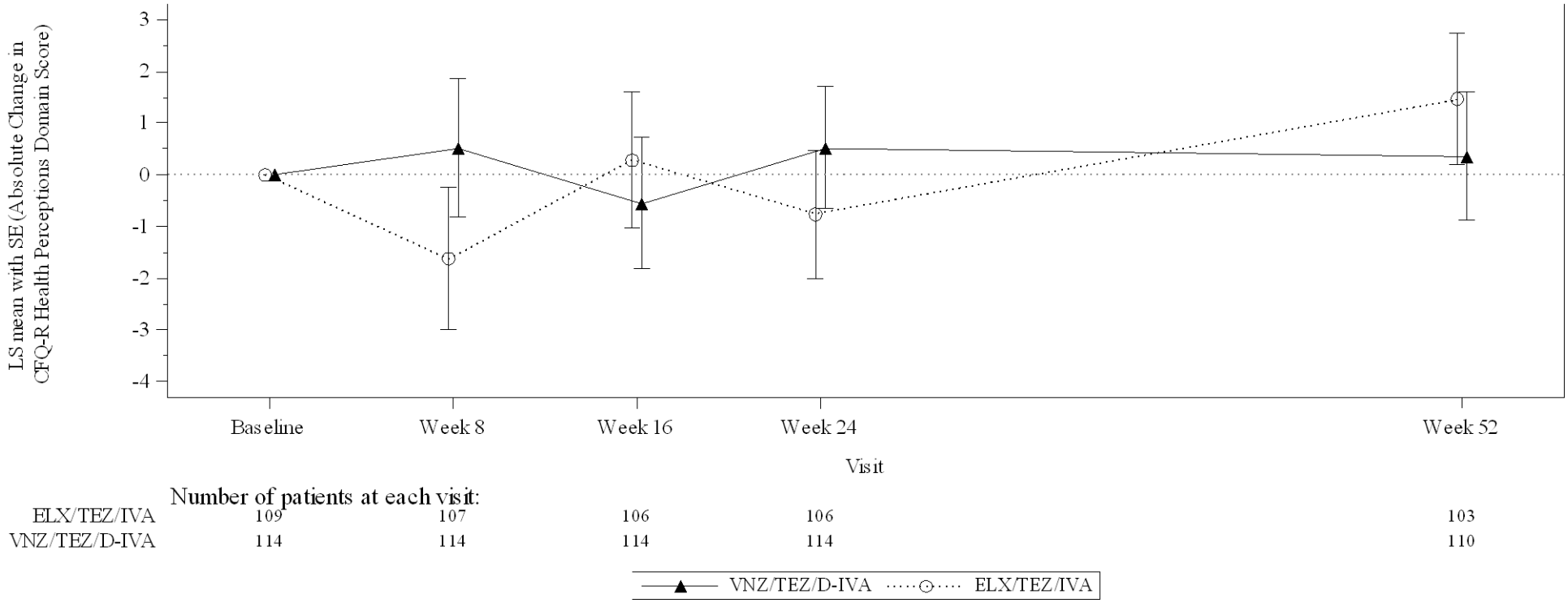
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L



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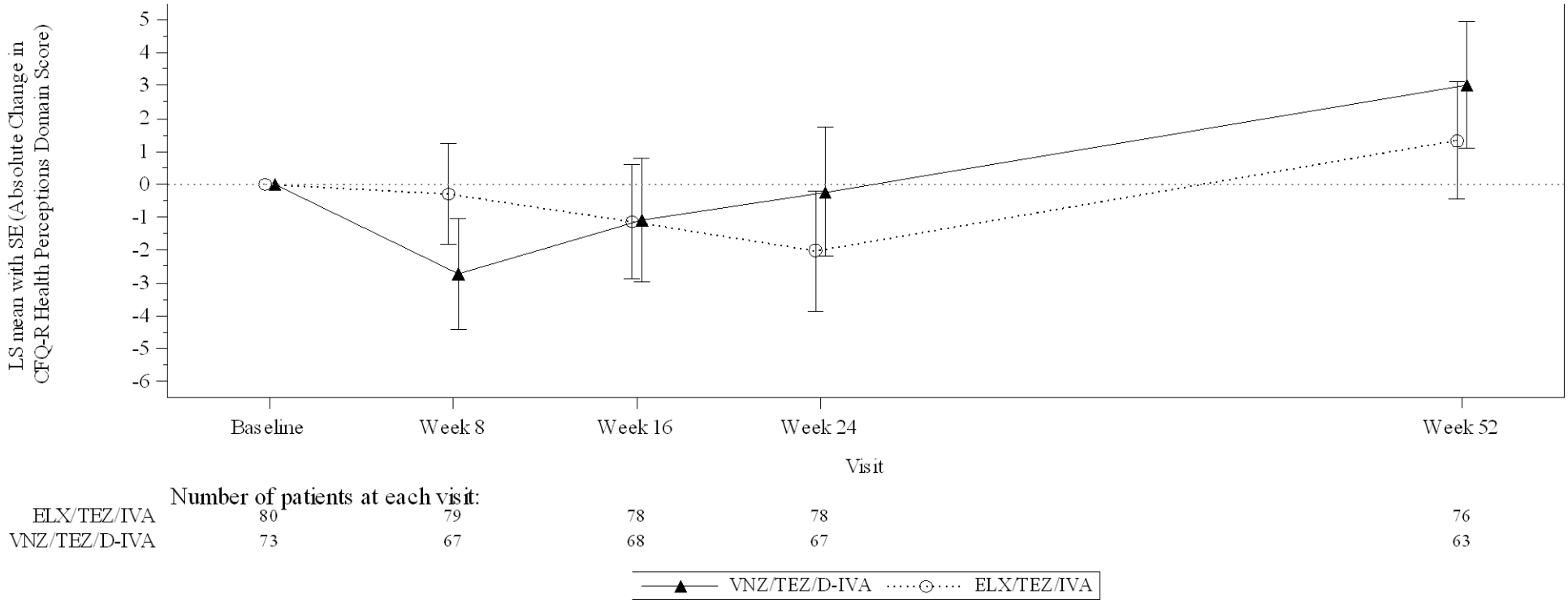
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male



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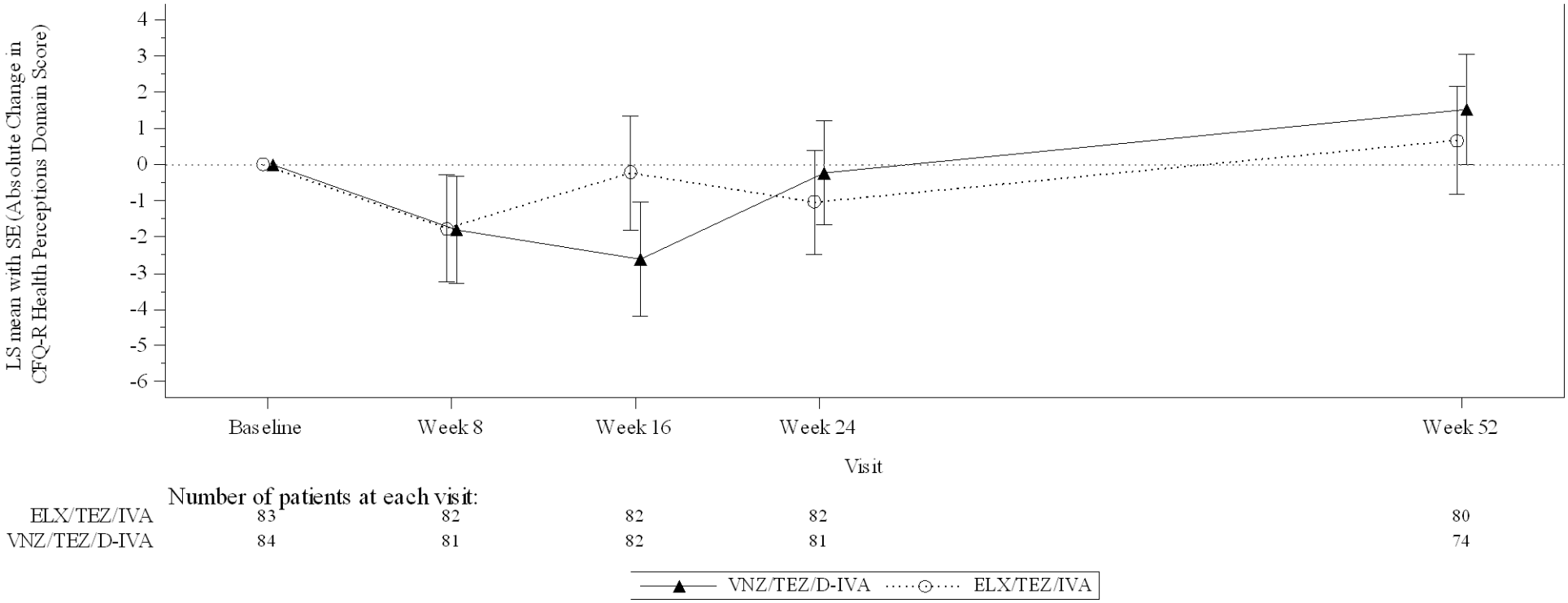
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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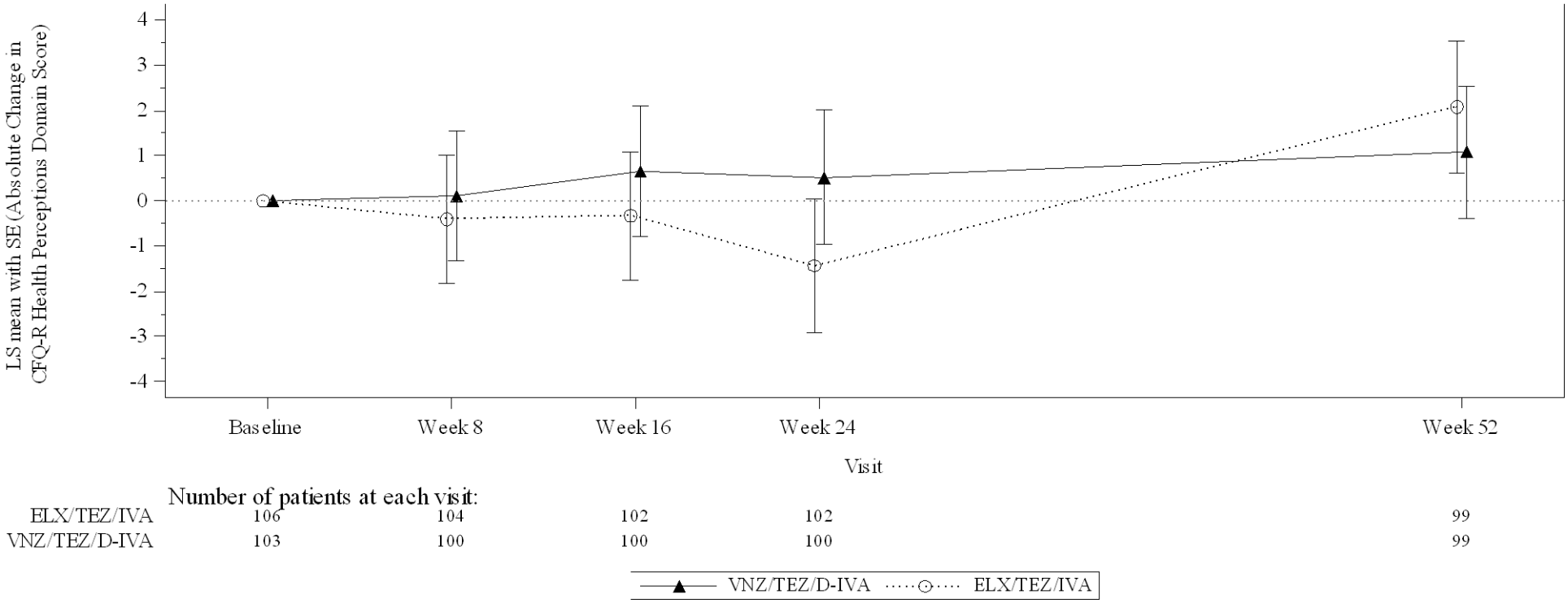
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America



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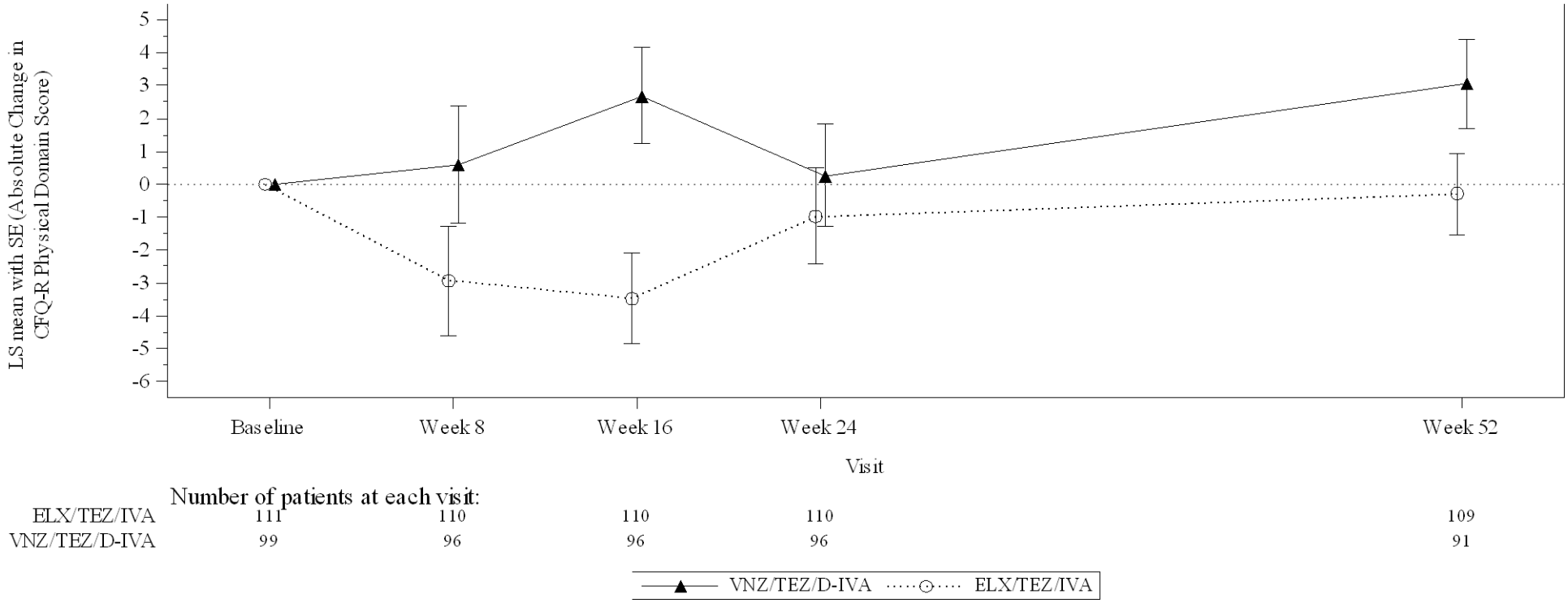
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Domain: Health Perceptions
Region = Rest of World



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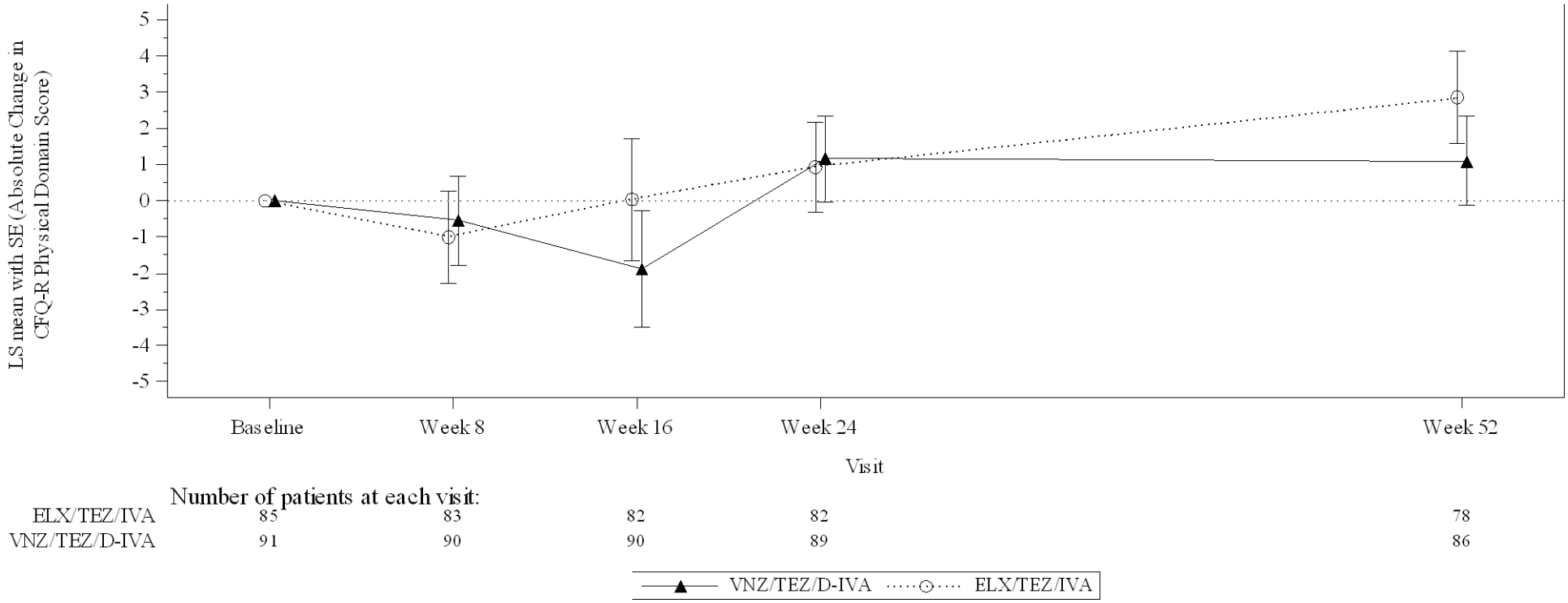
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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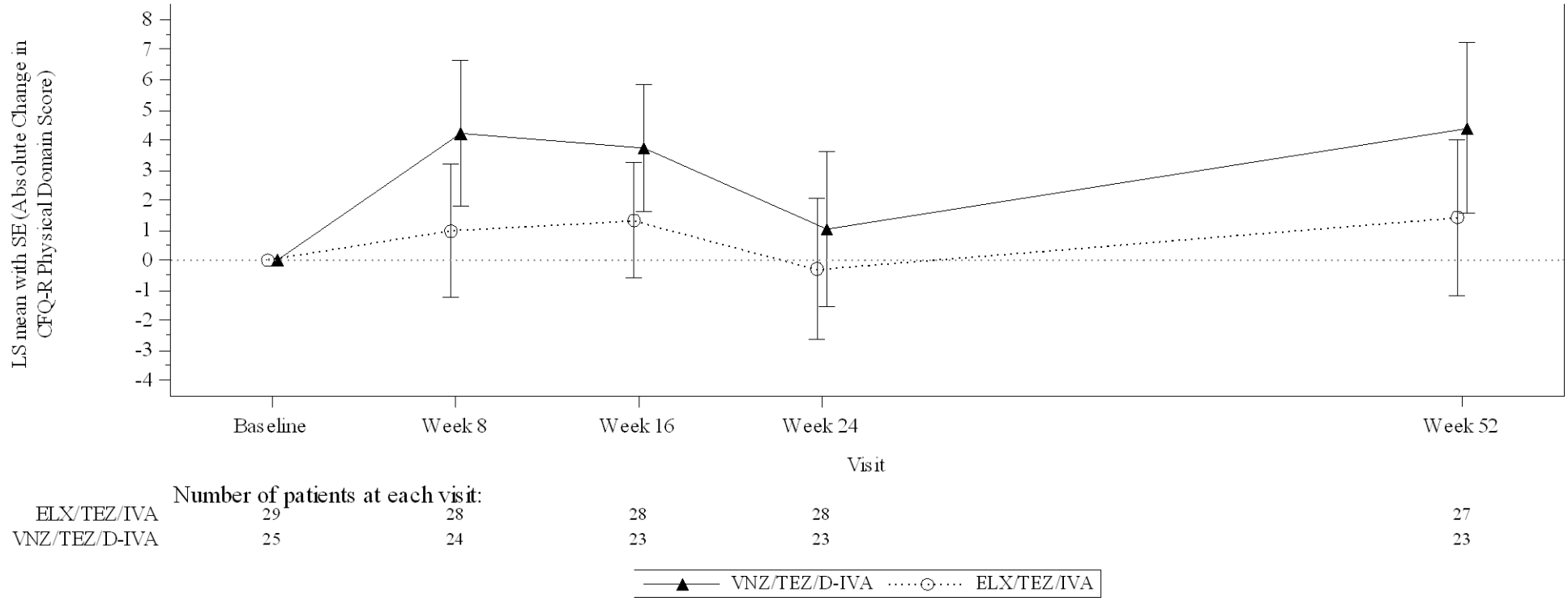
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline ≥70 %



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Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

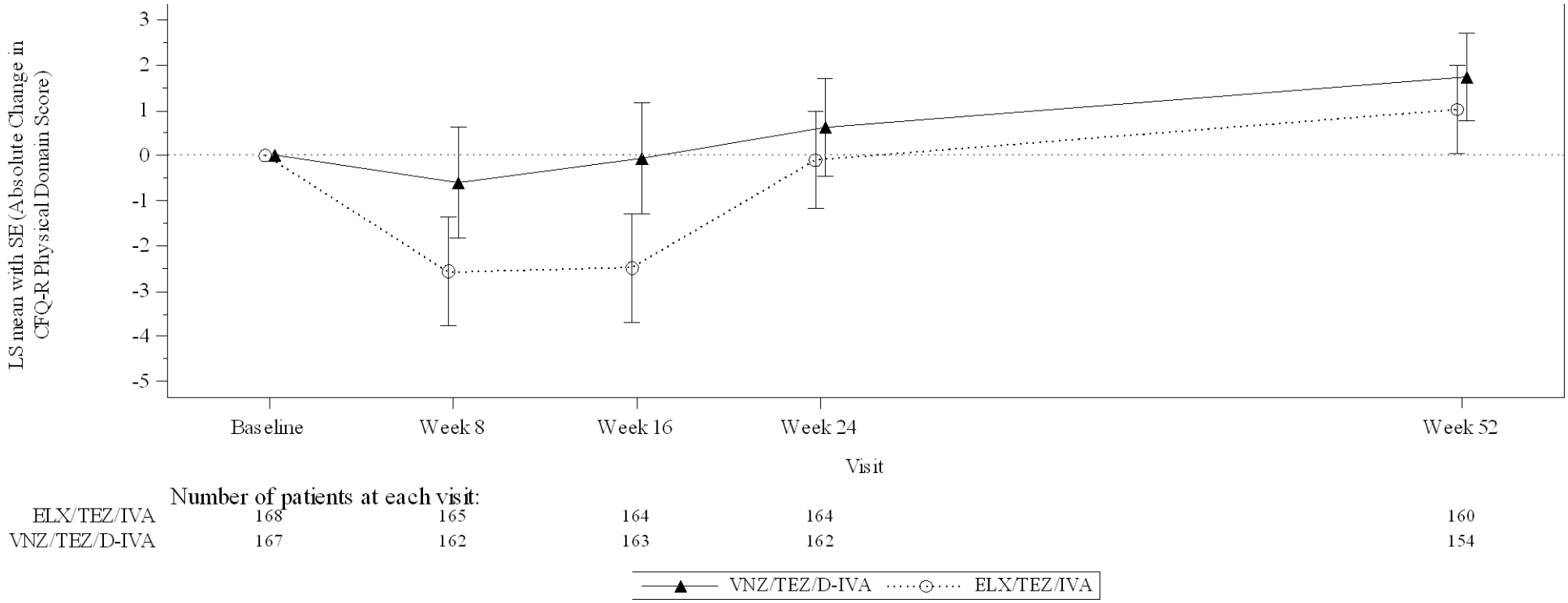
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

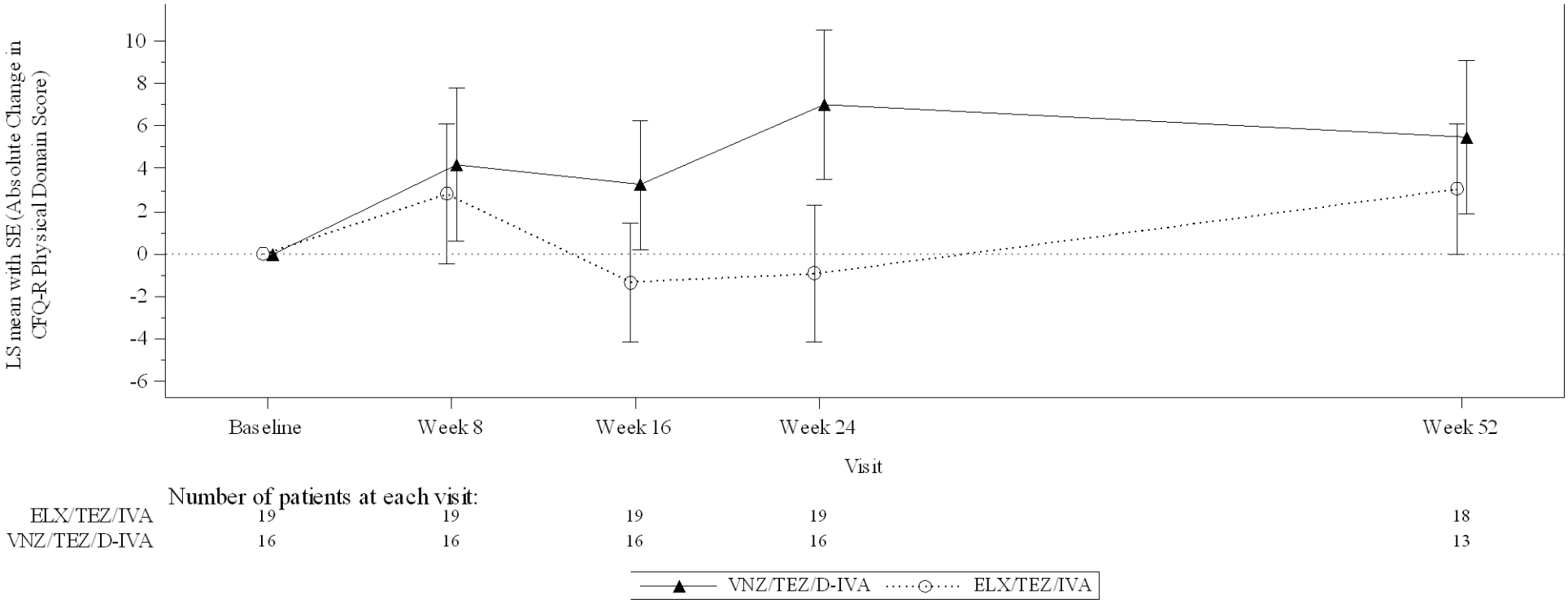
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years



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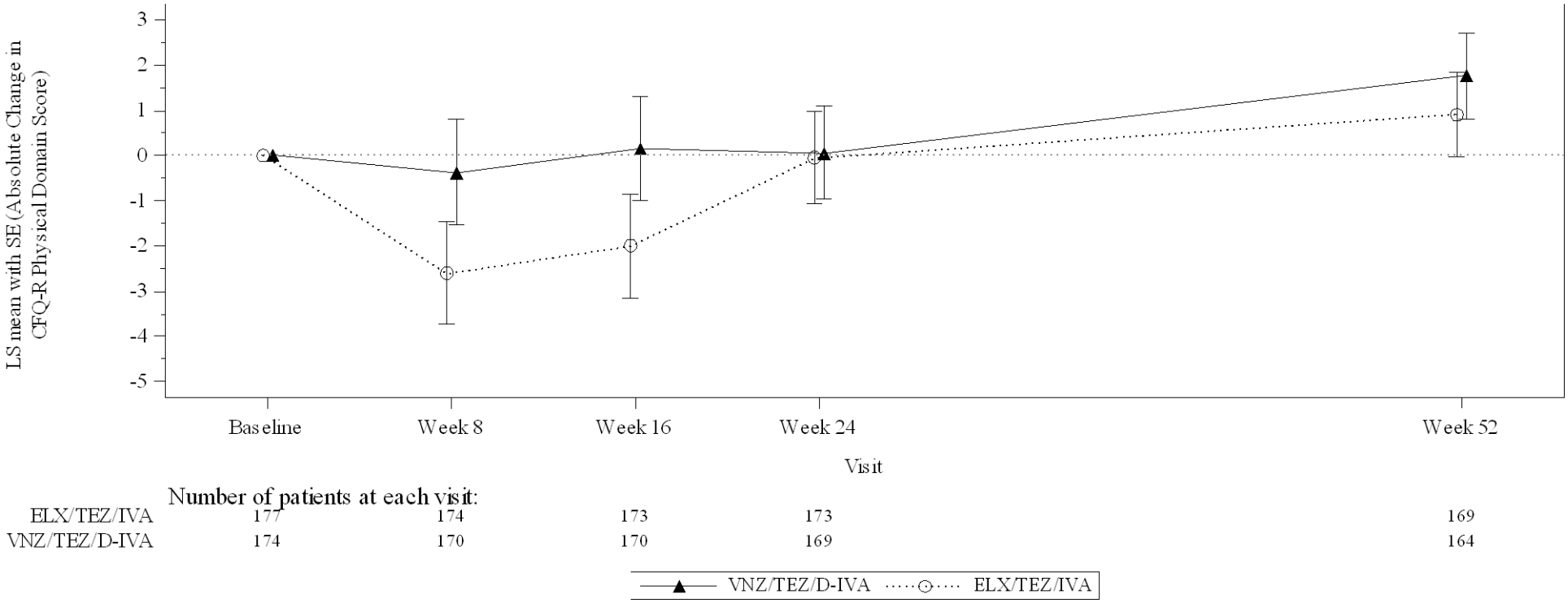
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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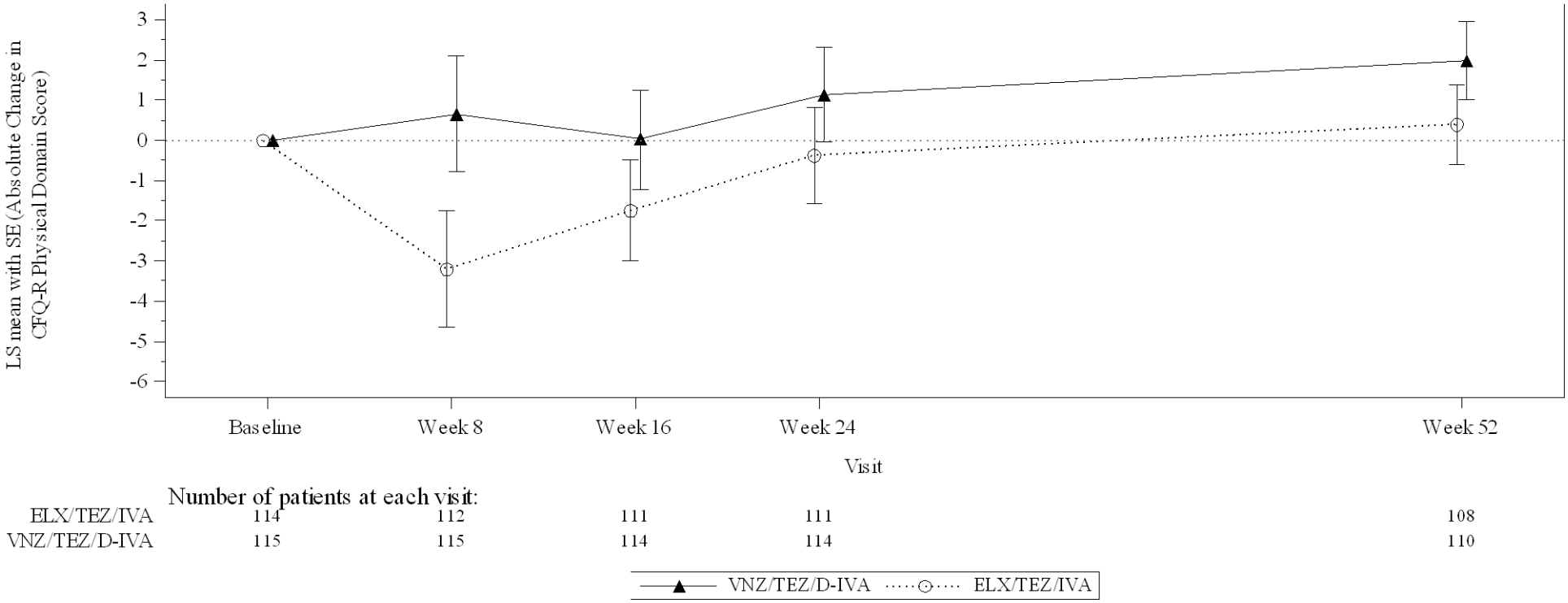
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L



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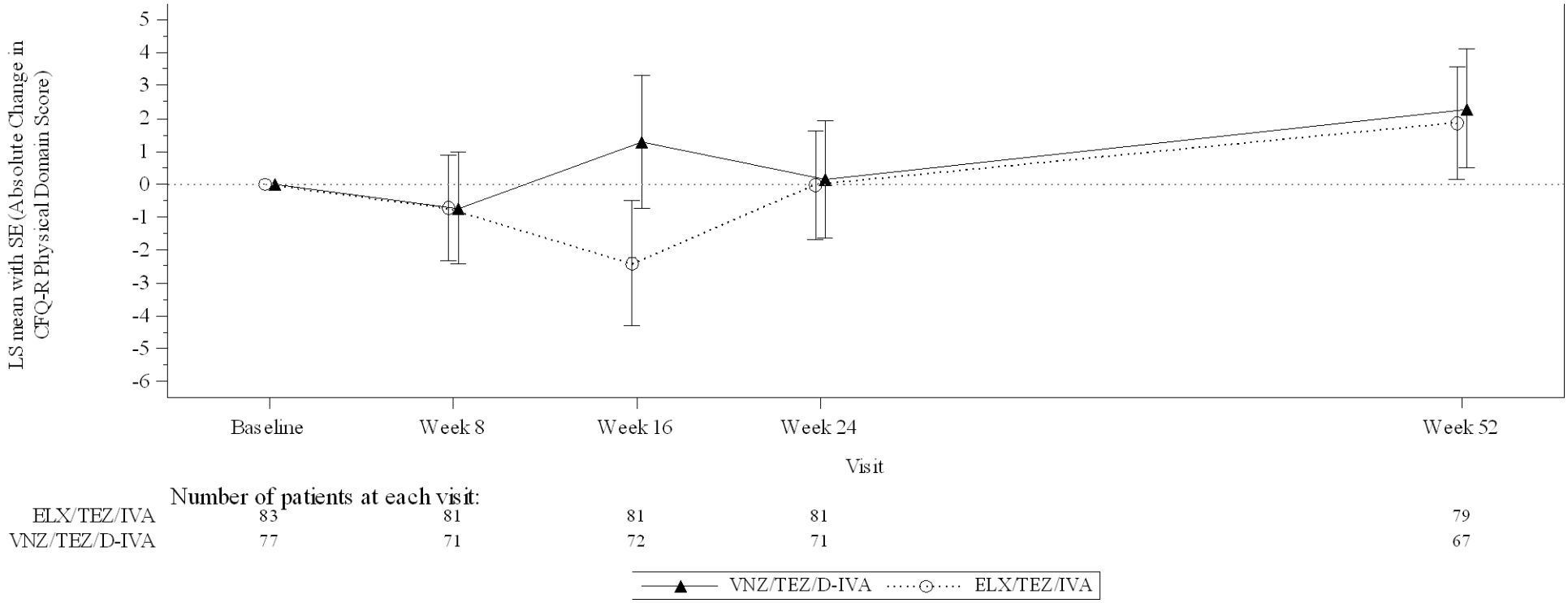
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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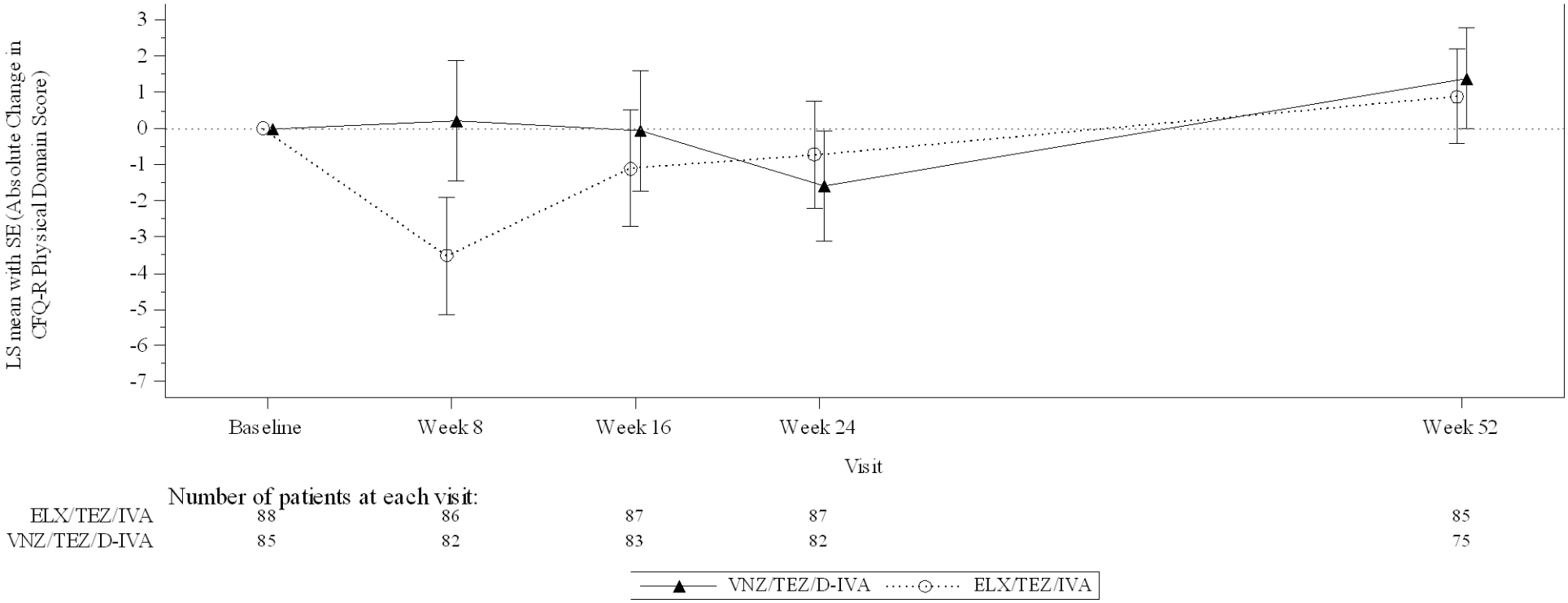
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female



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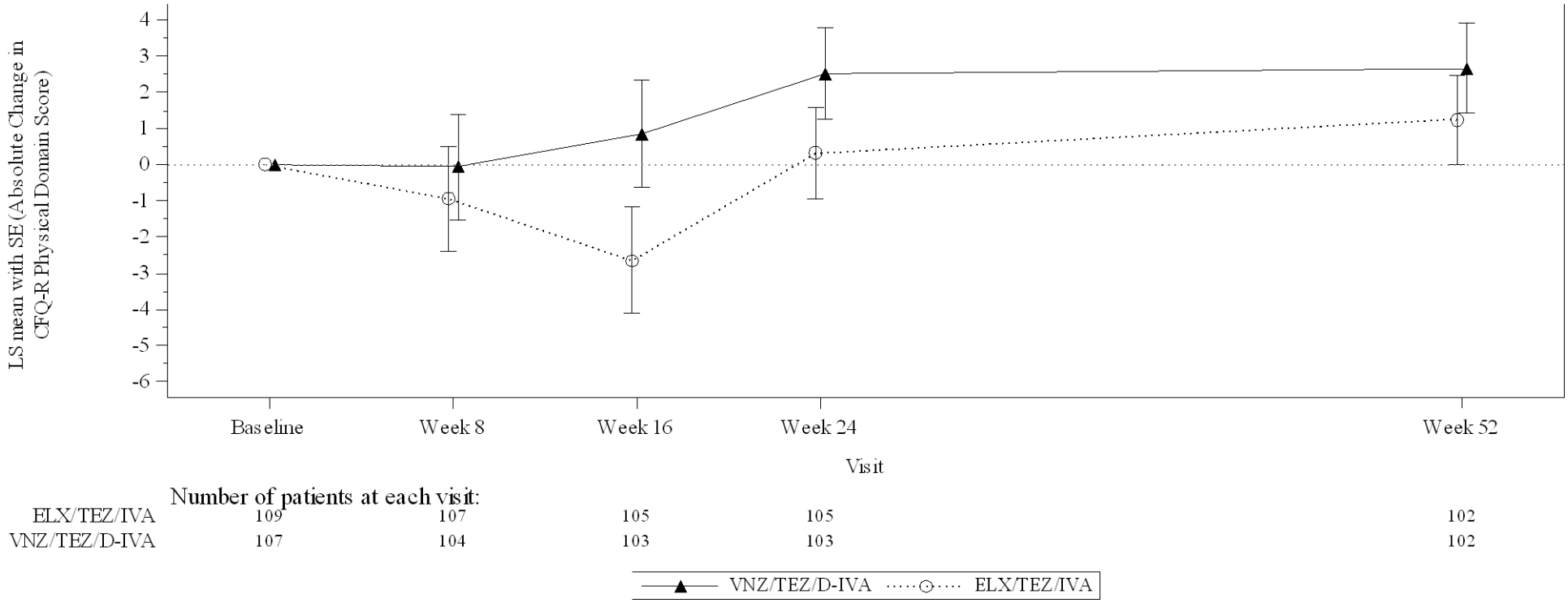
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America



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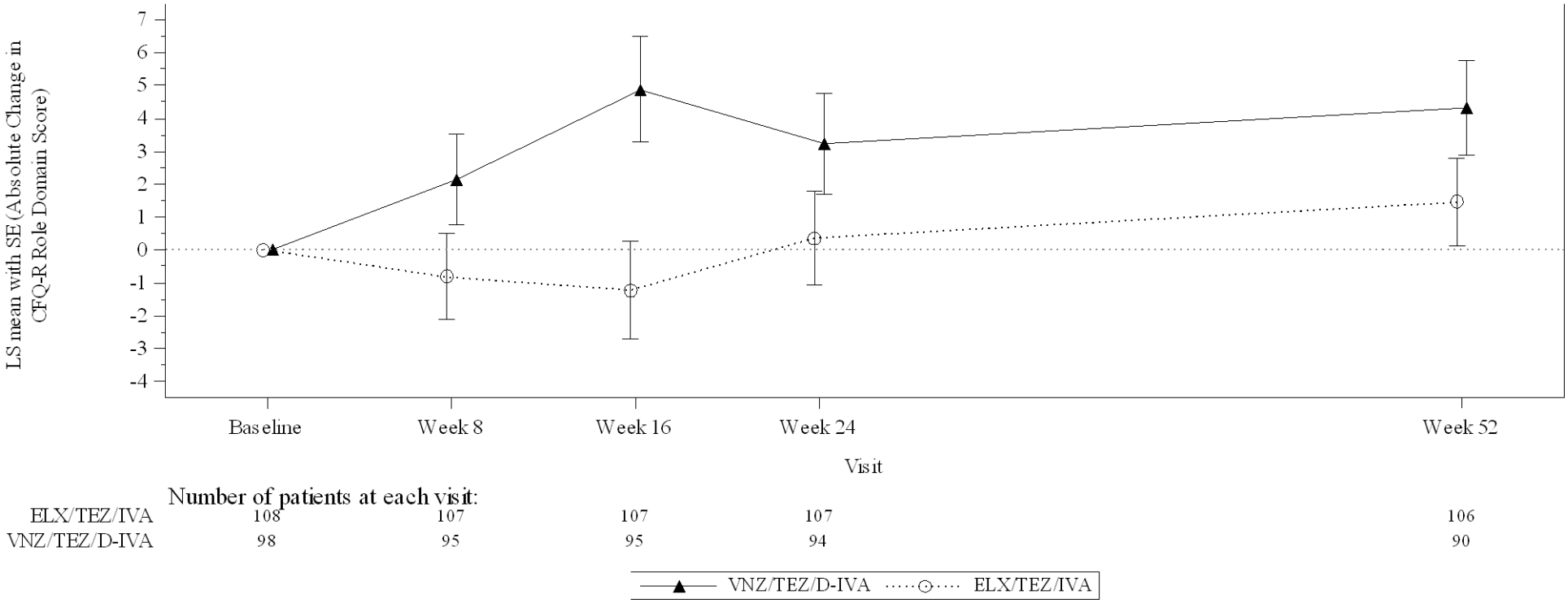
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World



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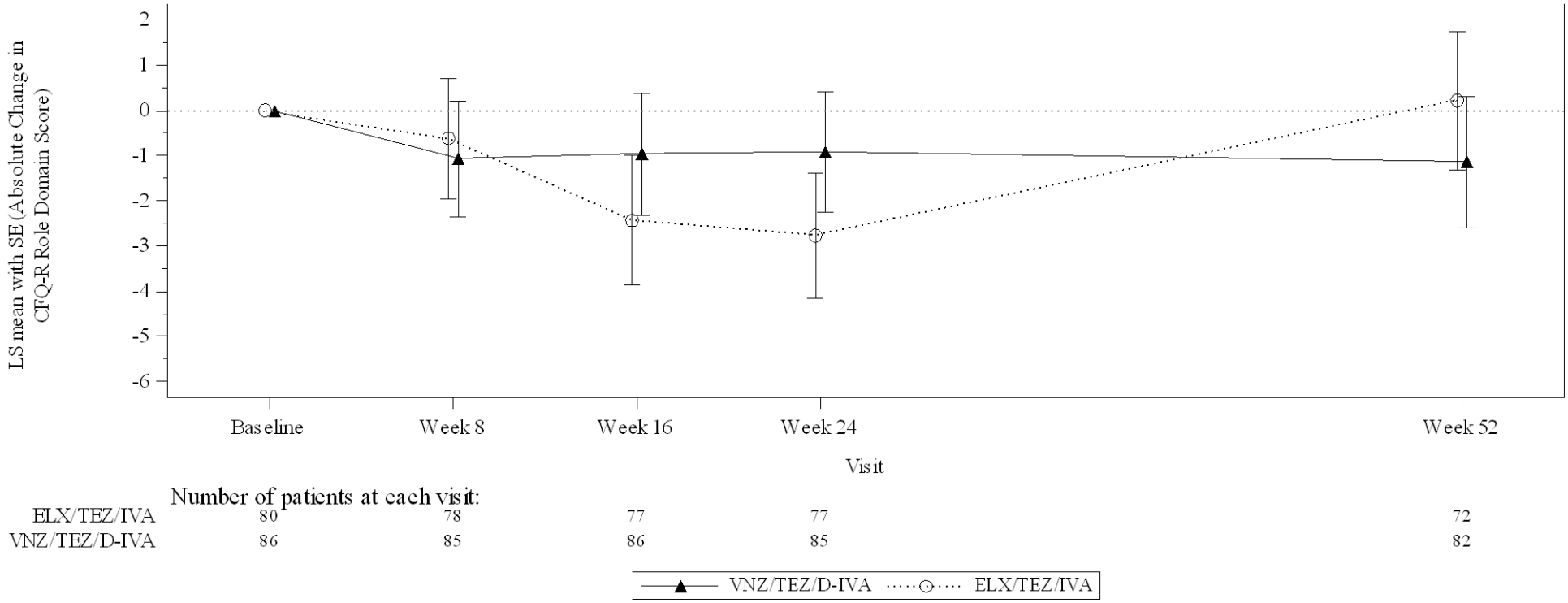
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %



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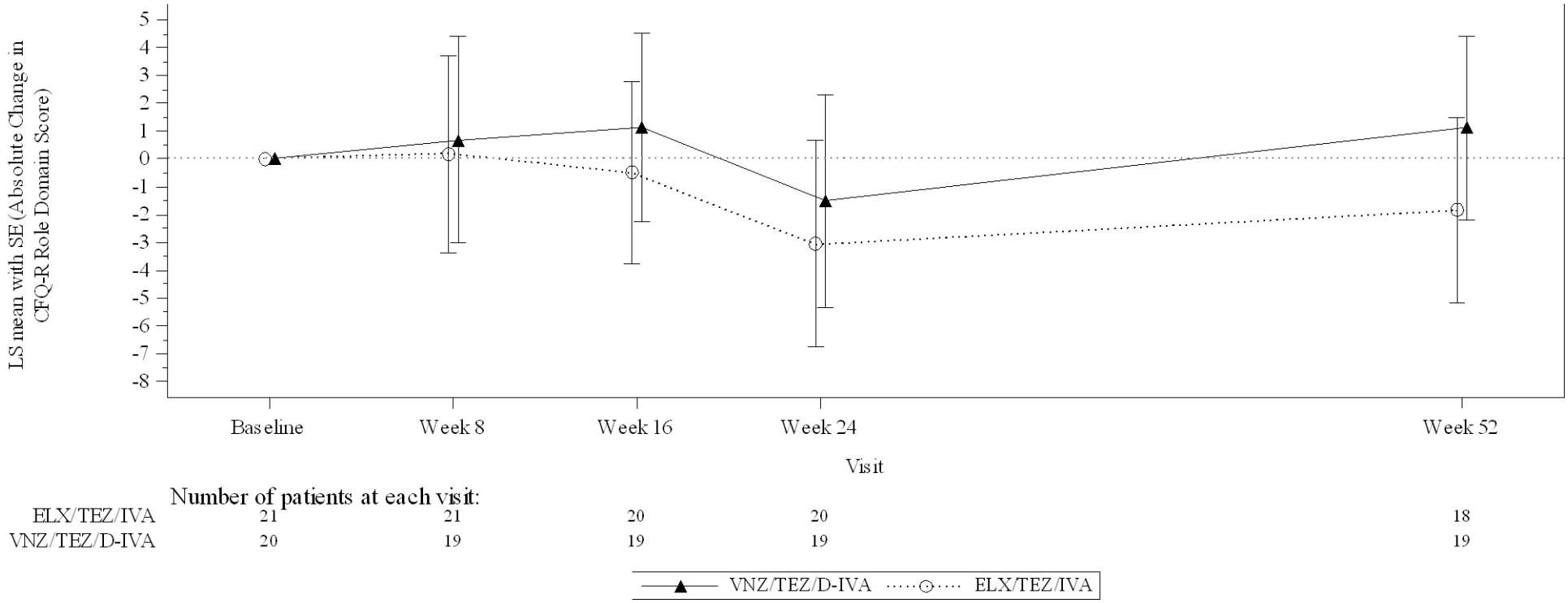
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
ppFEV$_1$ at baseline ≥70 %



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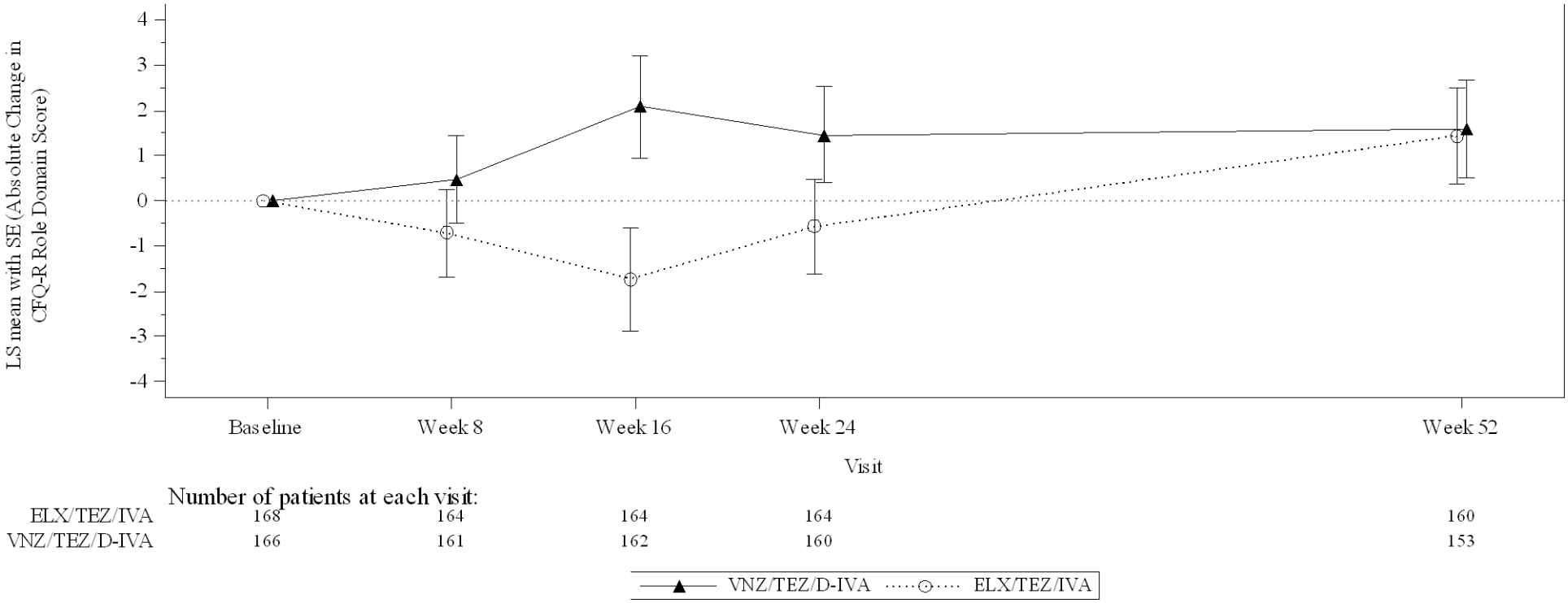
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years



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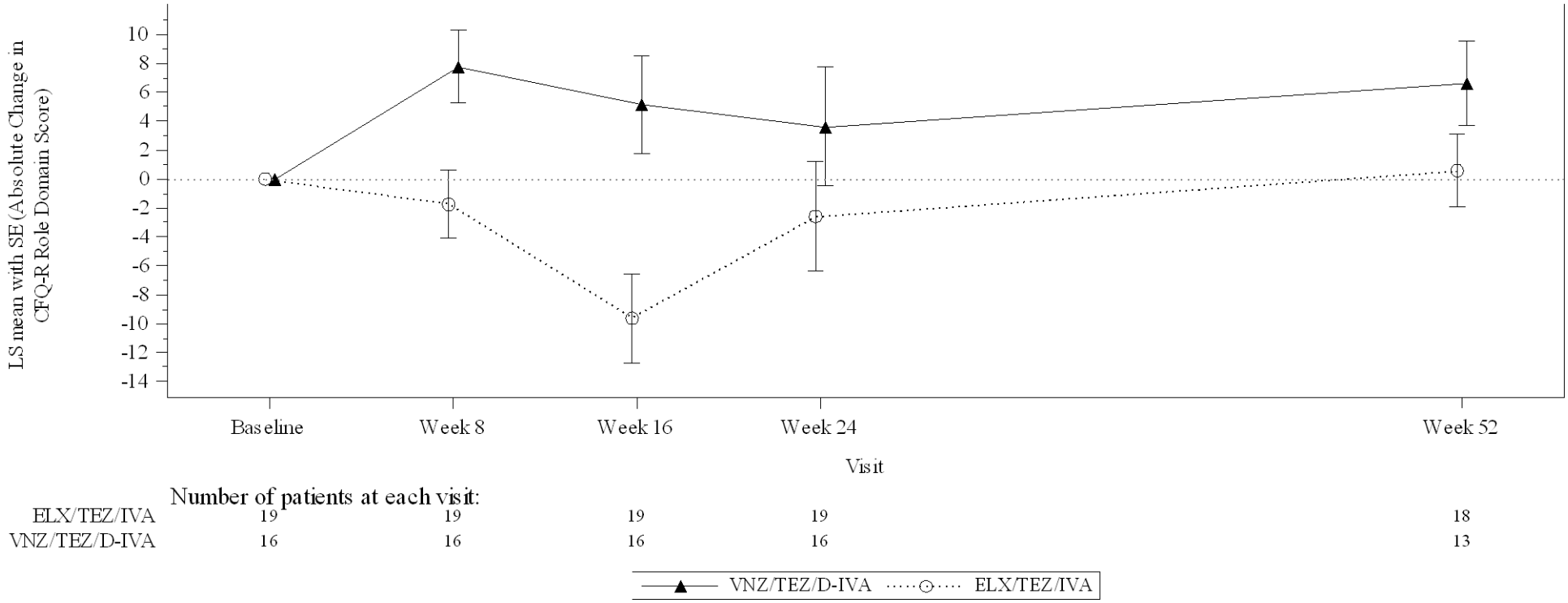
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years



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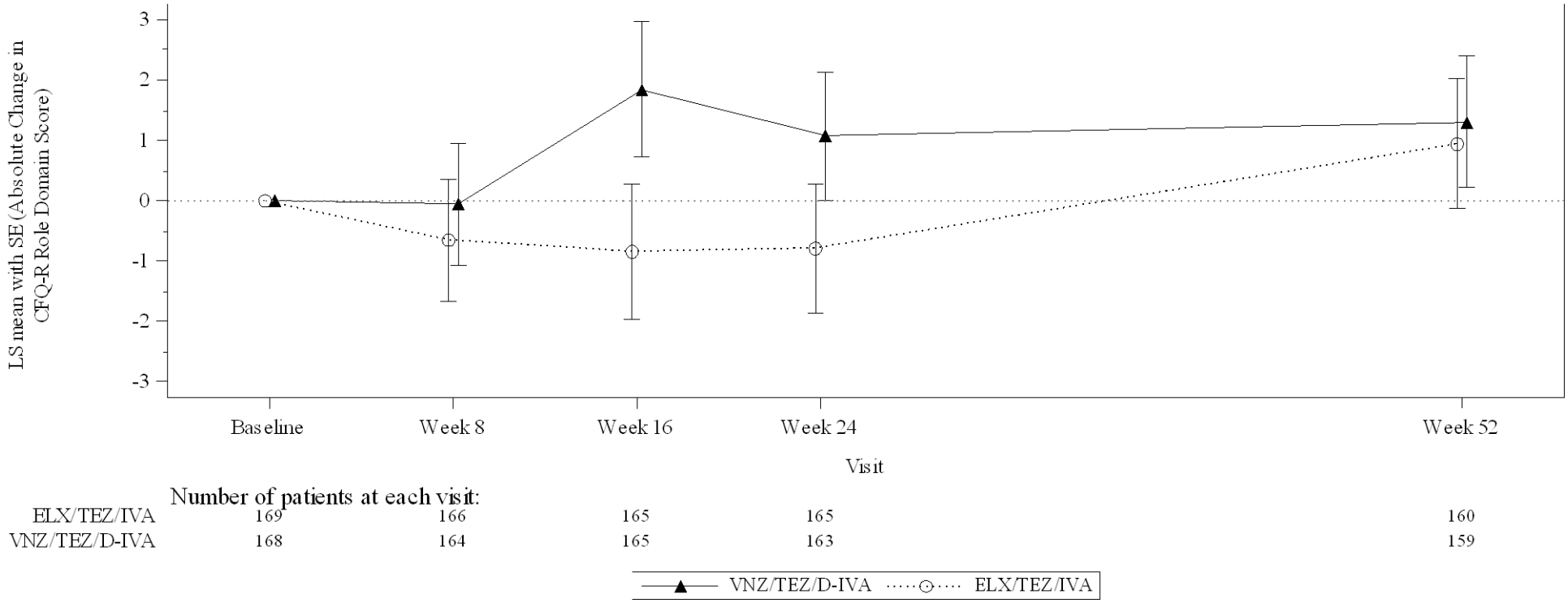
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L



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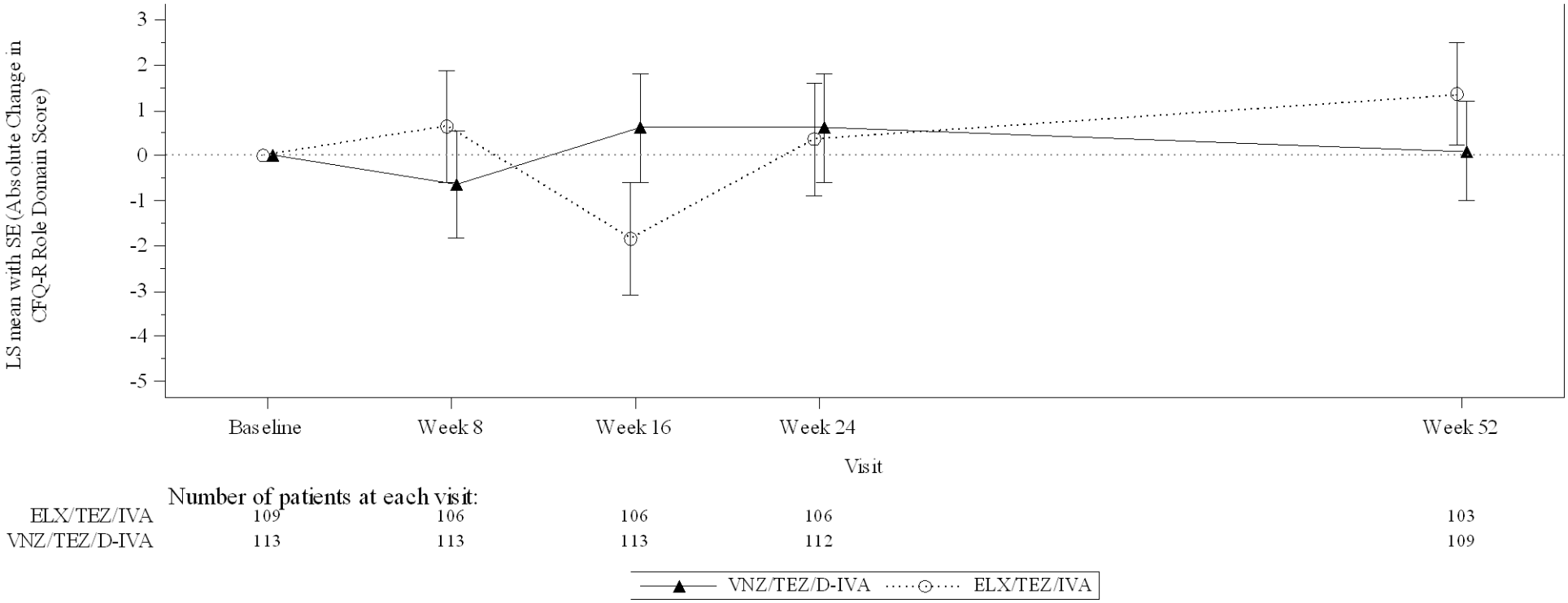
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L



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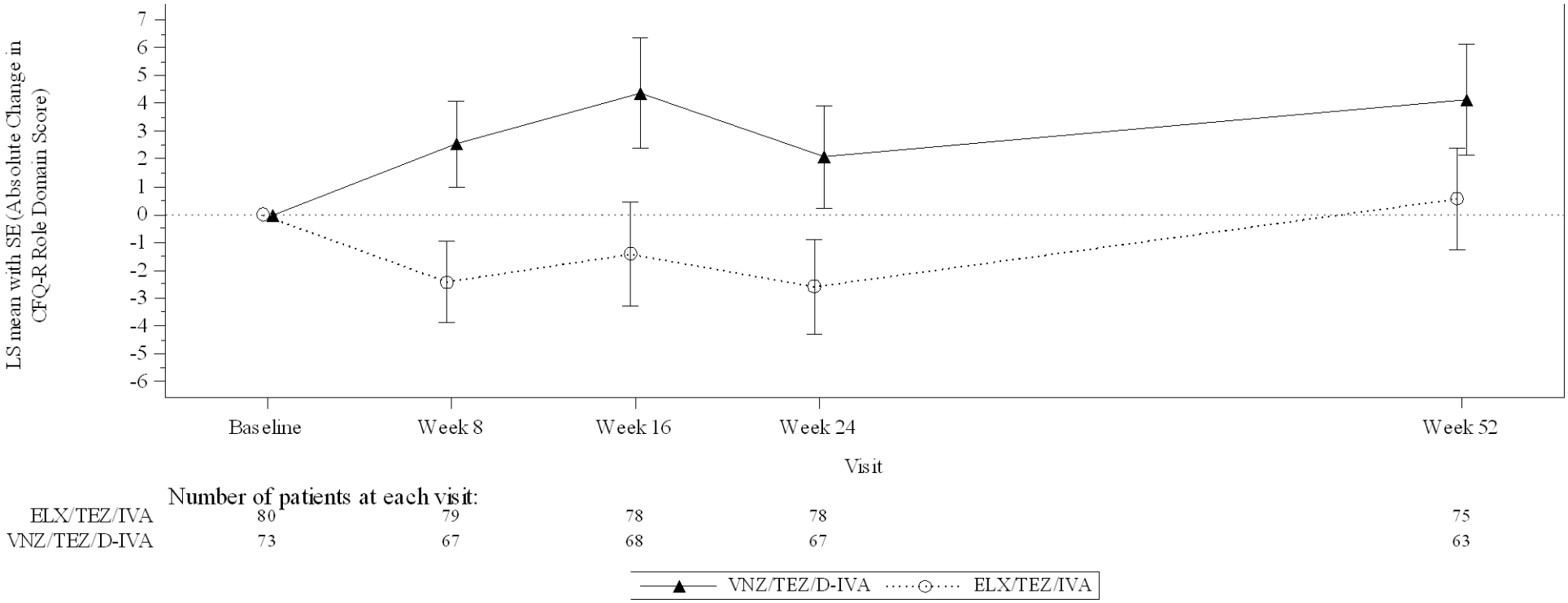
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Male



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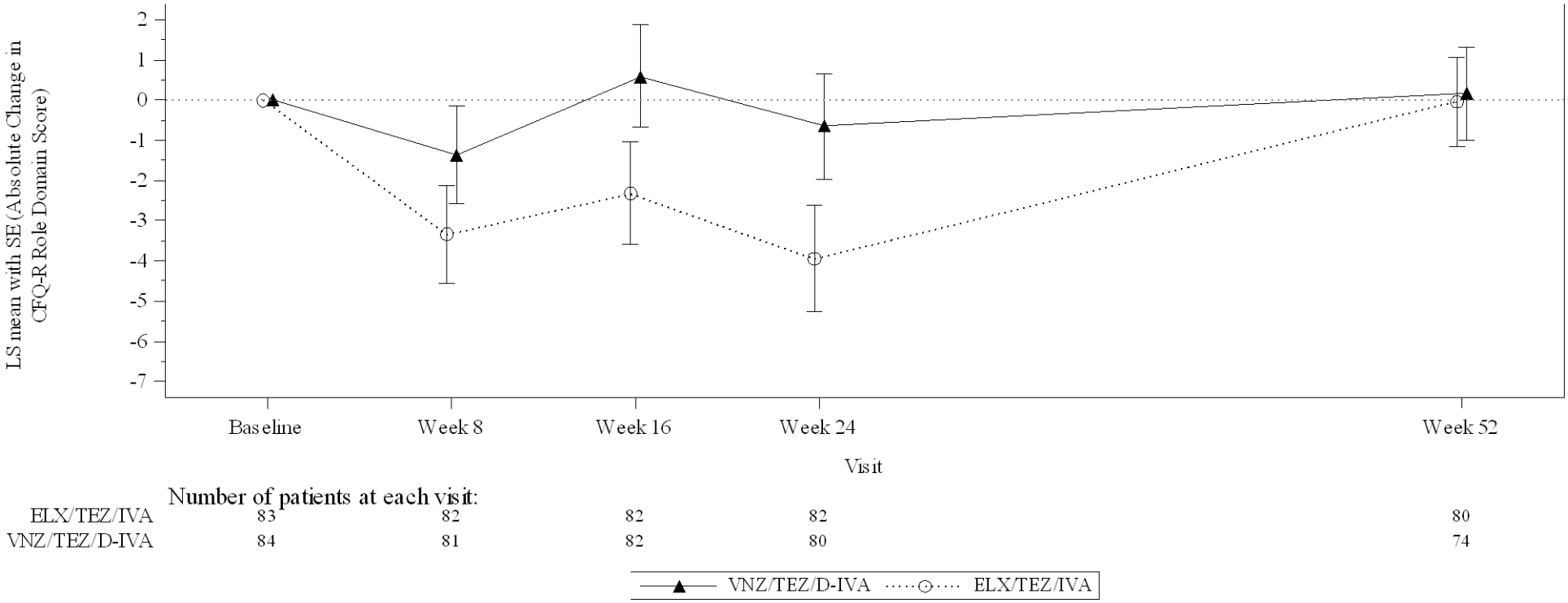
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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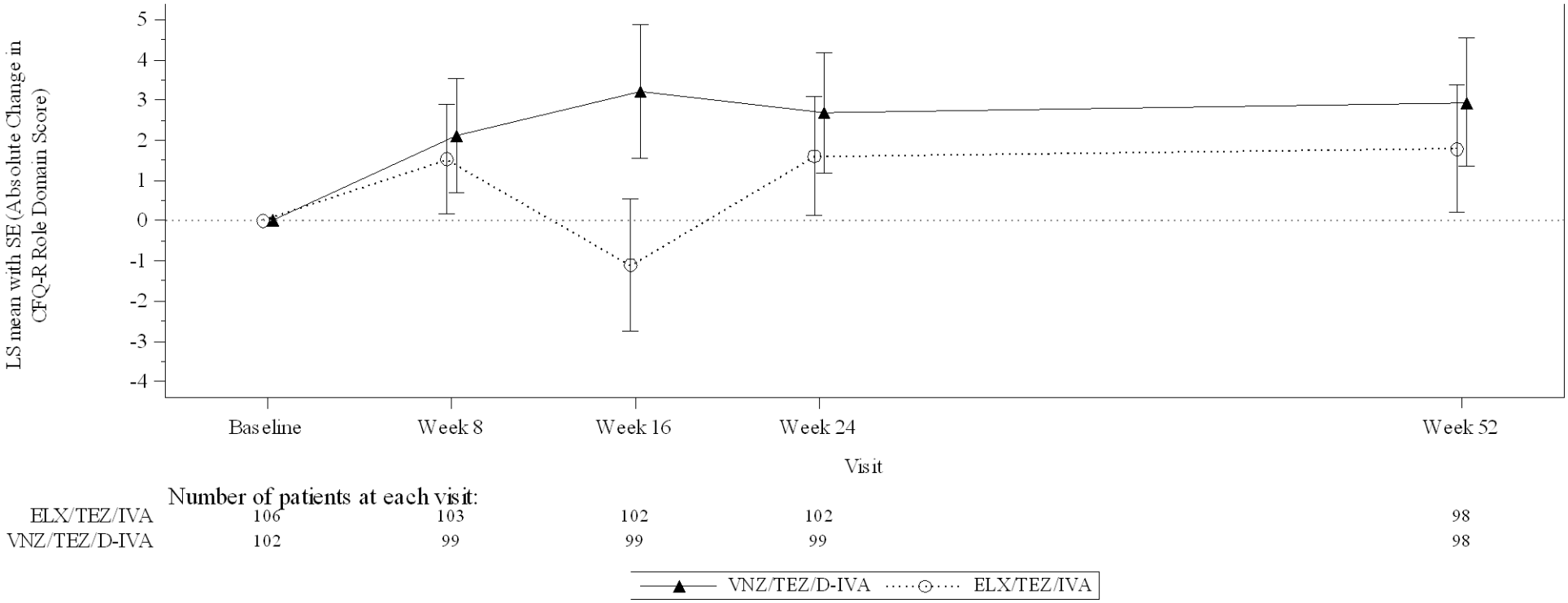
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = North America



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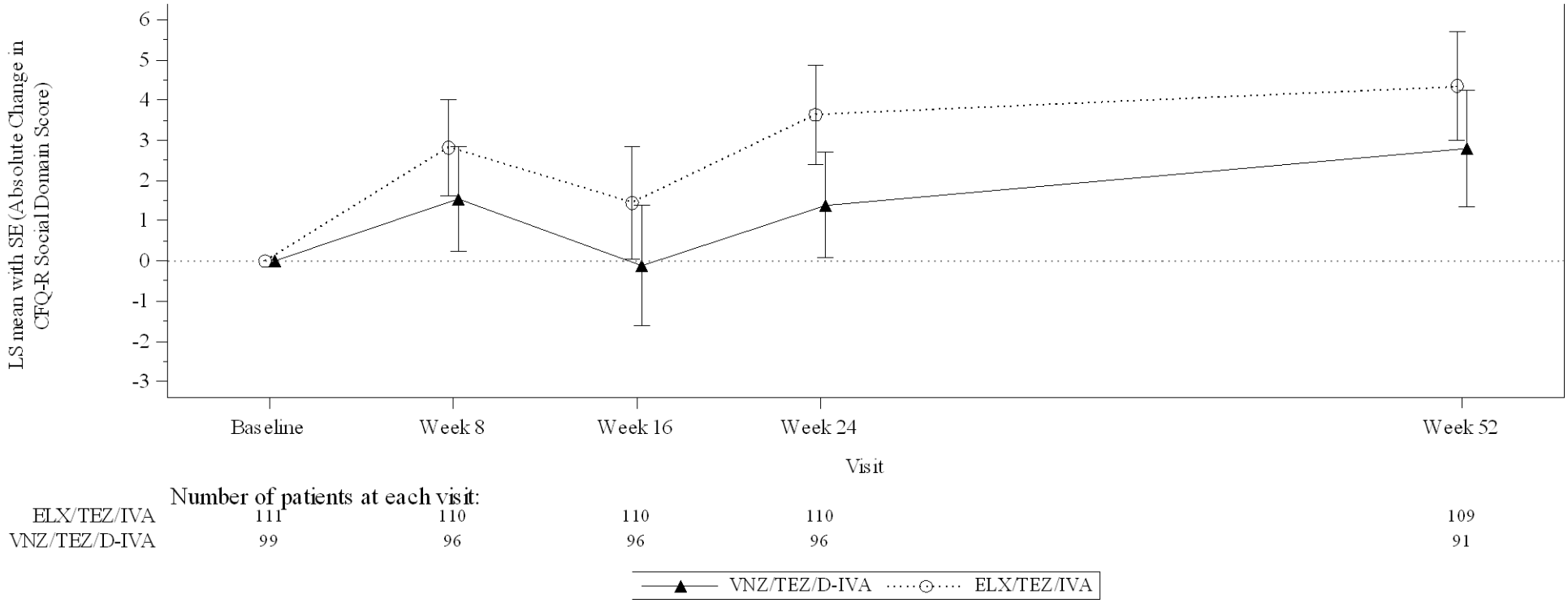
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World



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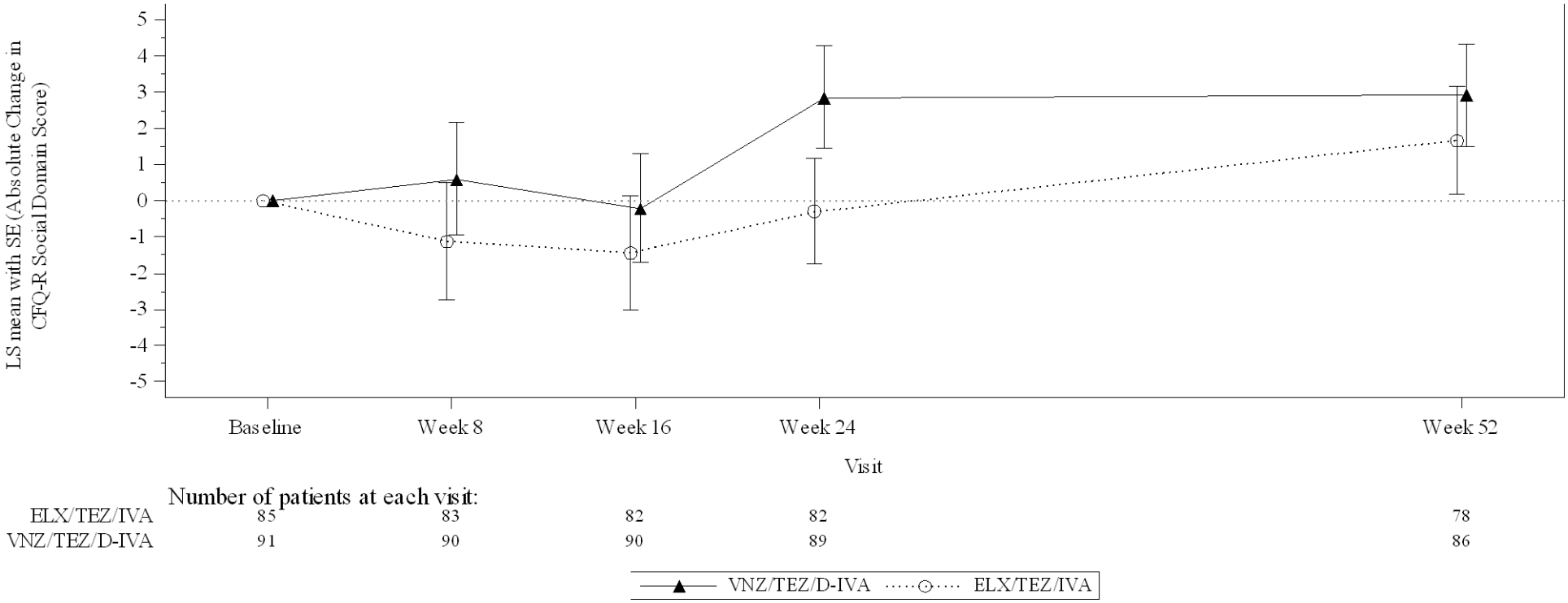
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

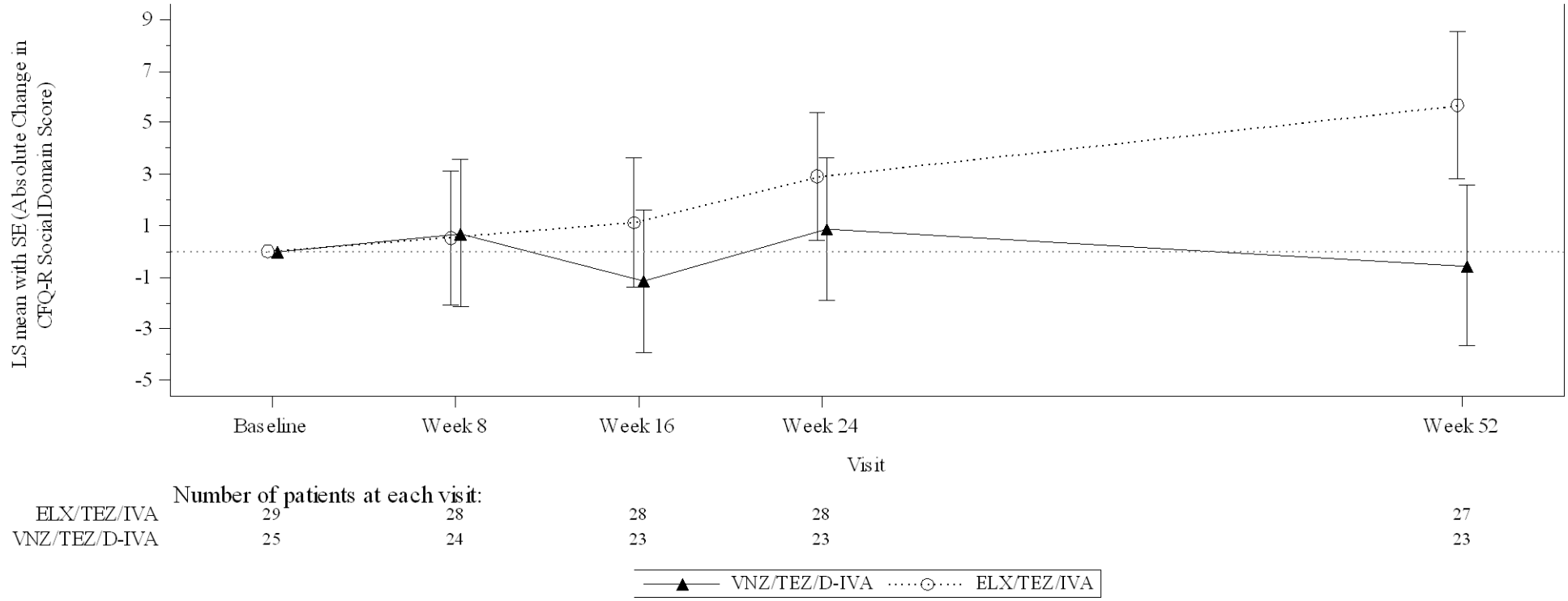
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

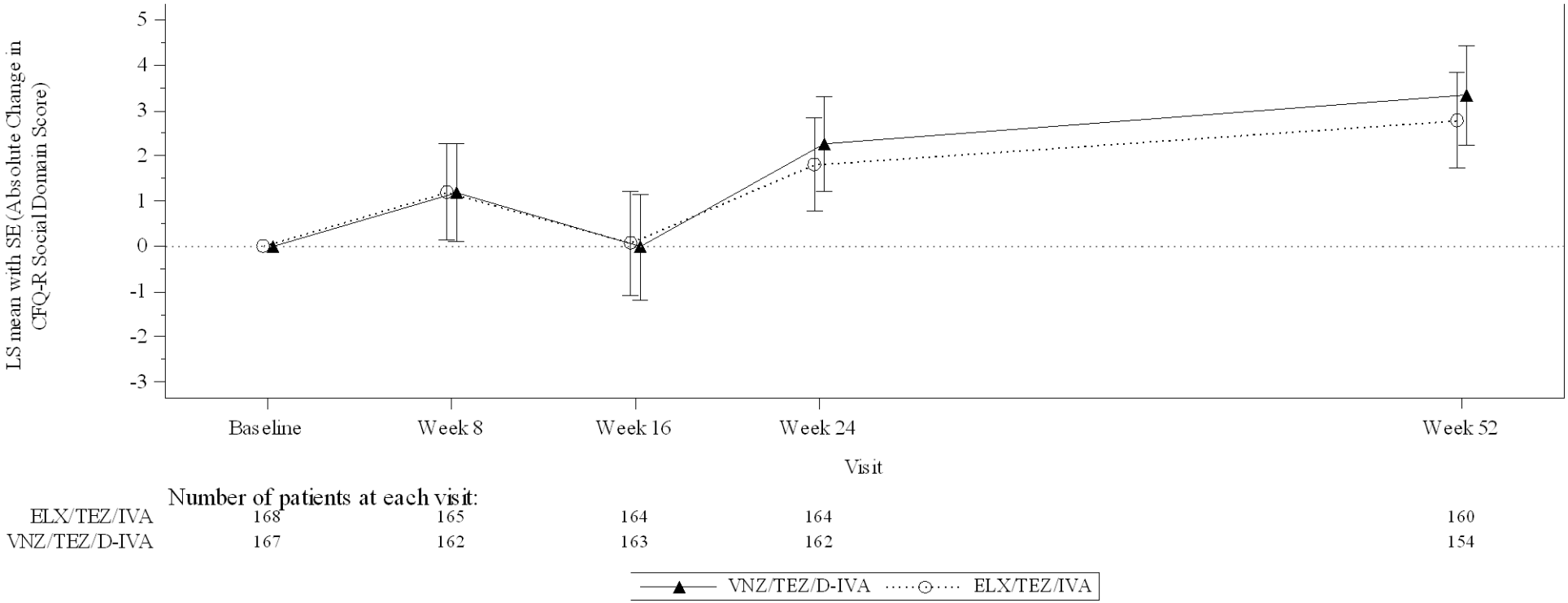
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years



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Full Analysis Set

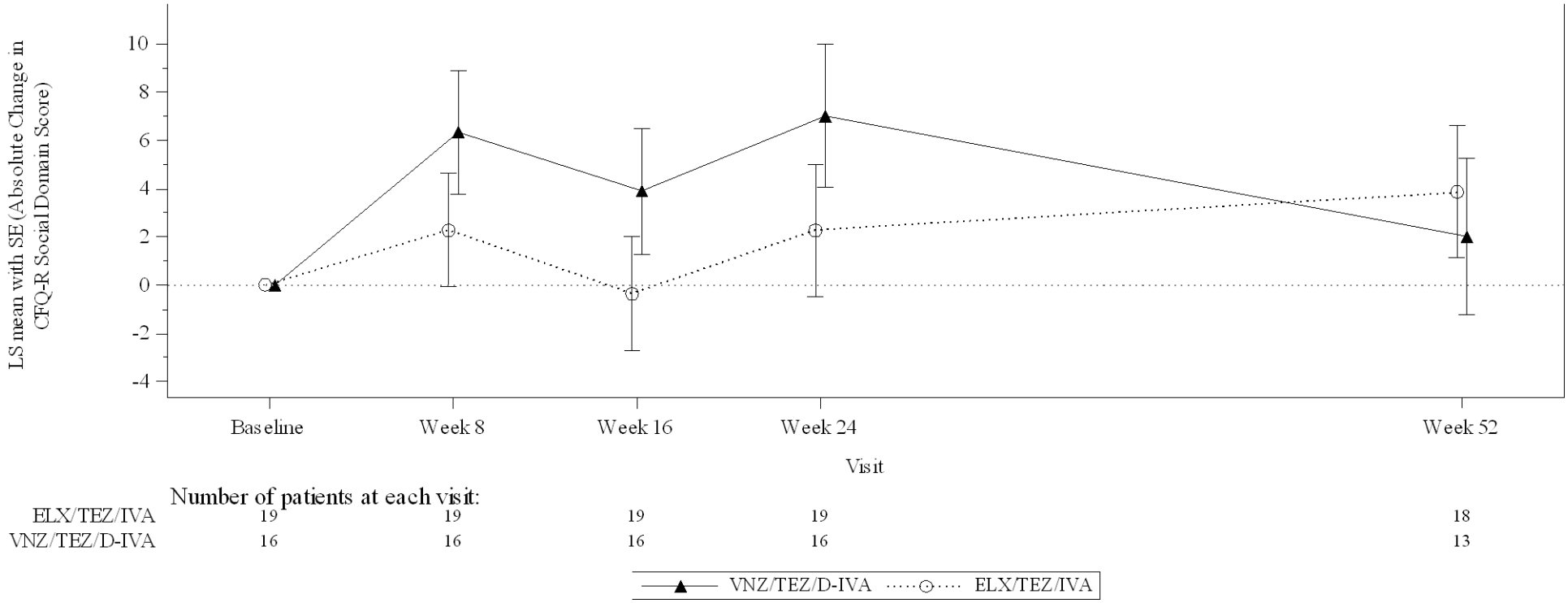
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years



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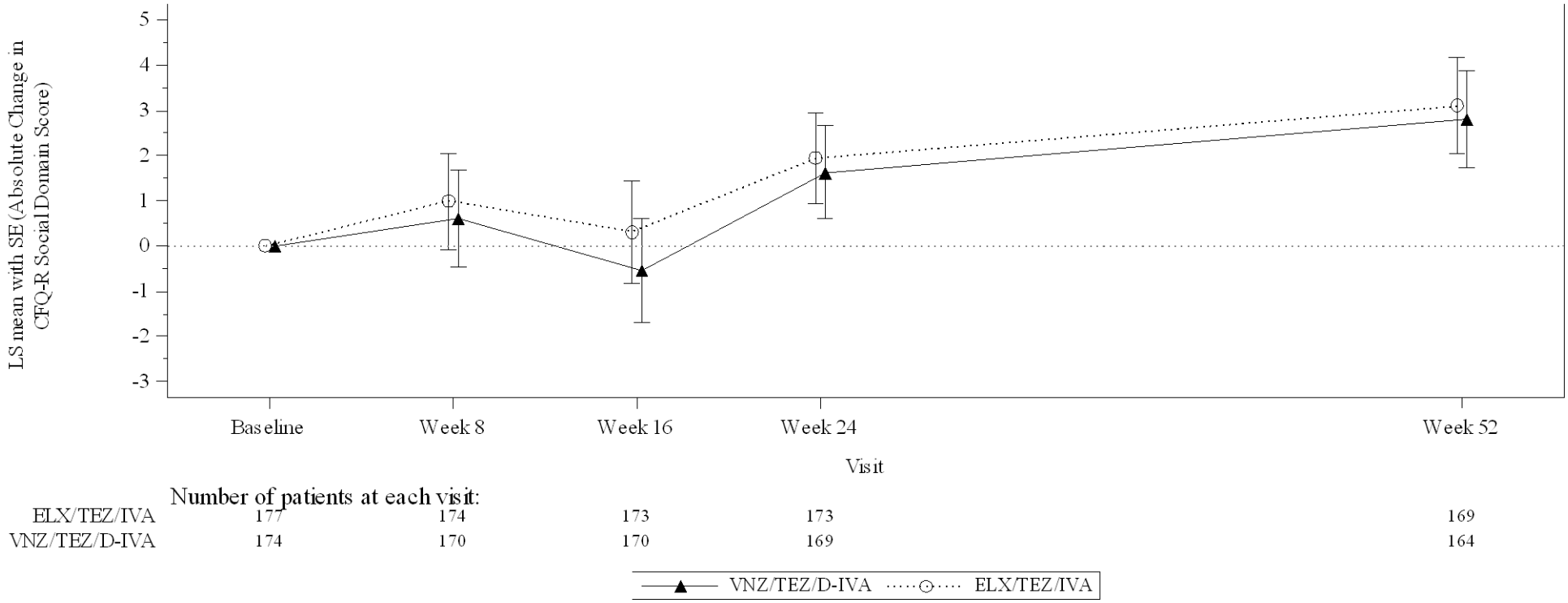
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L



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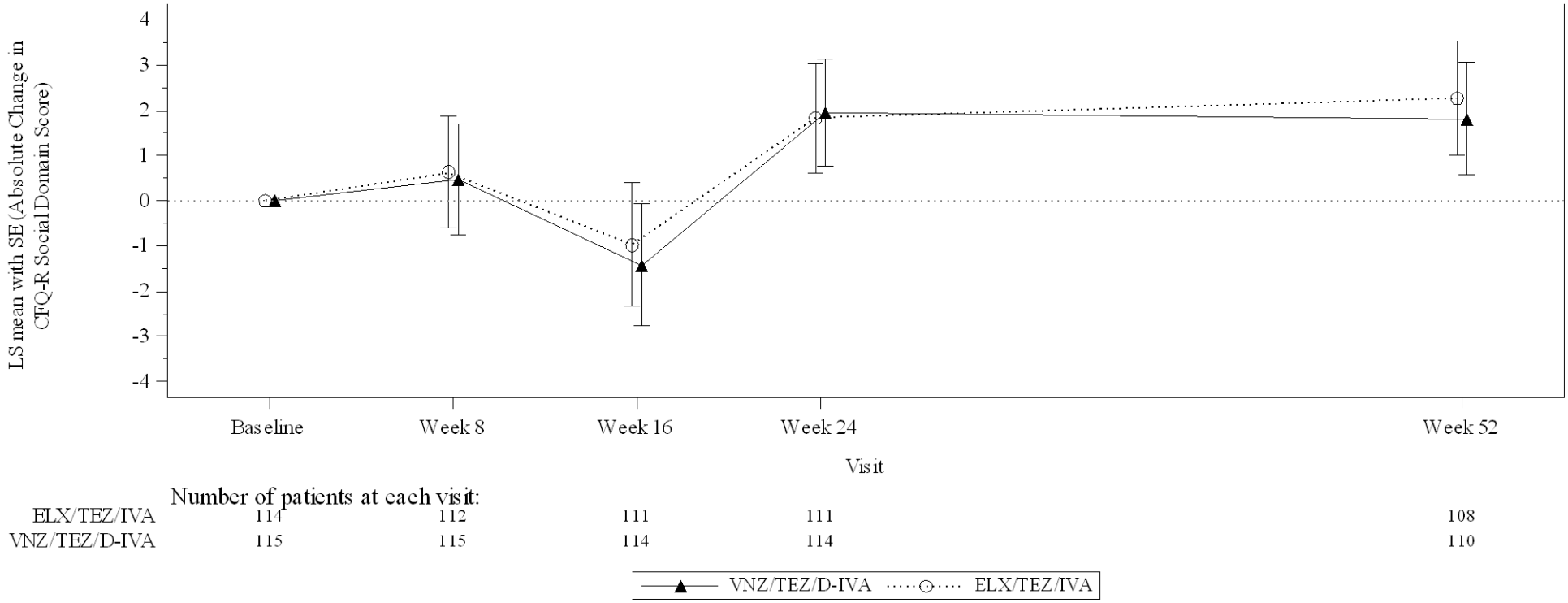
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L



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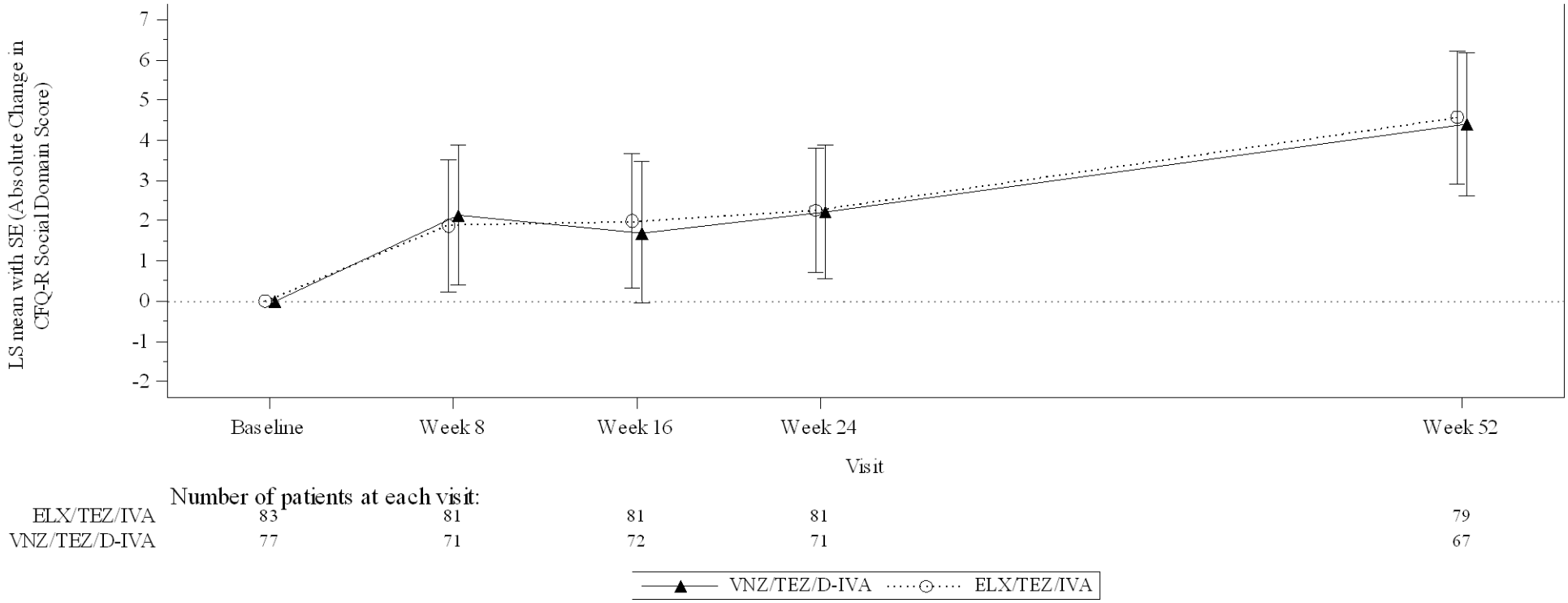
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male



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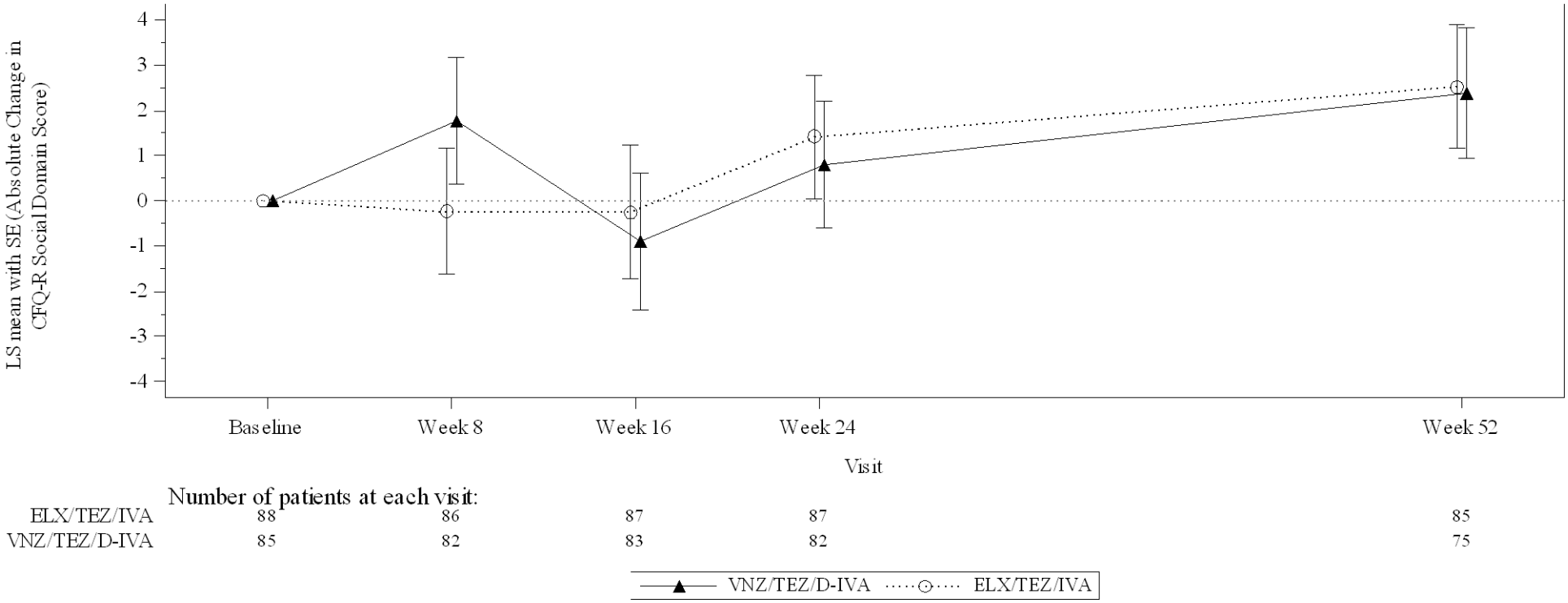
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female



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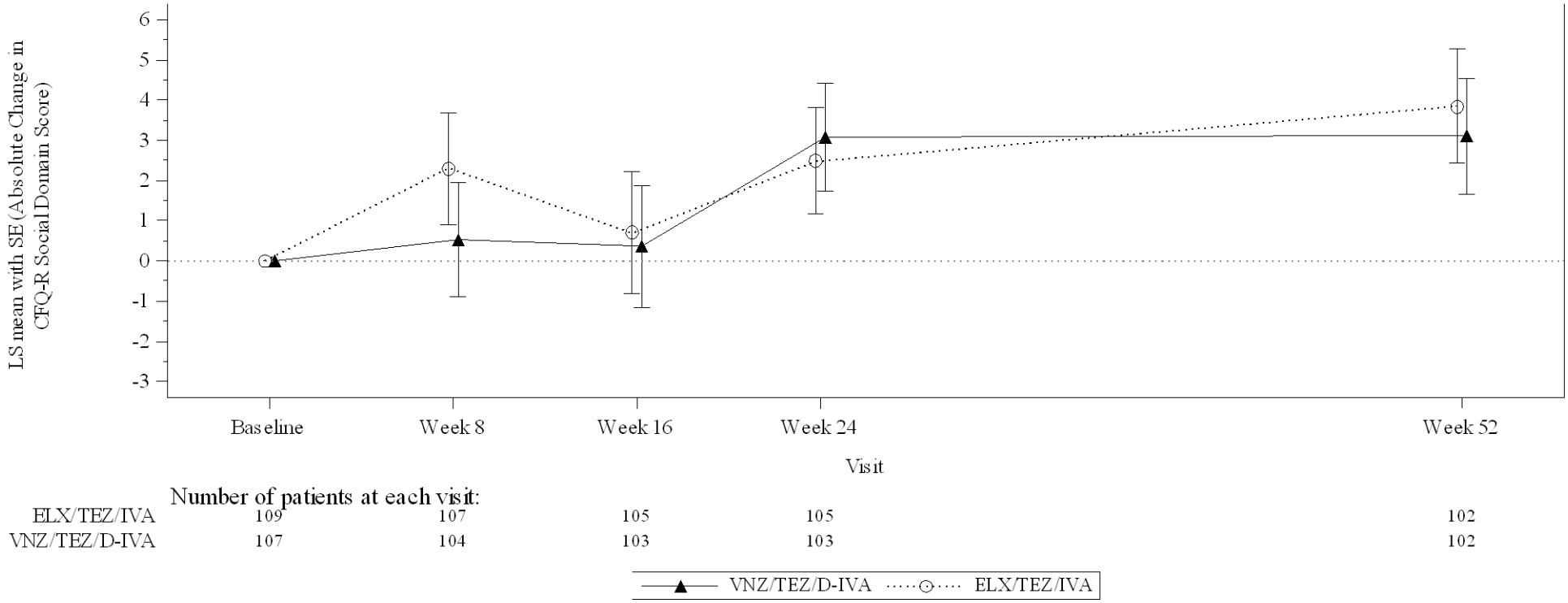
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America



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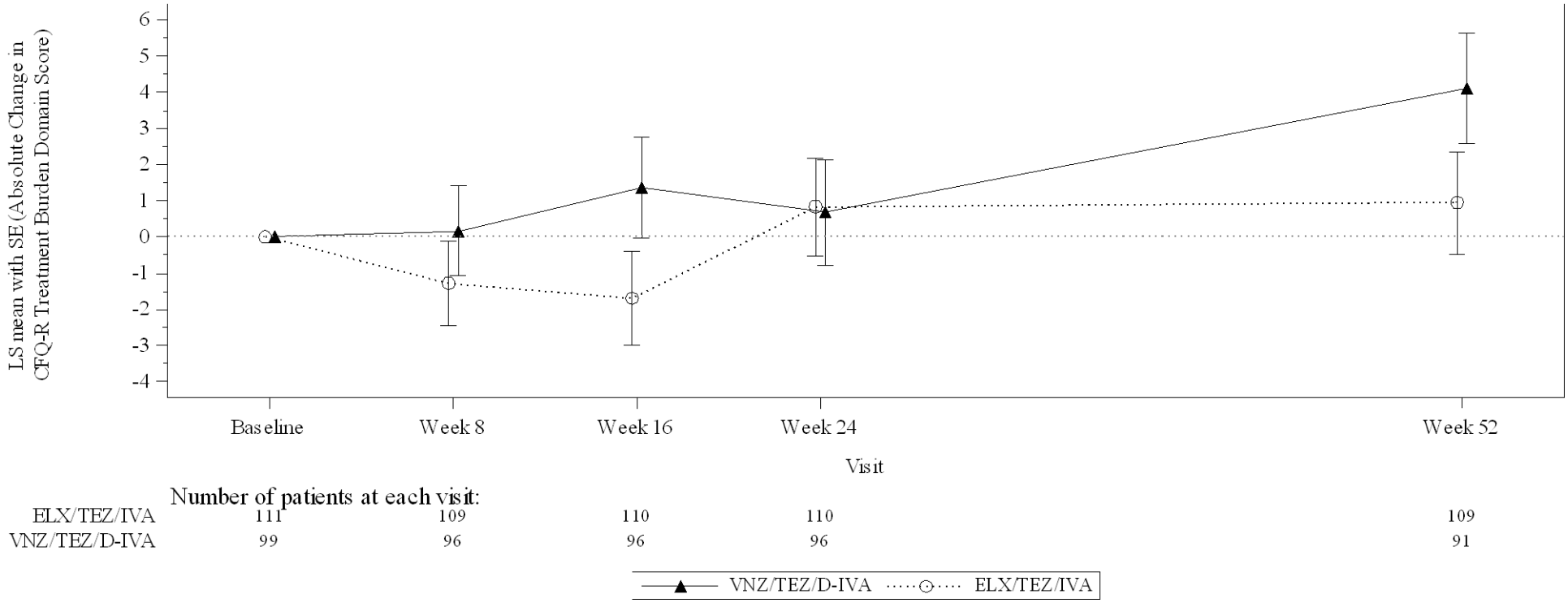
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World



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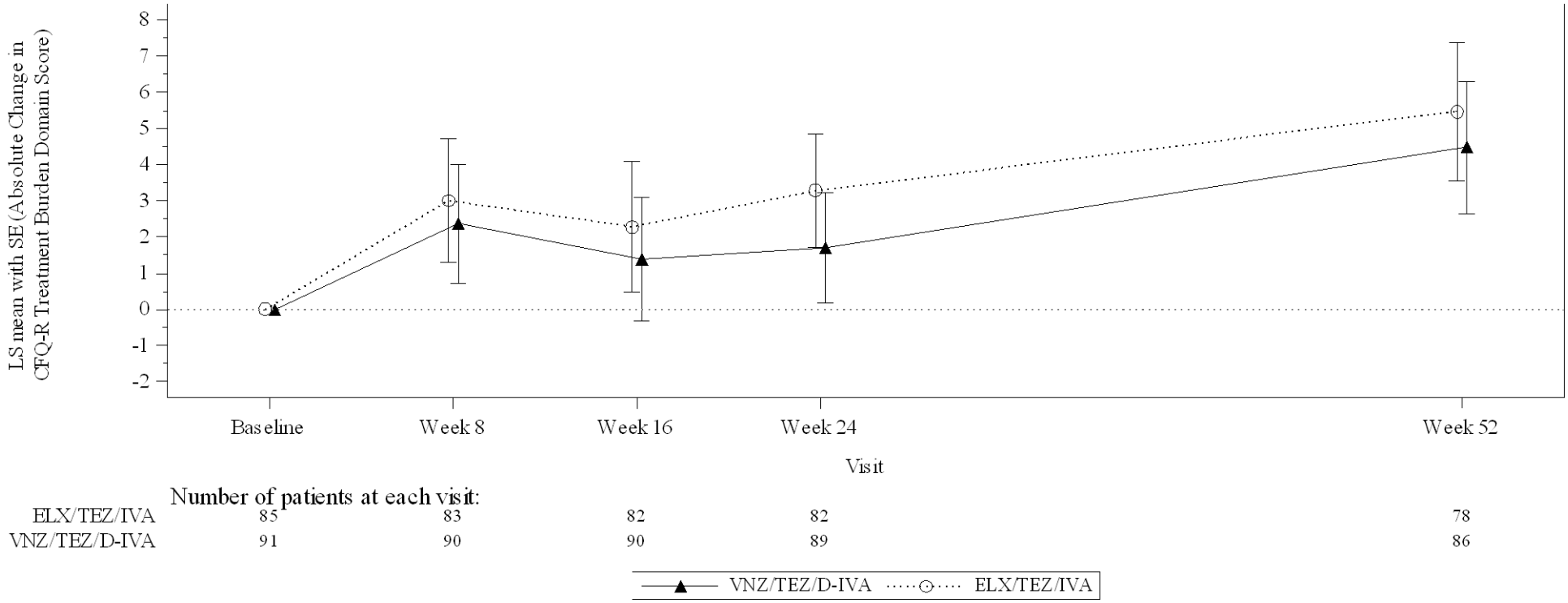
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %



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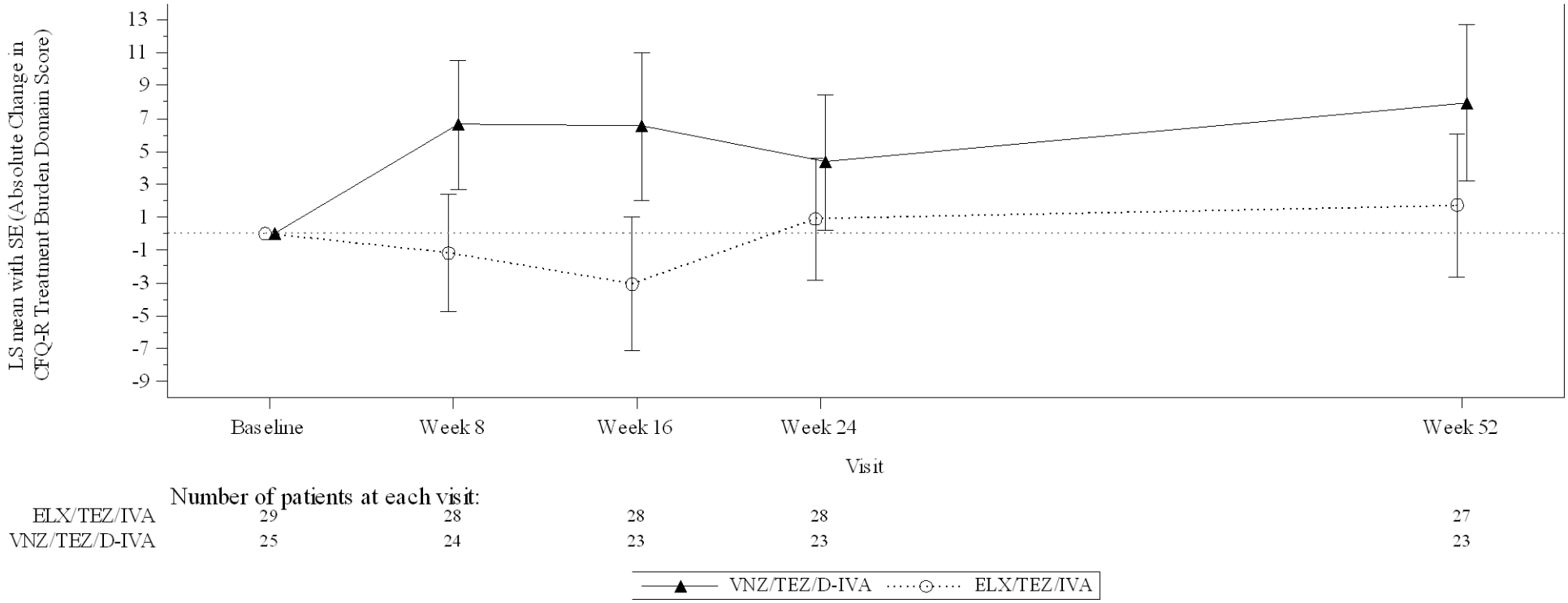
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %



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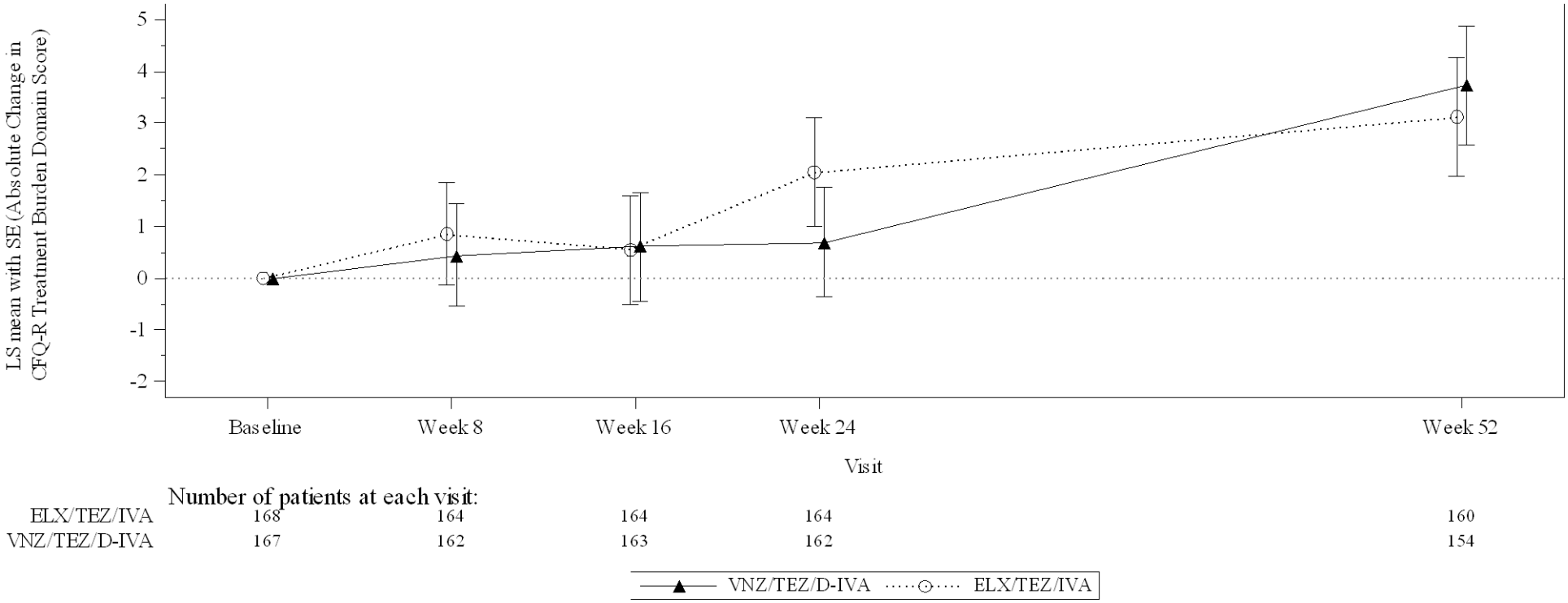
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years



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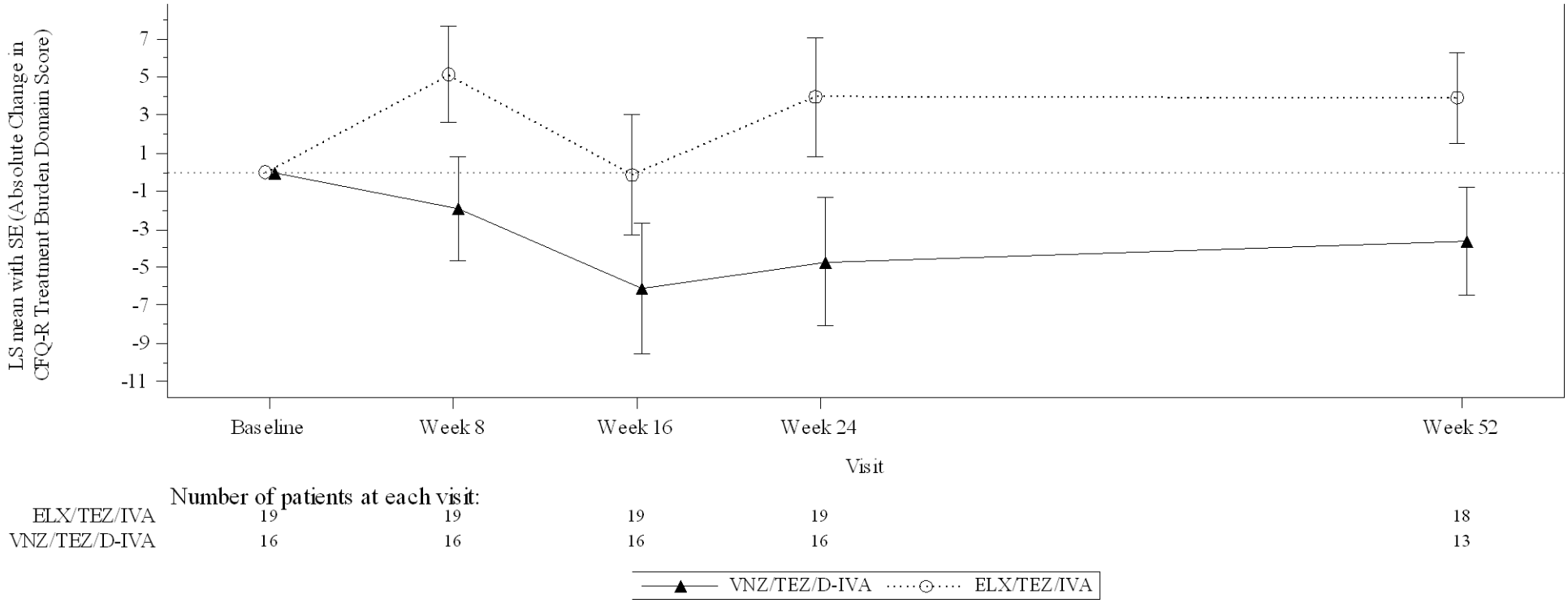
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years



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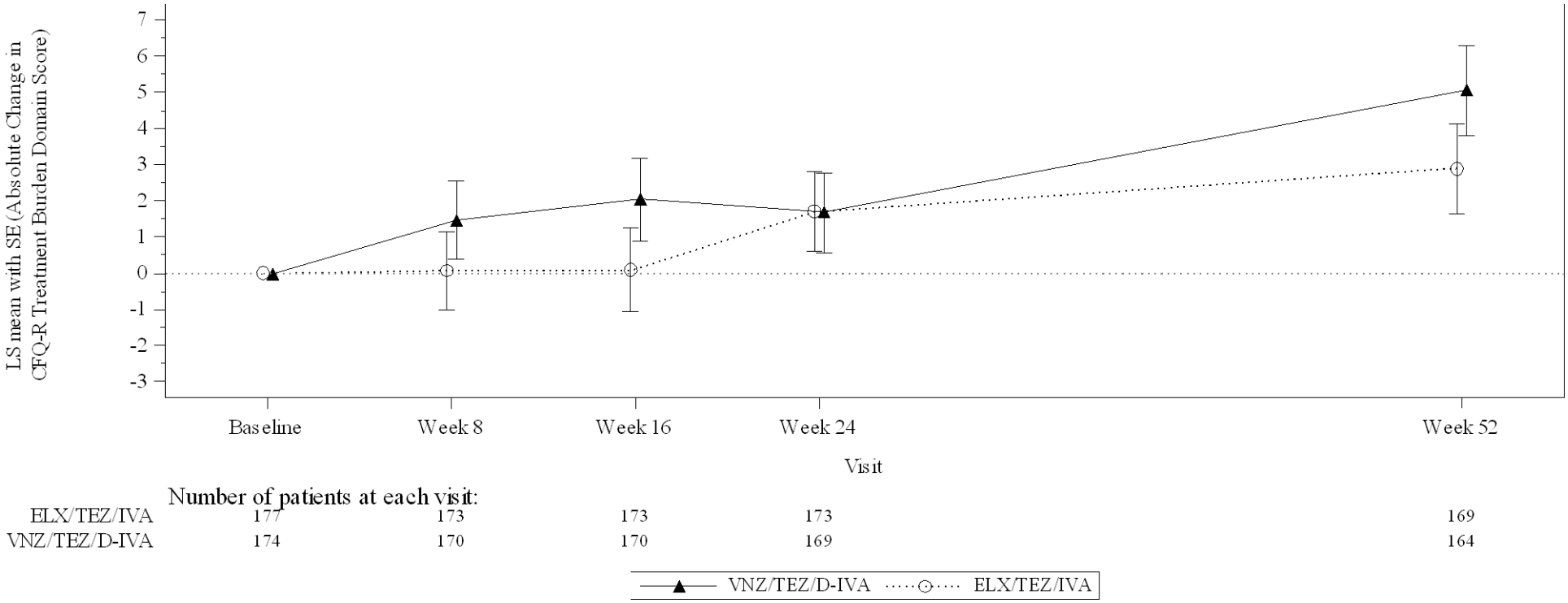
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L



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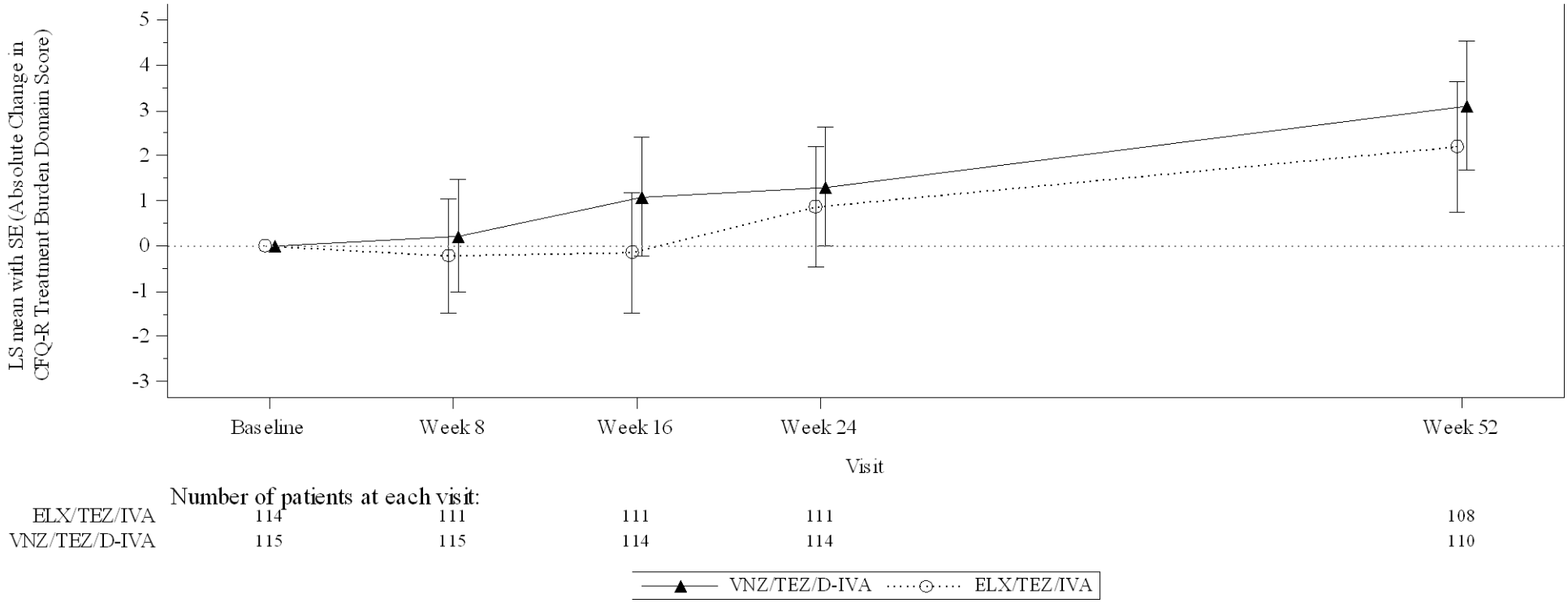
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L



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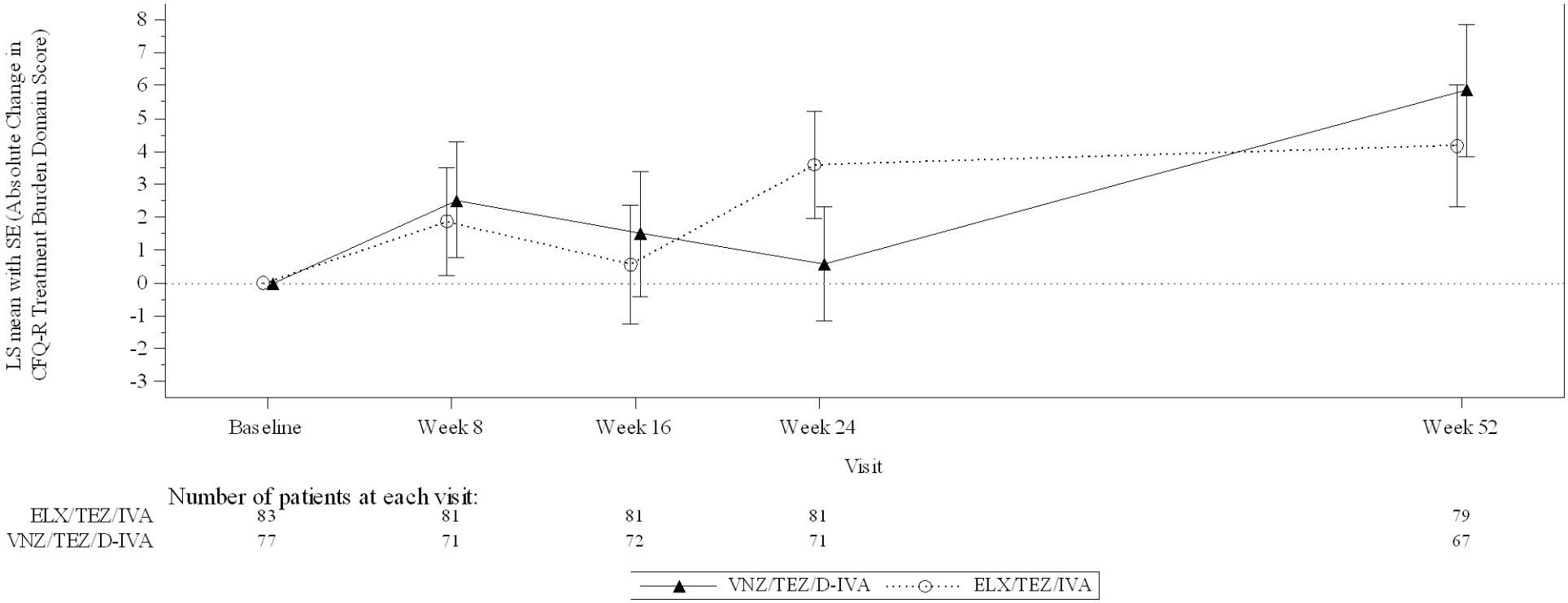
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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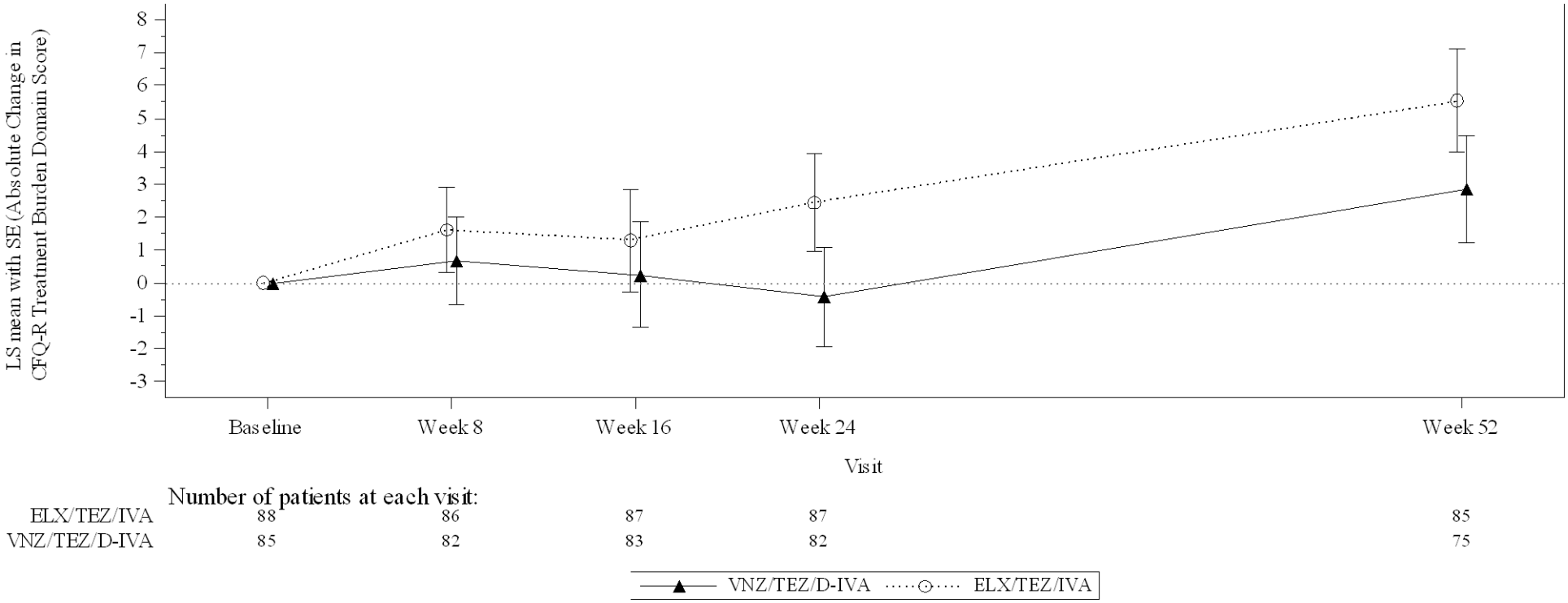
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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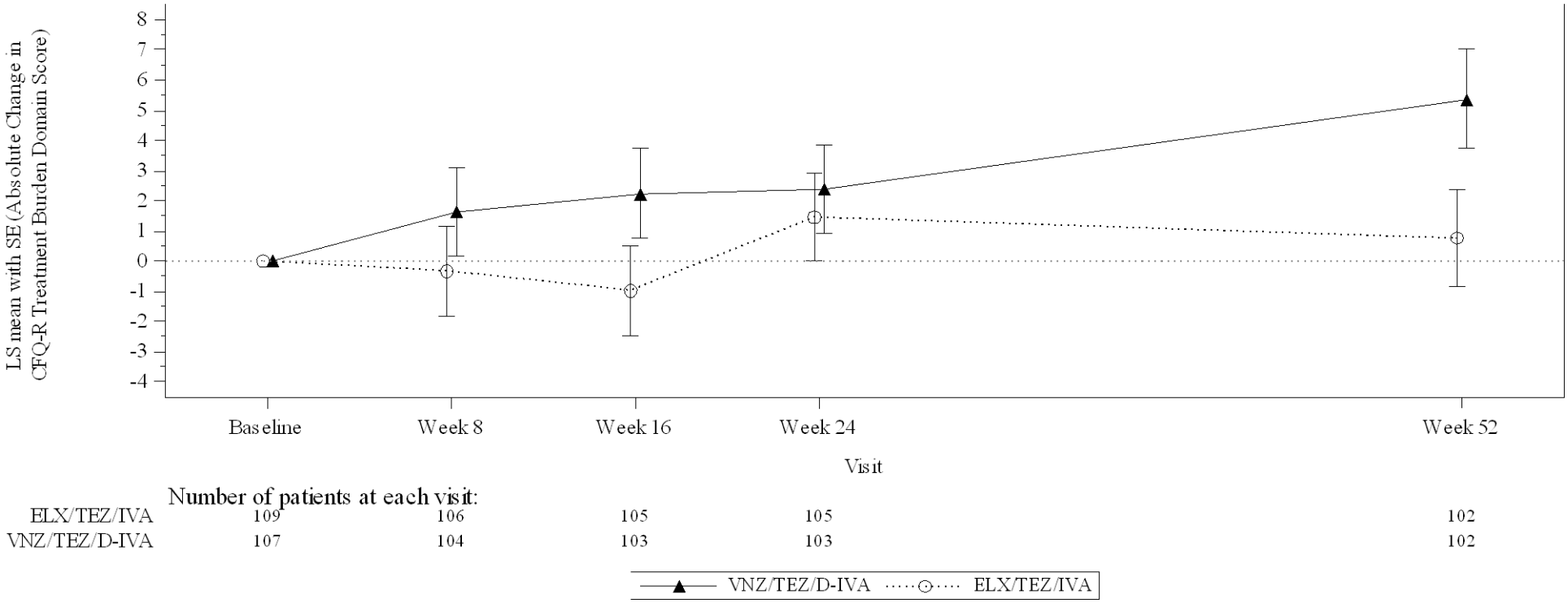
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America



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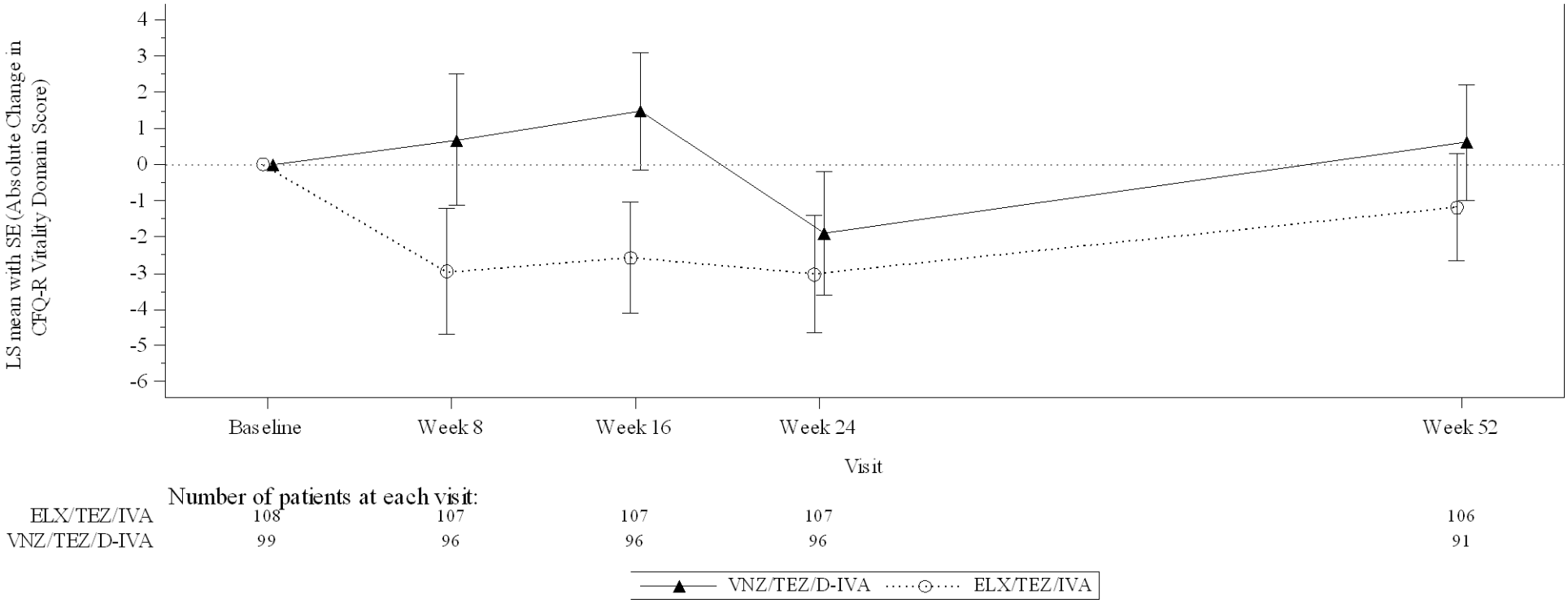
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World



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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

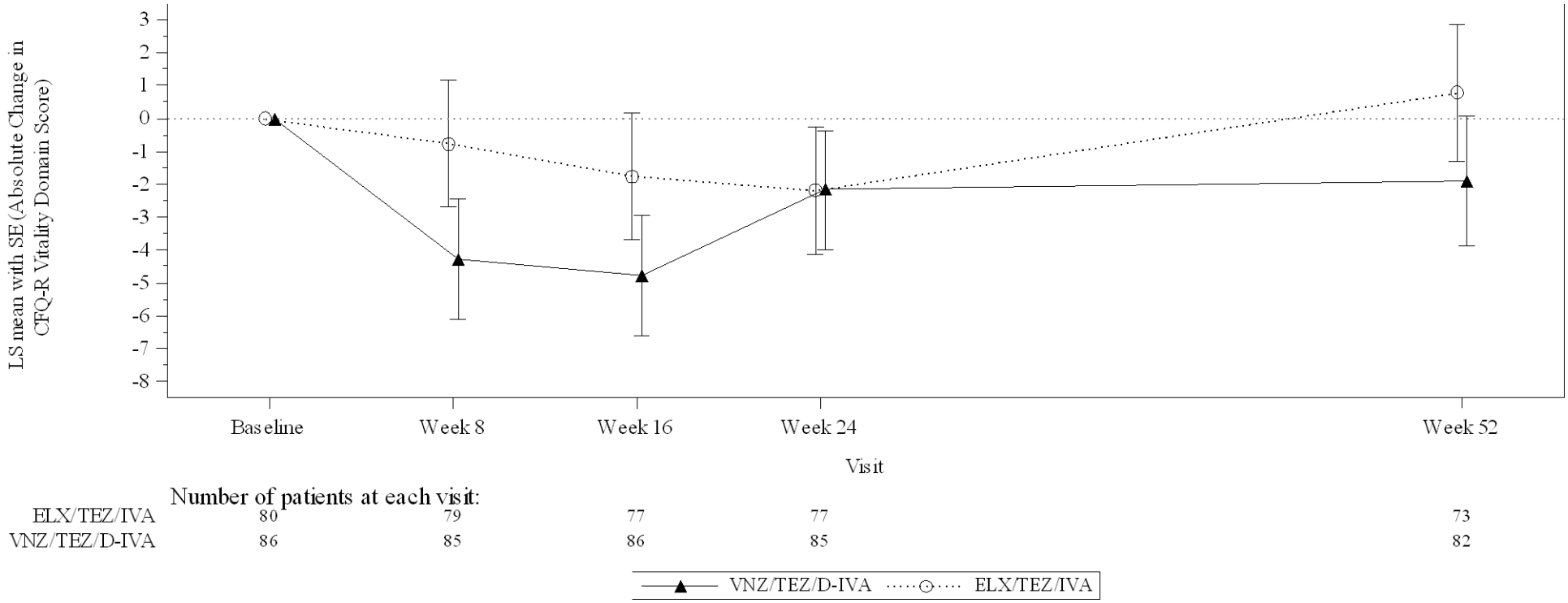
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

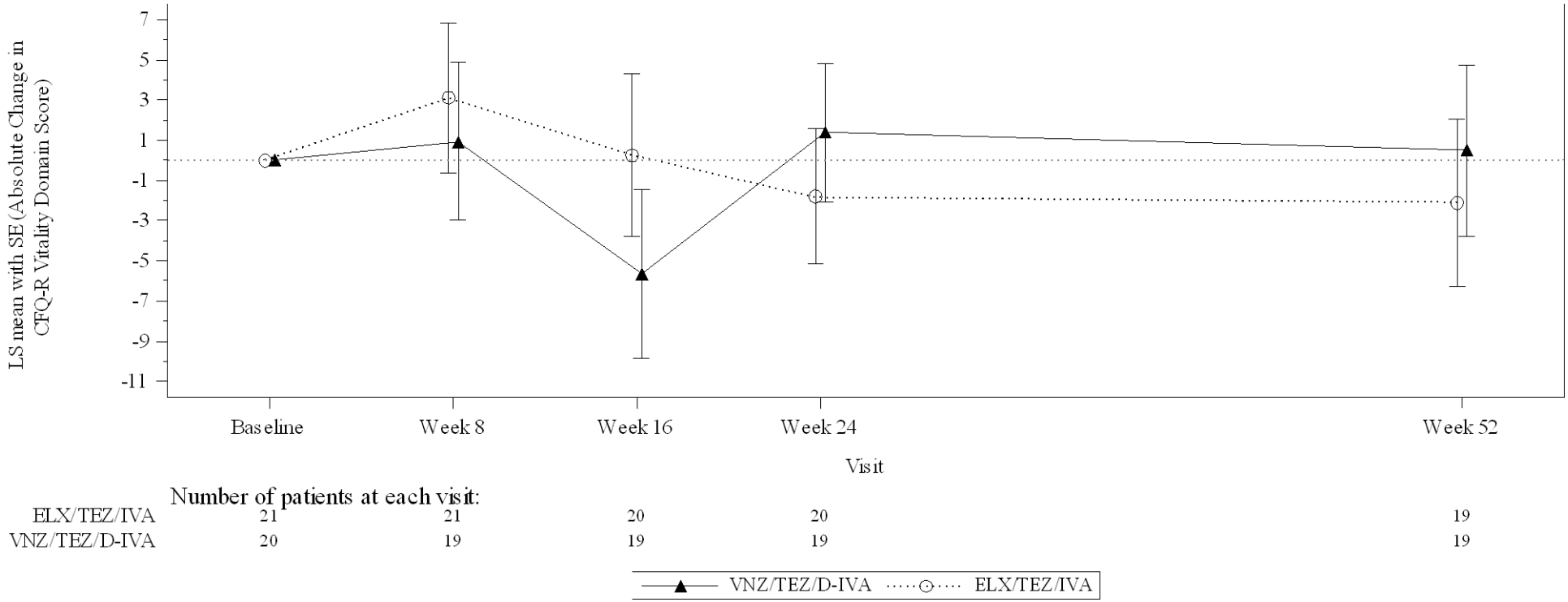
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

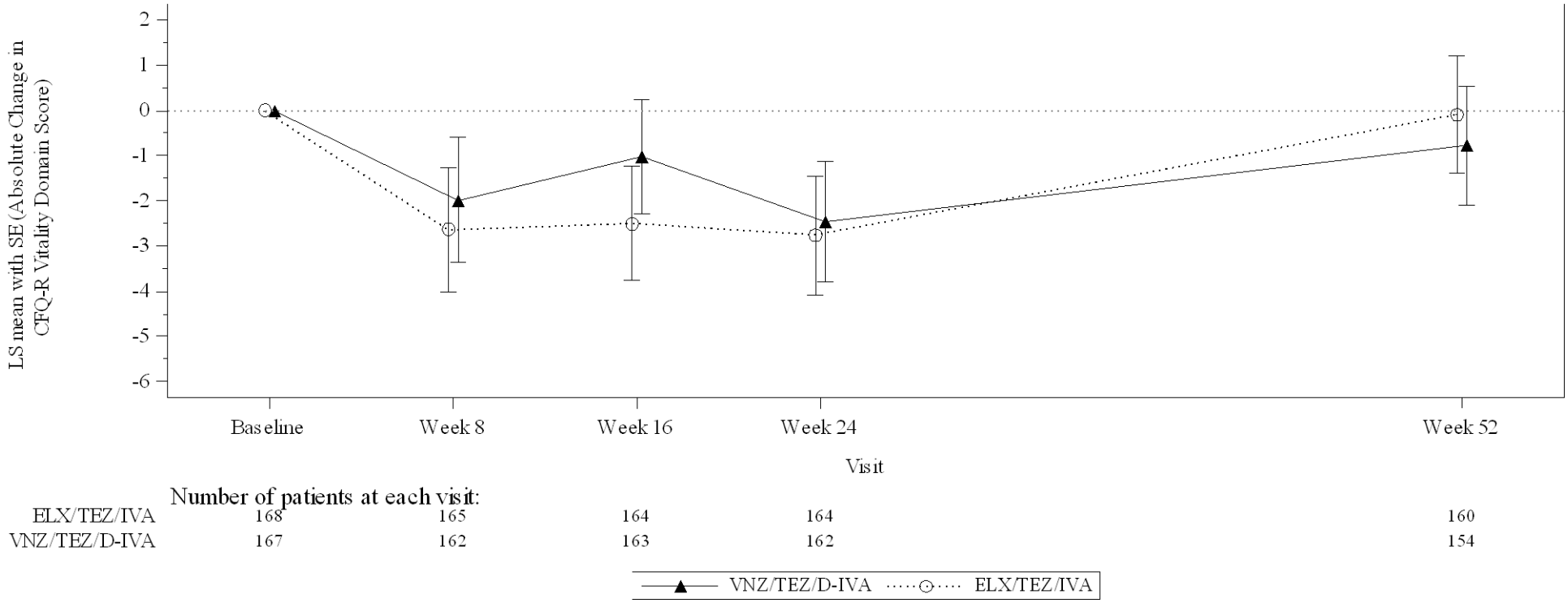
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years



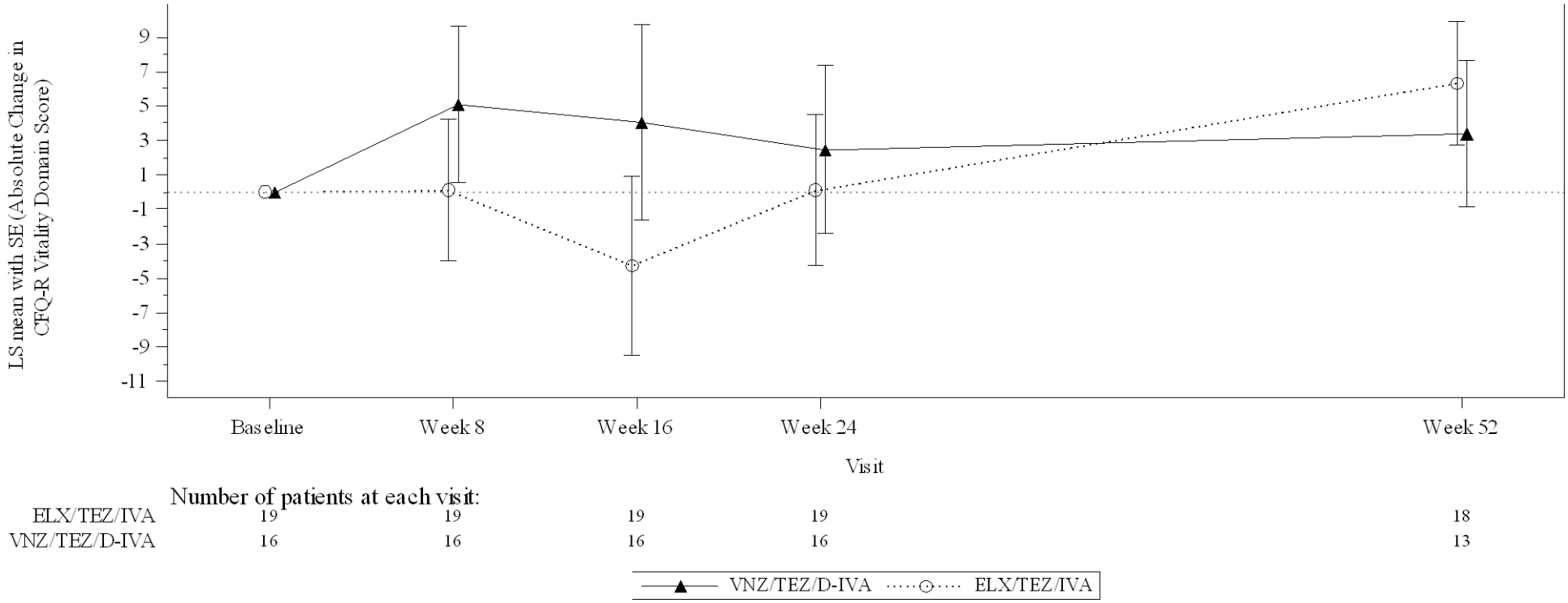
Number of patients at each visit:

ELX/TEZ/IVA	168	165	164	164	160
VNZ/TEZ/D-IVA	167	162	163	162	154

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

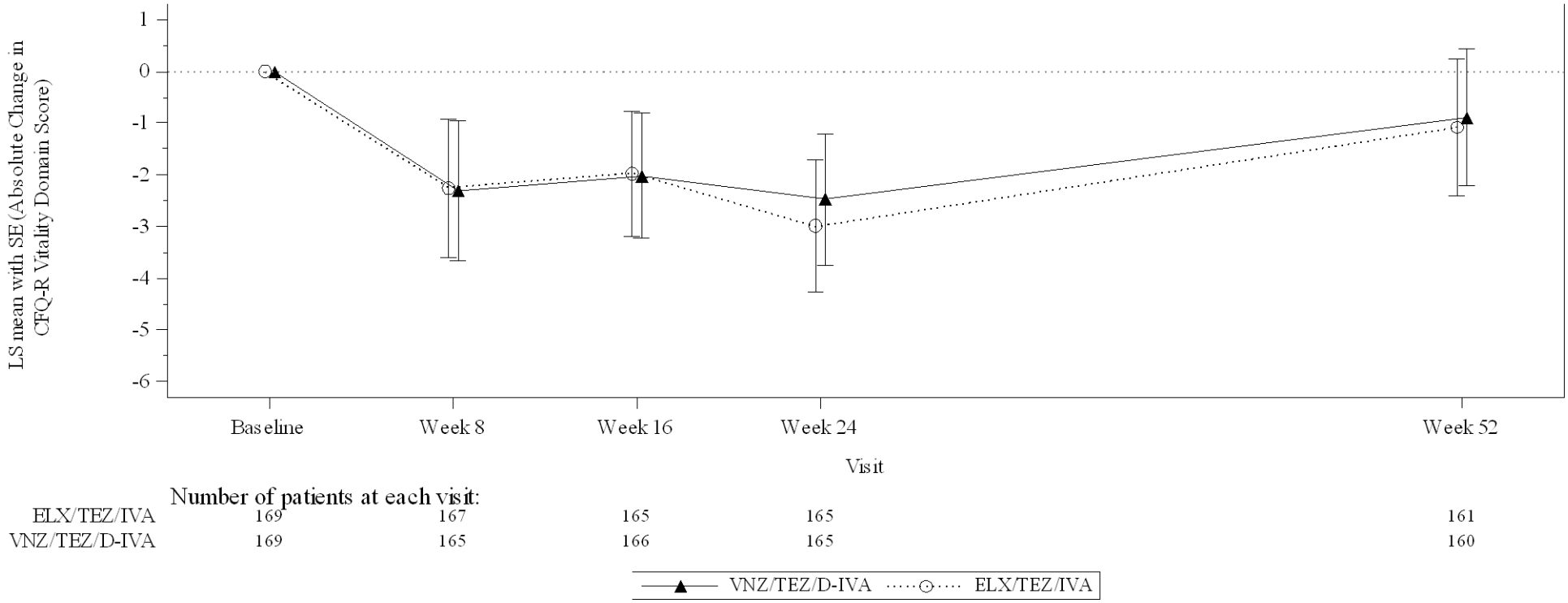
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L



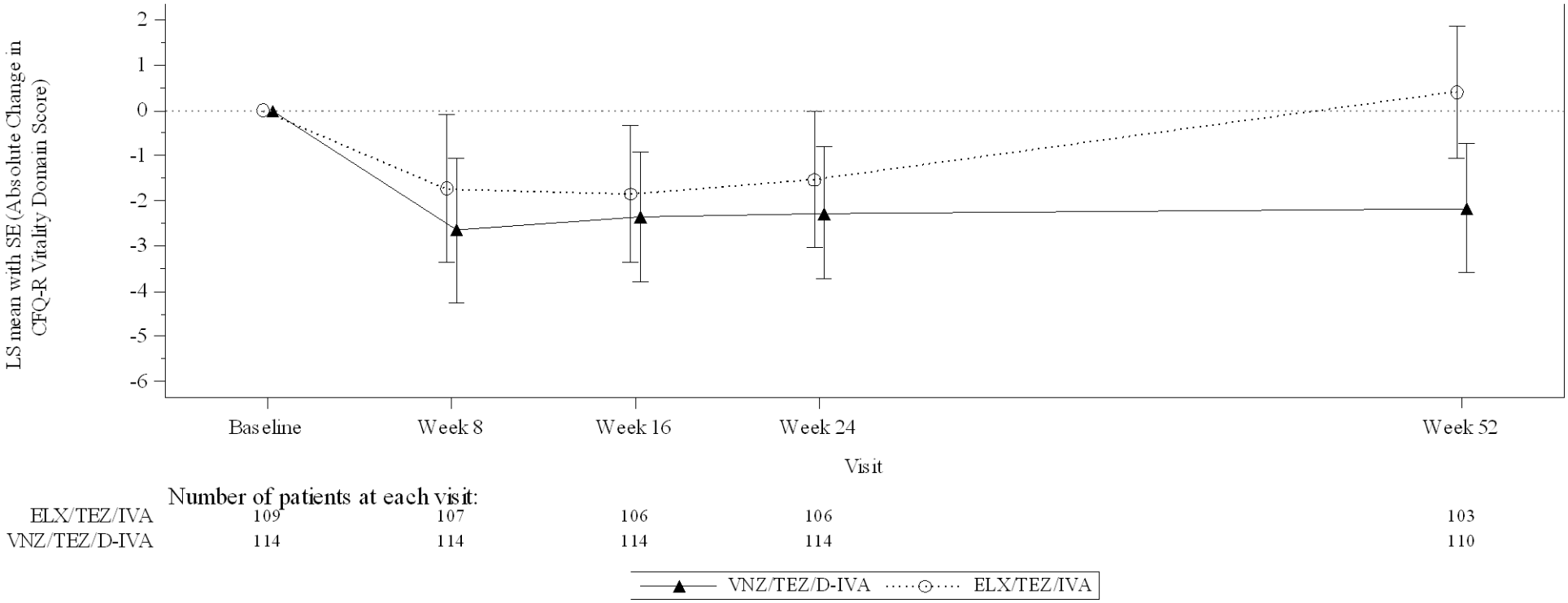
Number of patients at each visit:

	Baseline	Week 8	Week 16	Week 24	Week 52
ELX/TEZ/IVA	169	167	165	165	161
VNZ/TEZ/D-IVA	169	165	166	165	160

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

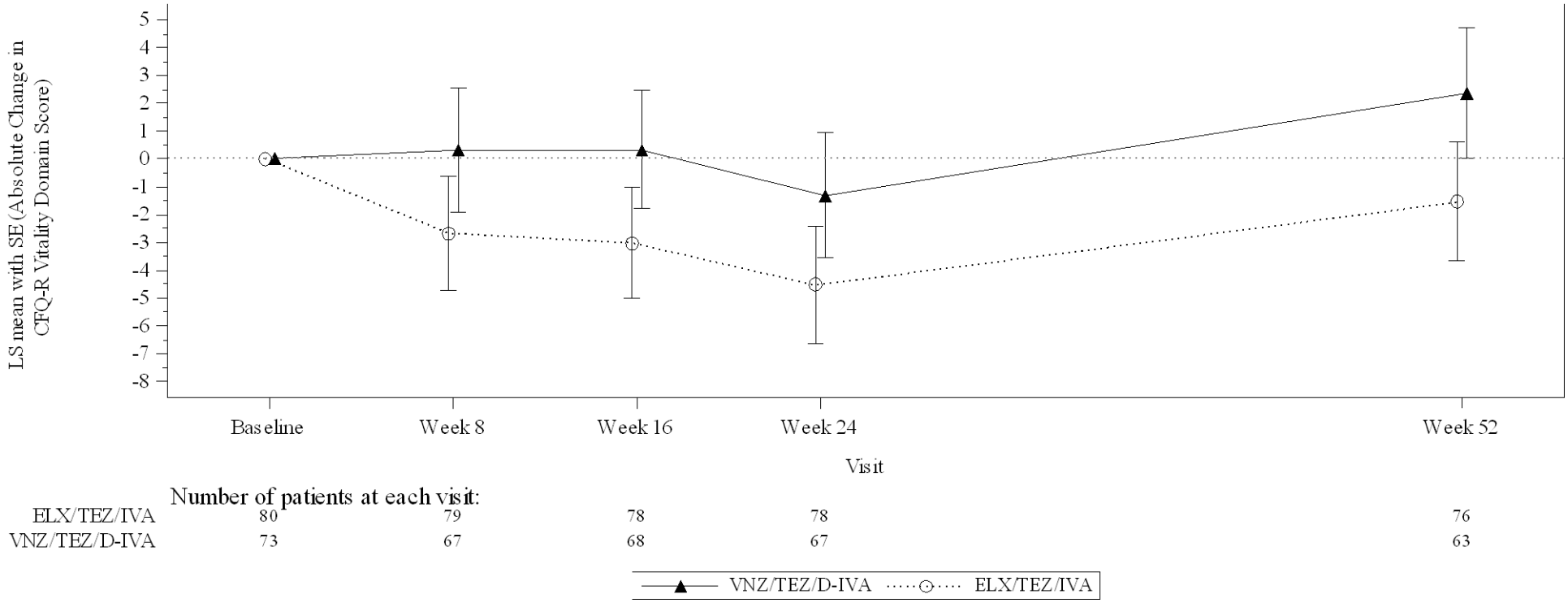
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

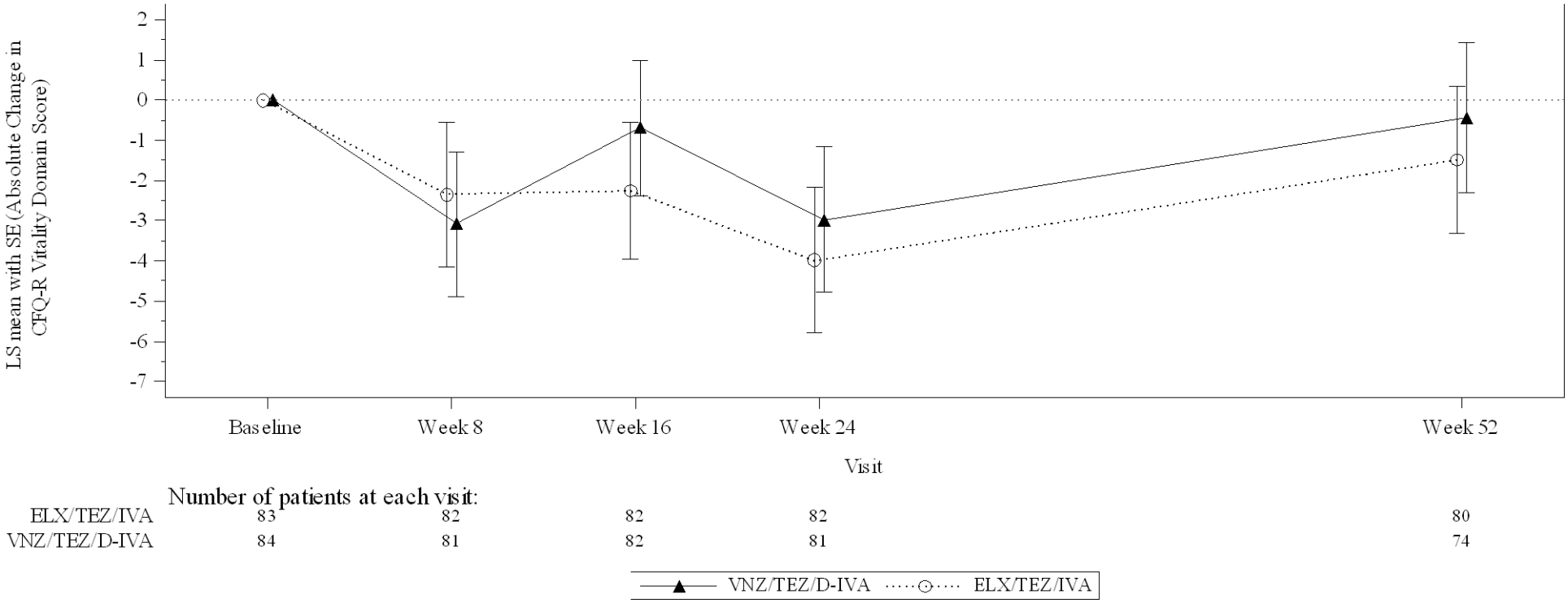
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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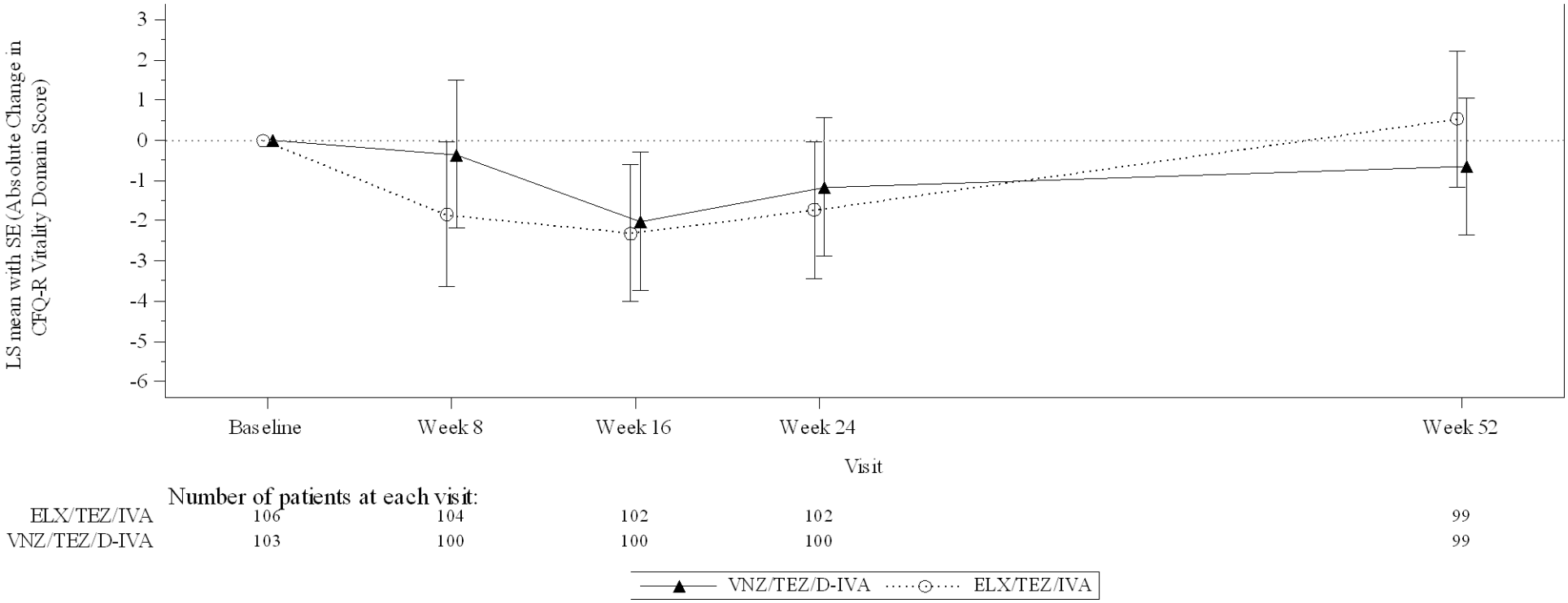
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

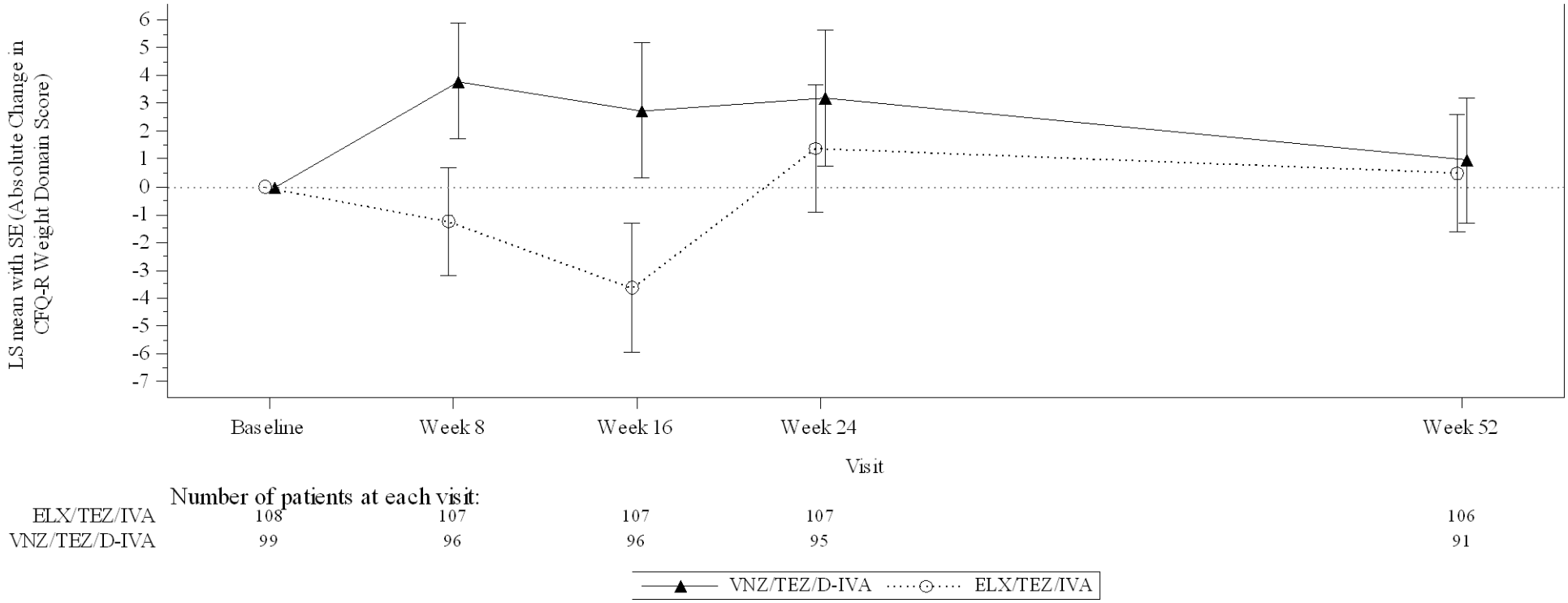
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

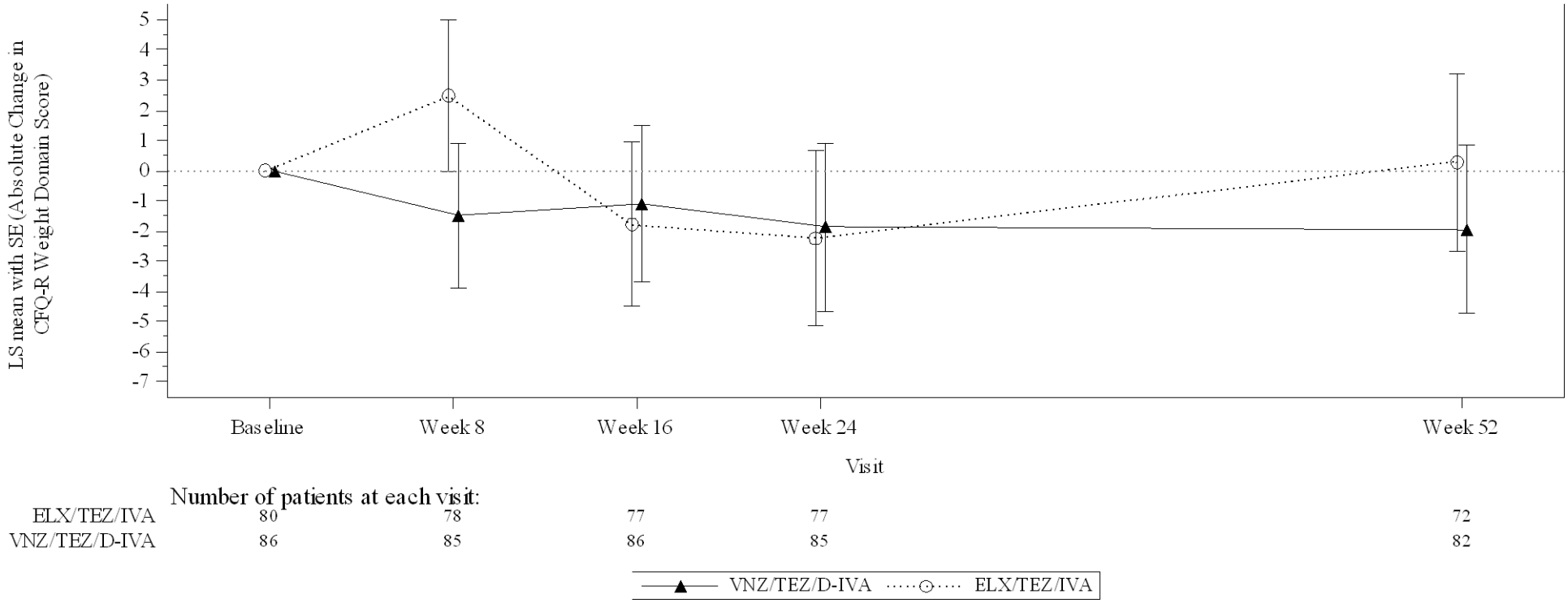
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5
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Full Analysis Set

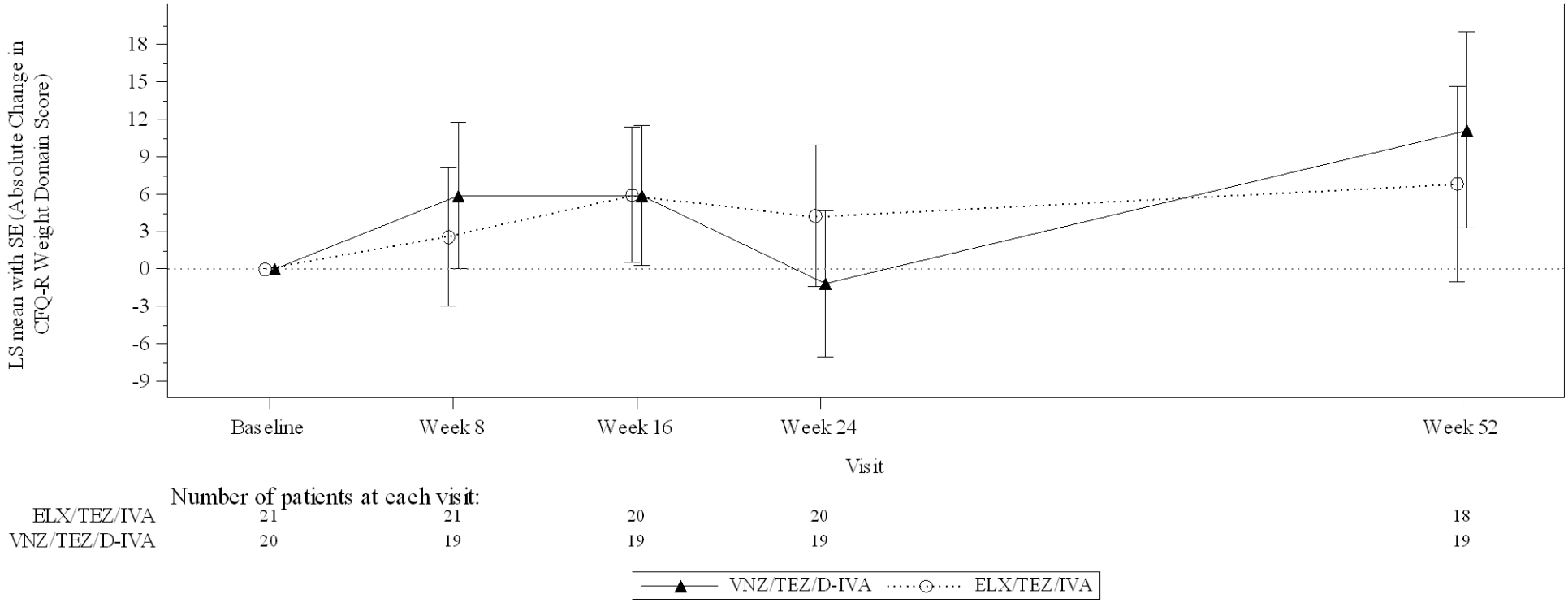
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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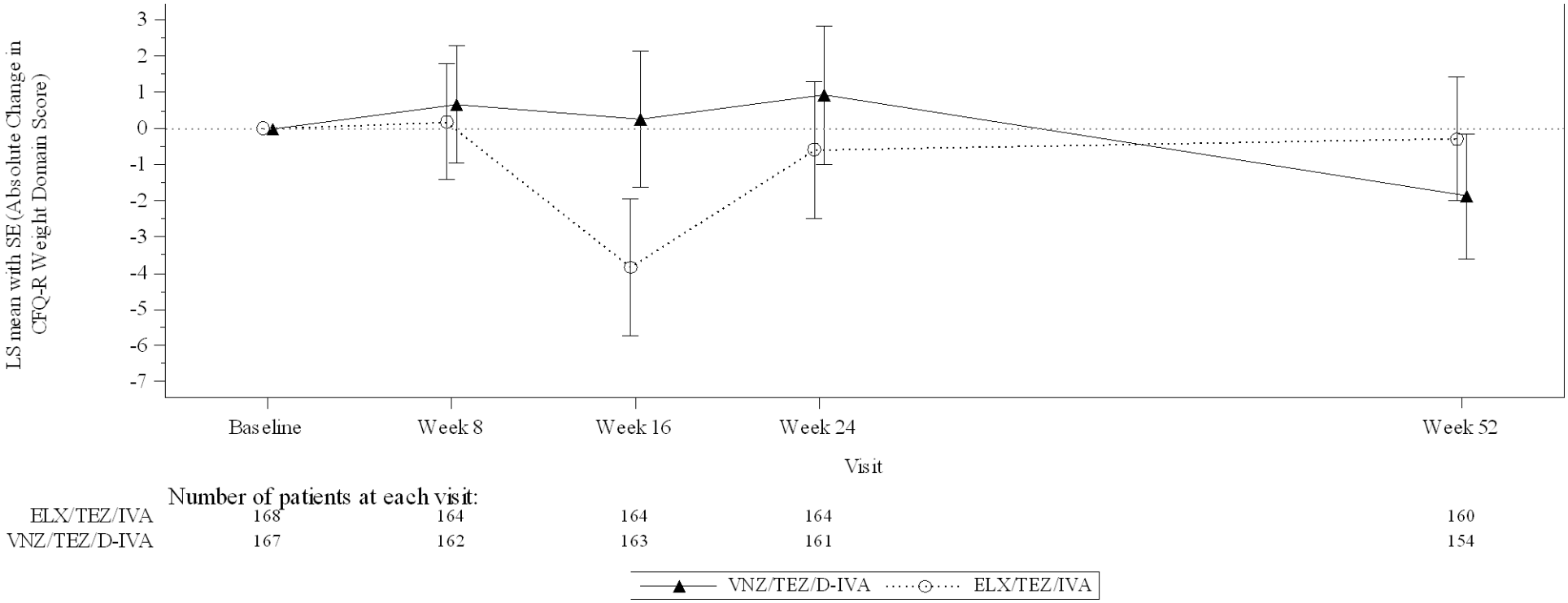
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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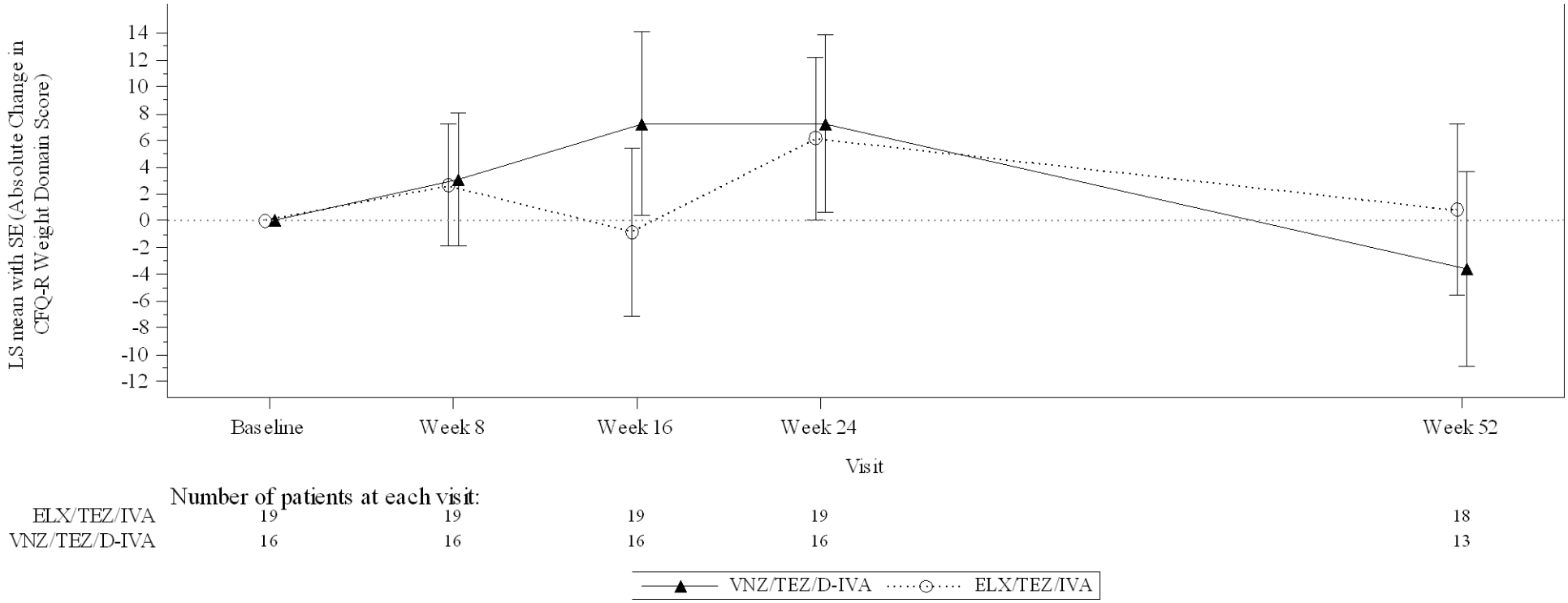
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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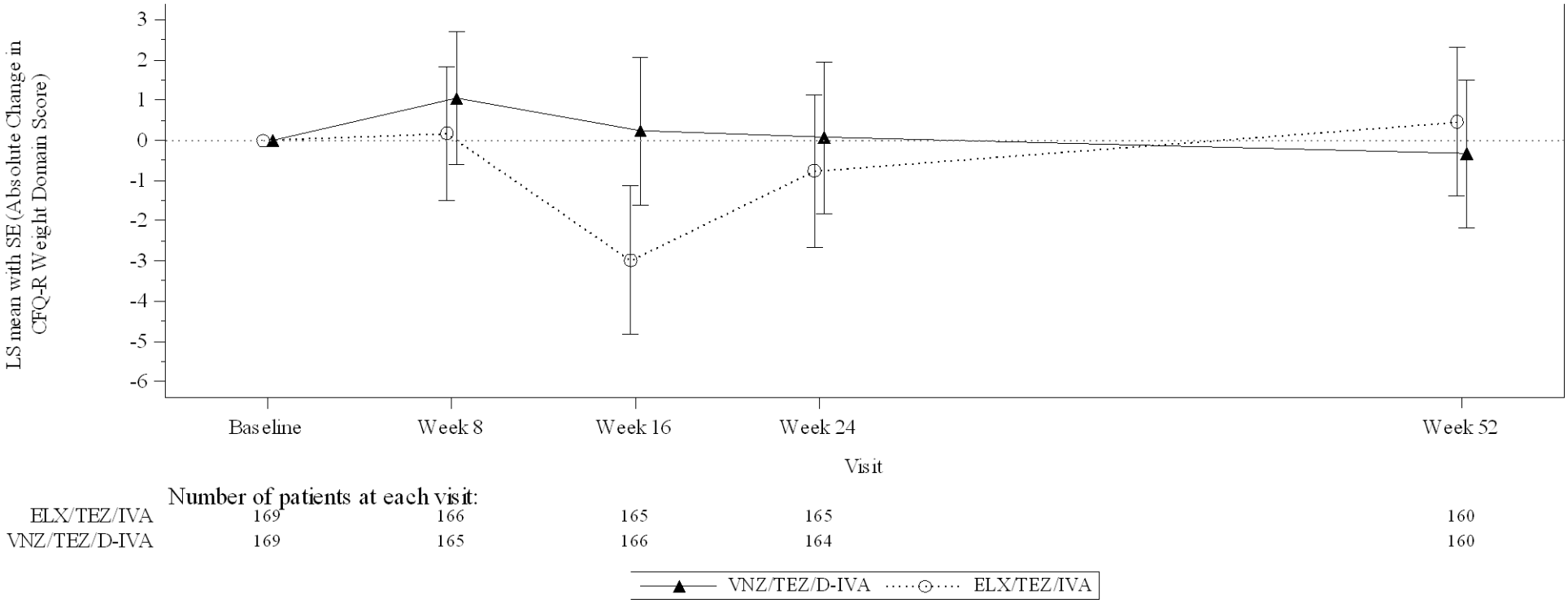
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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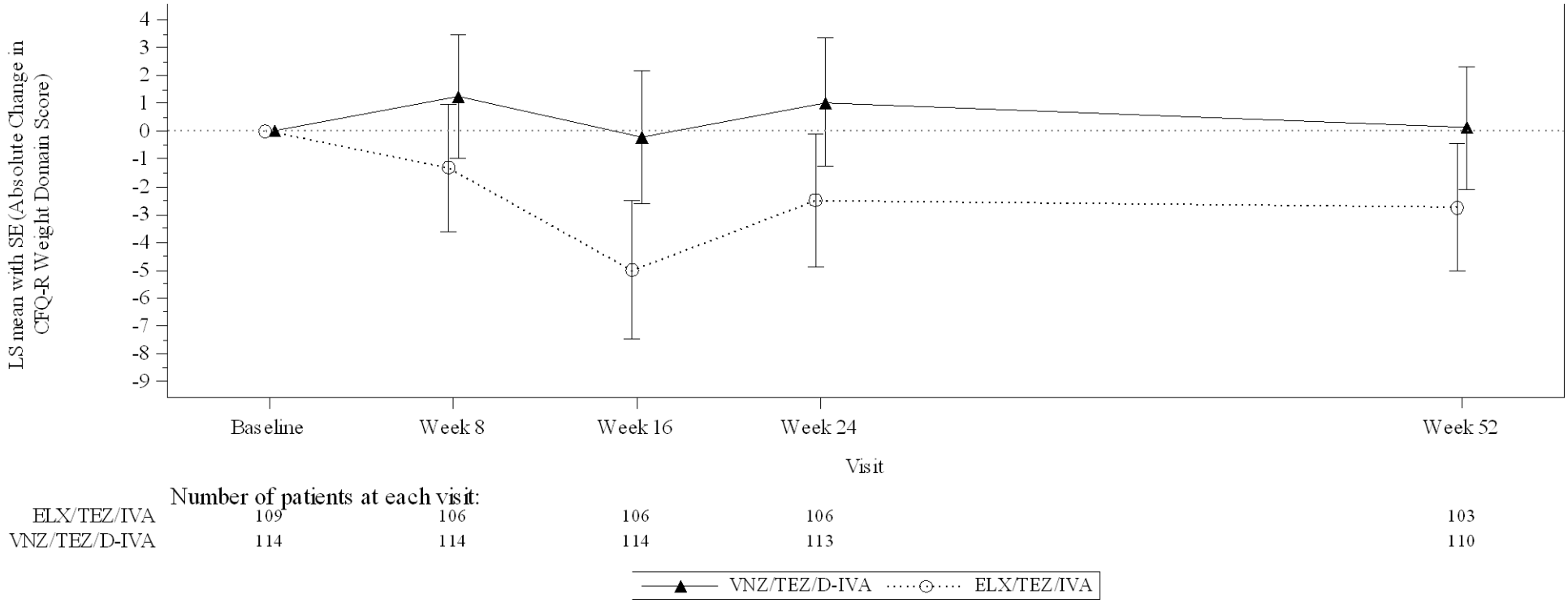
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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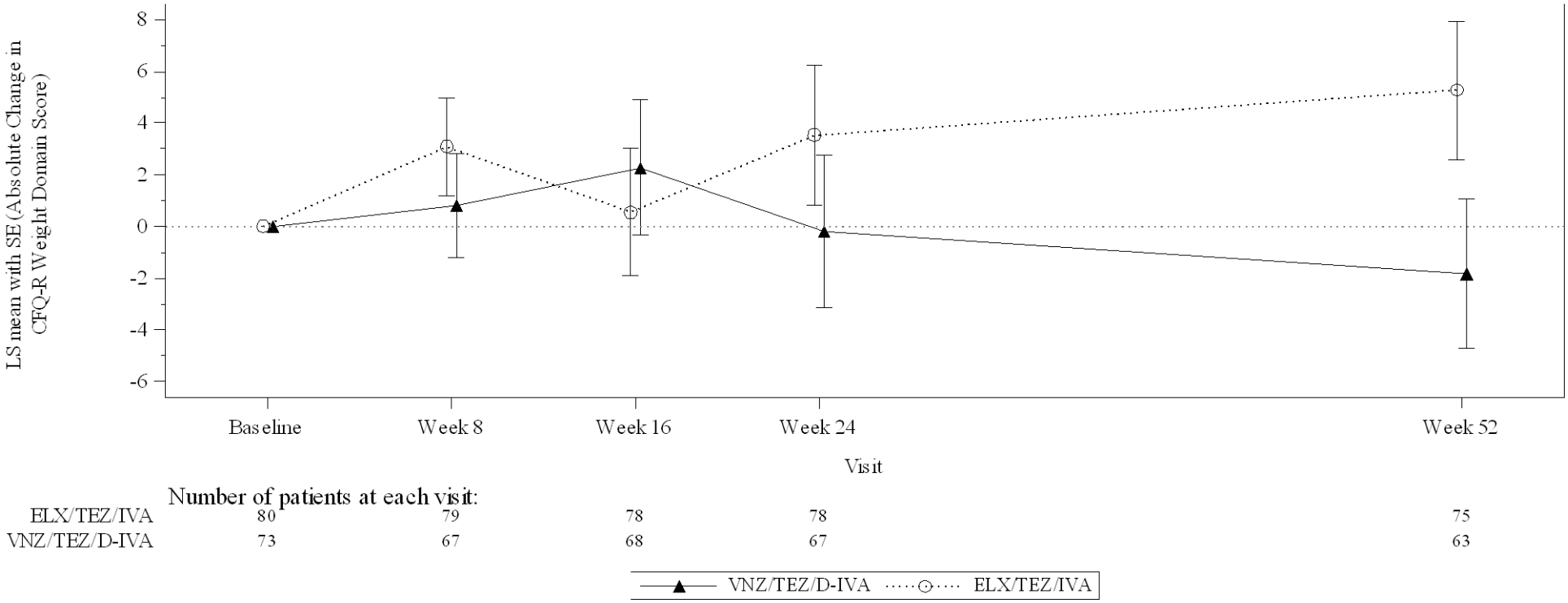
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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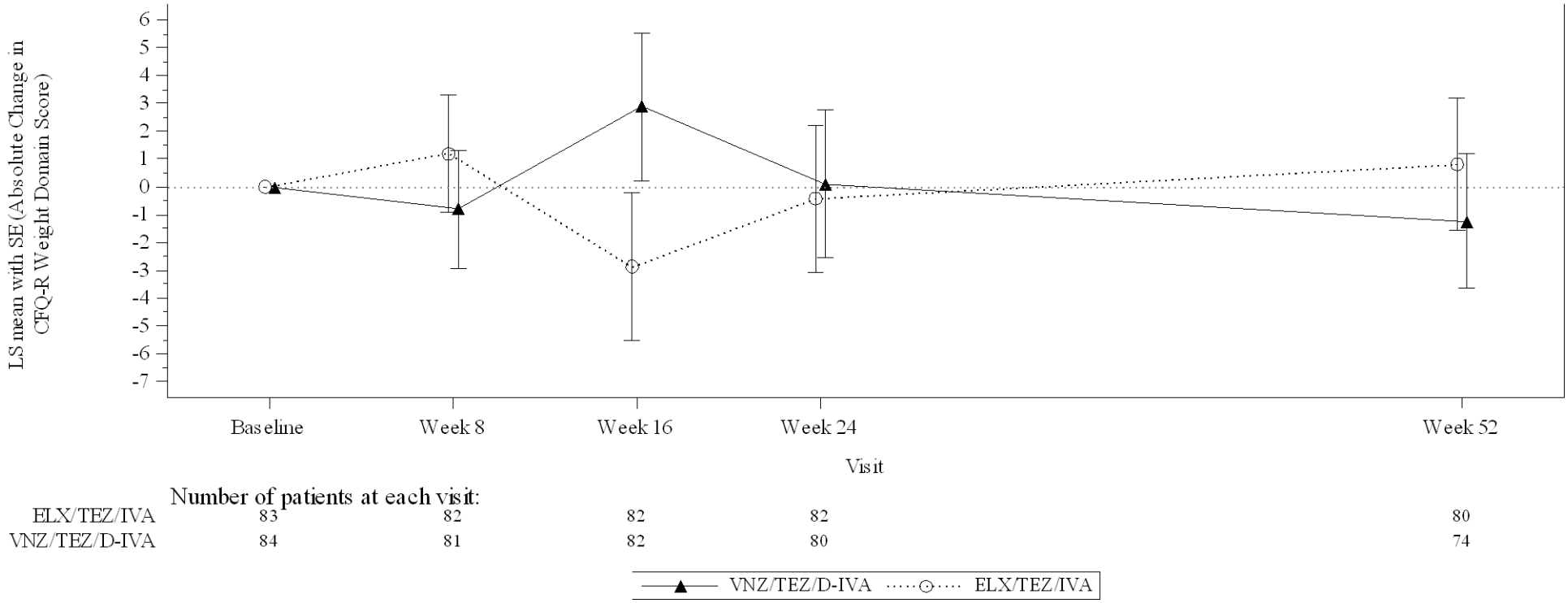
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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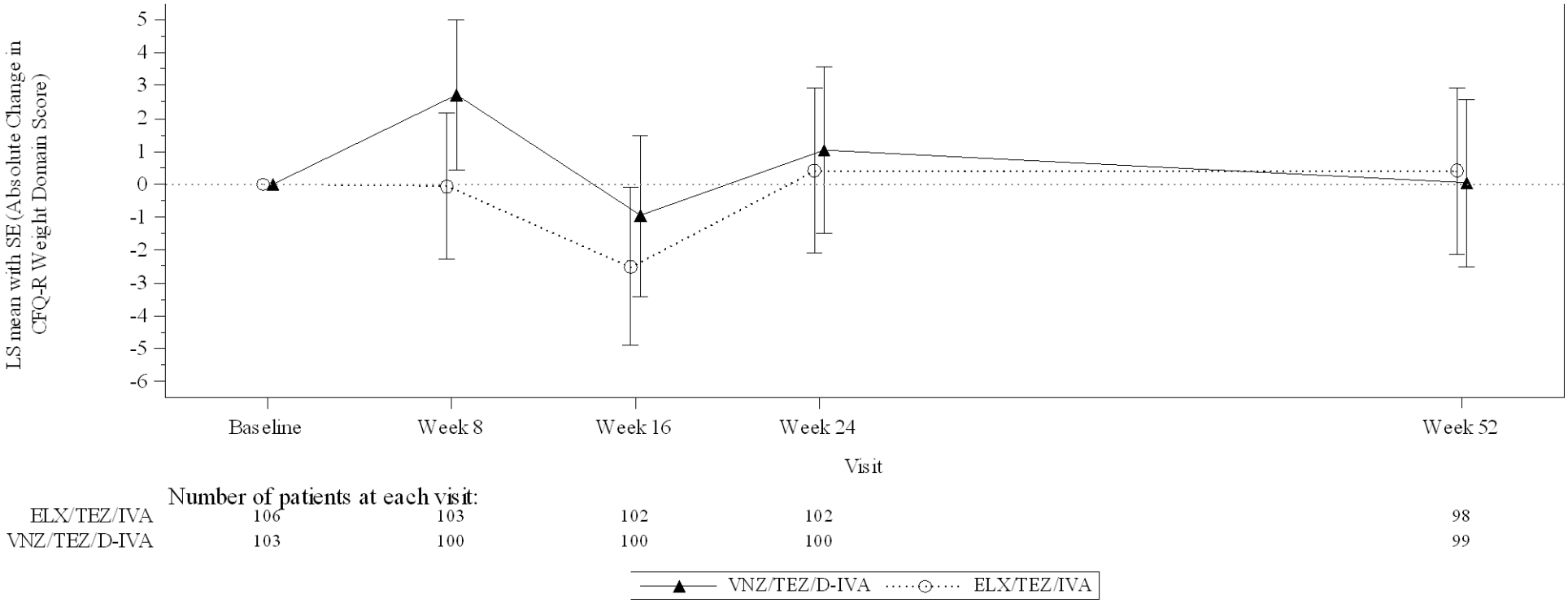
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Figure 1.2.2.9.5
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

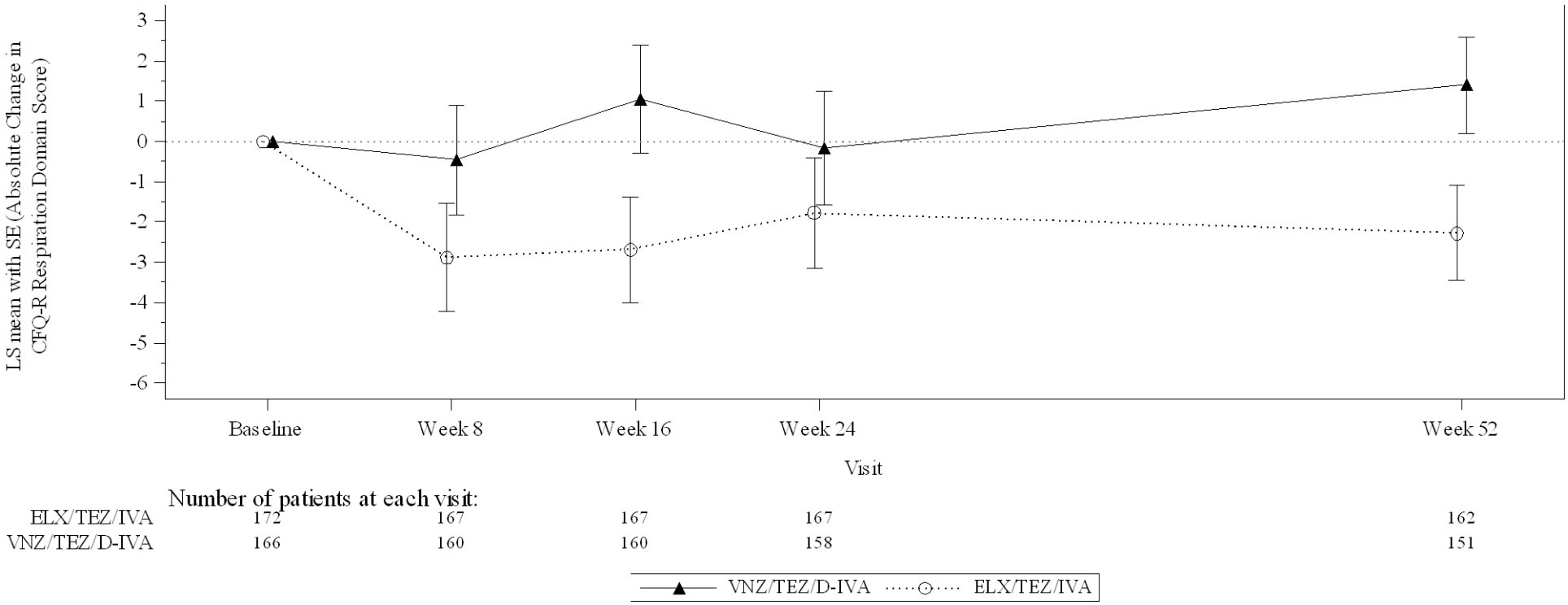
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

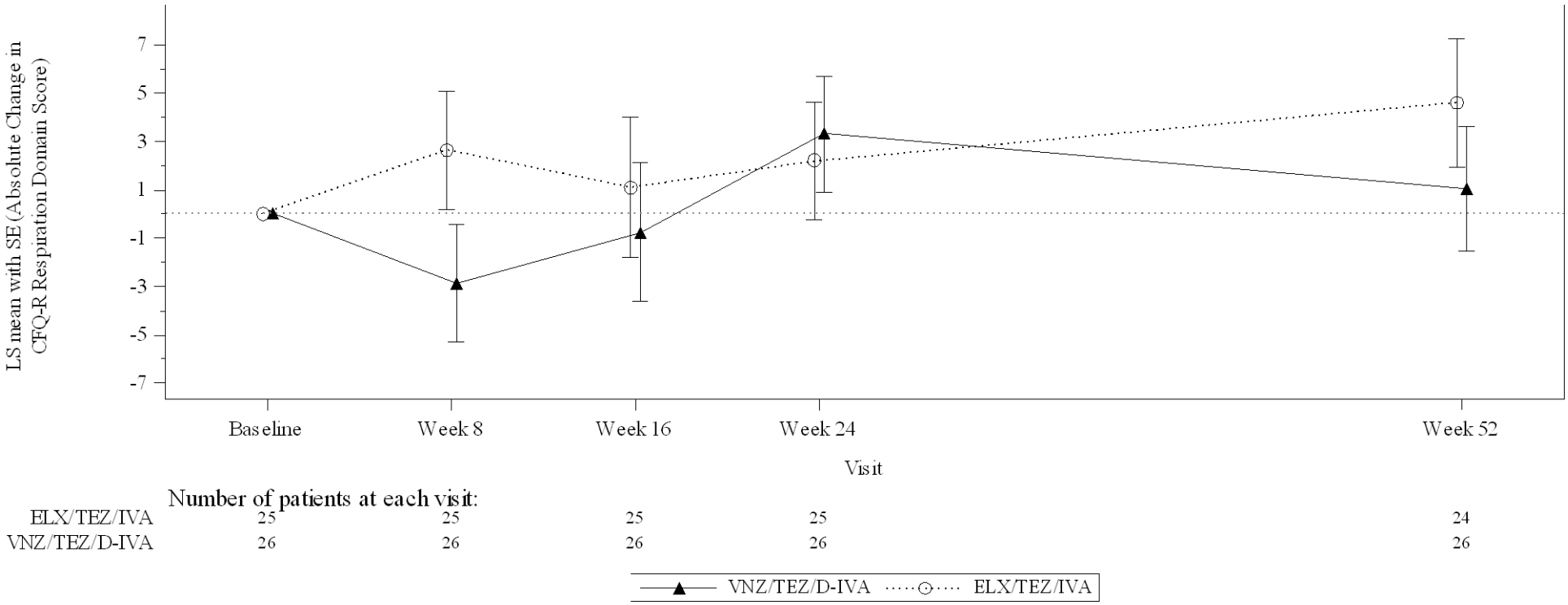
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

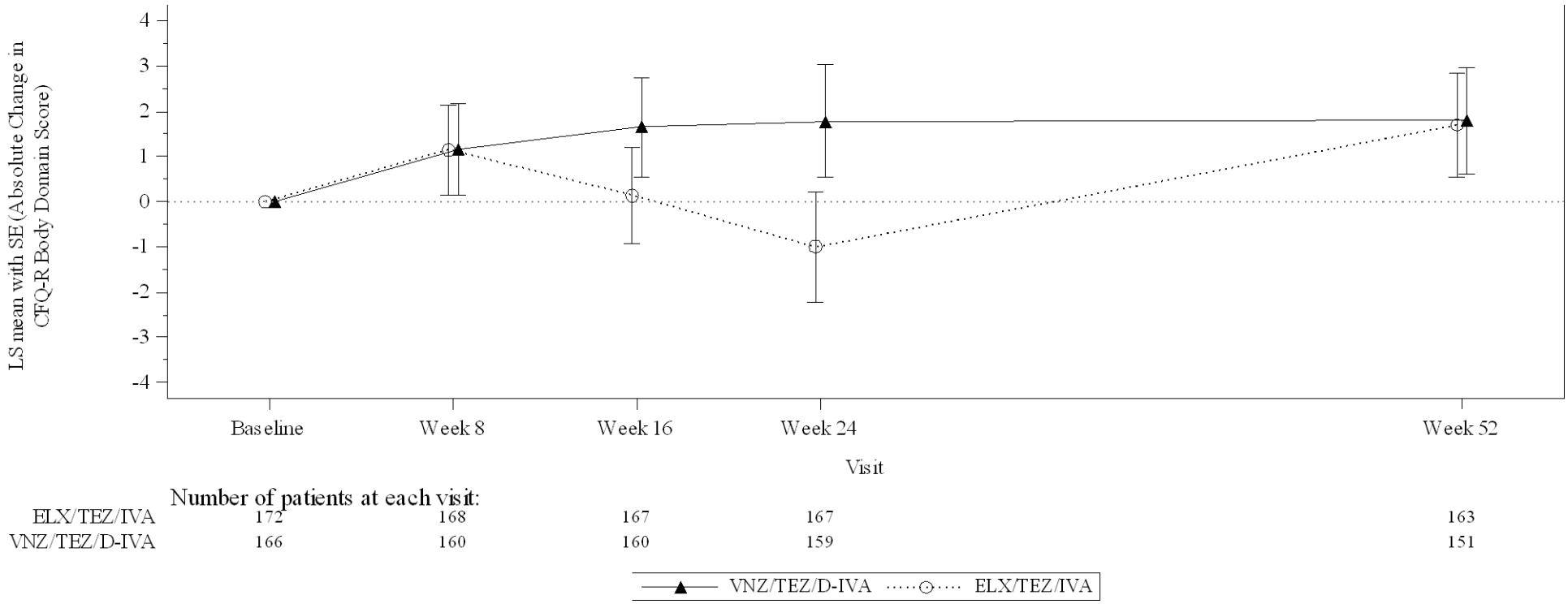
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

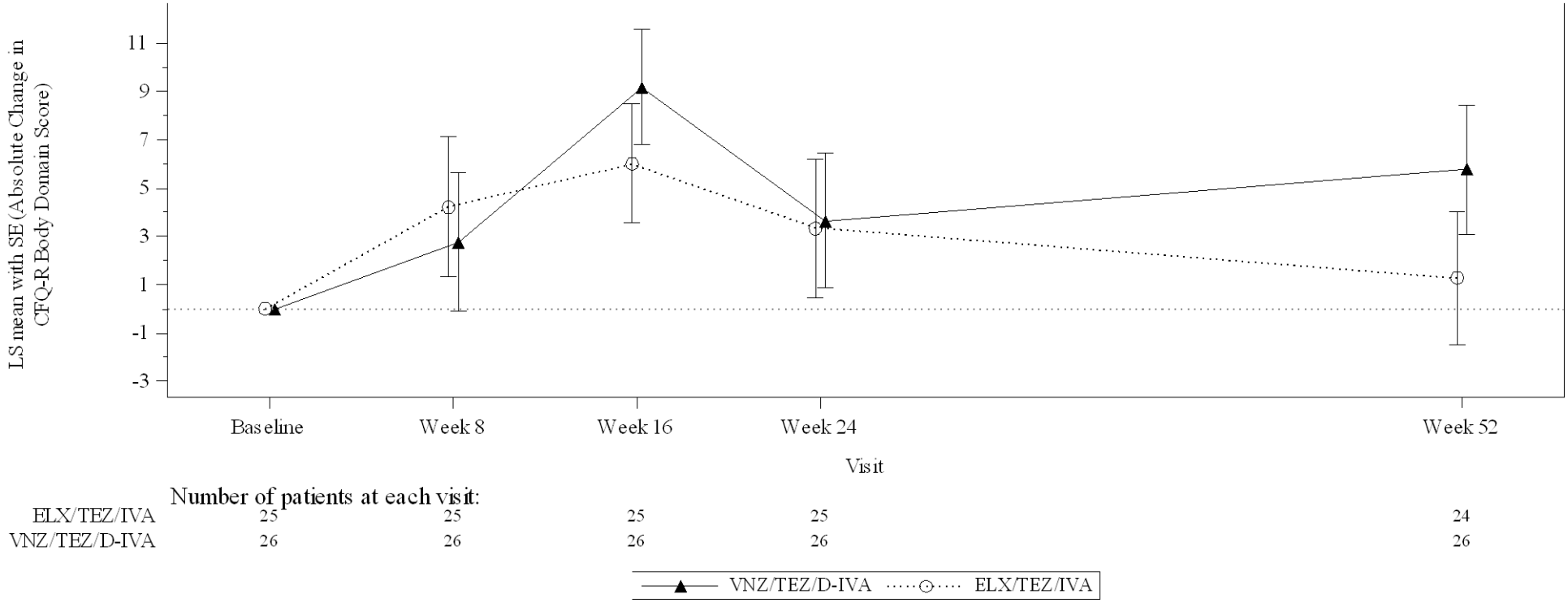
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

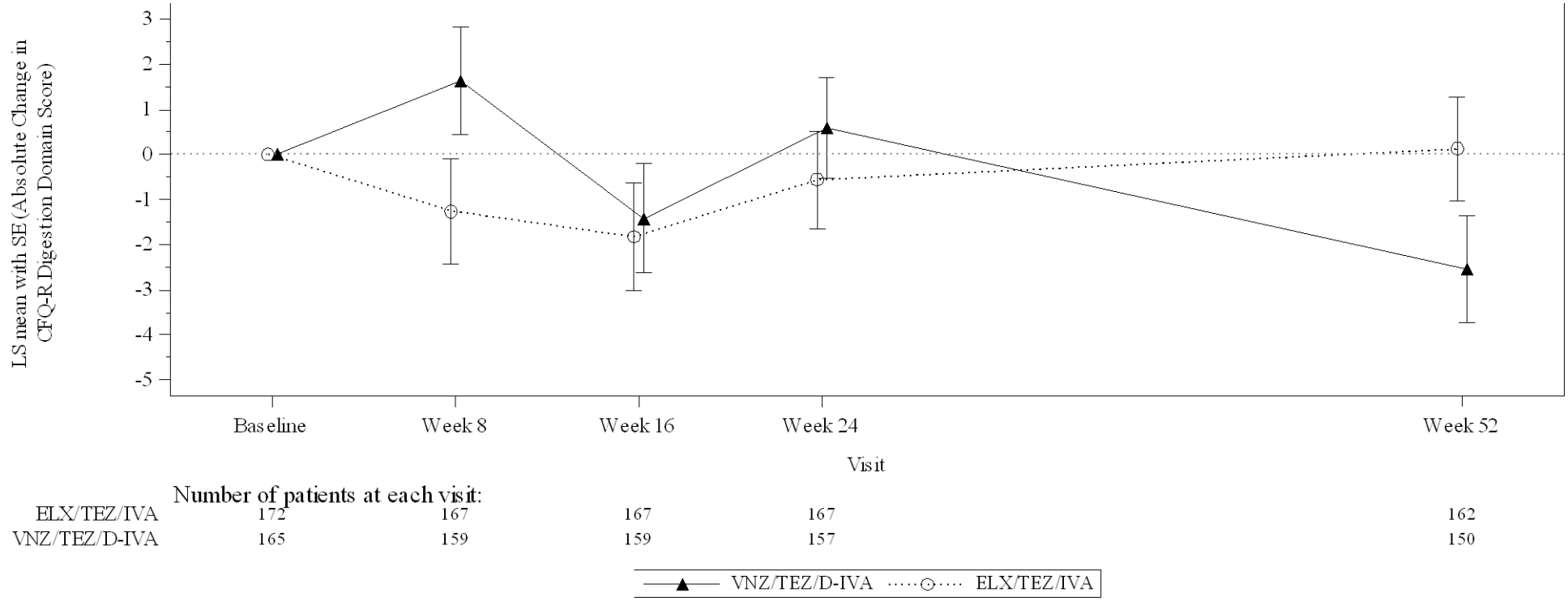
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

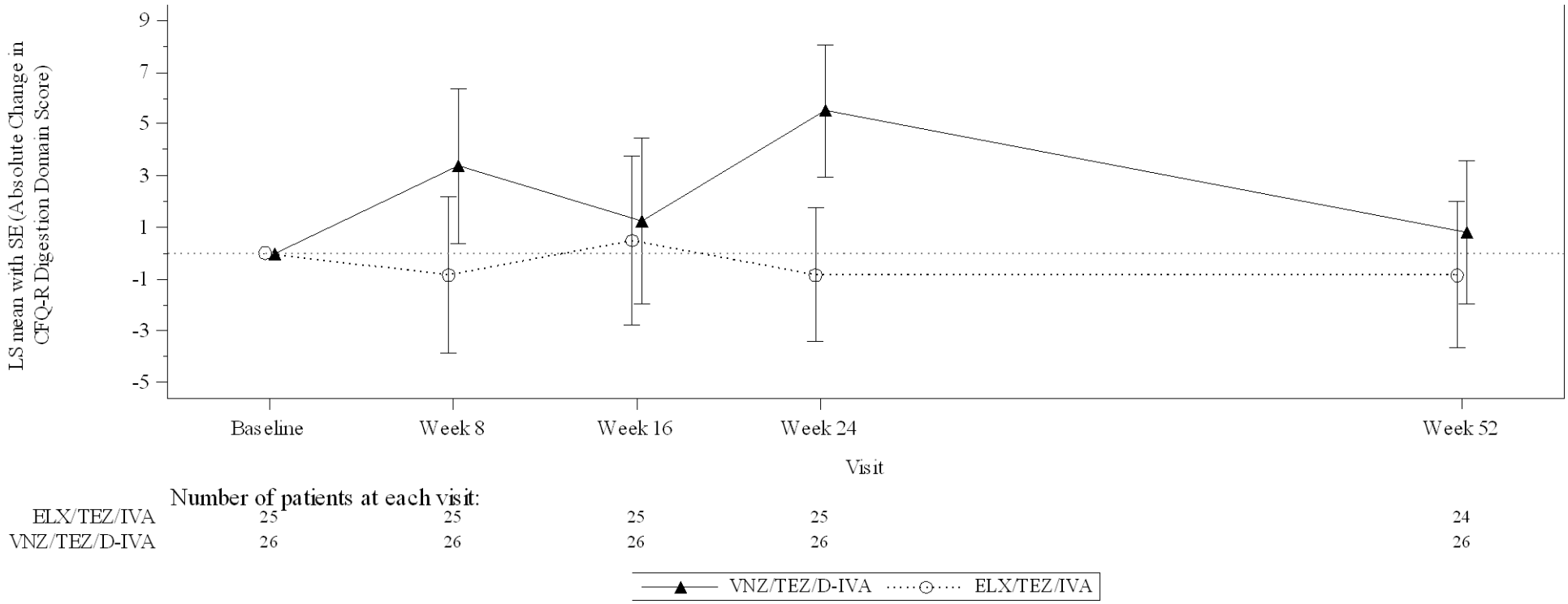
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

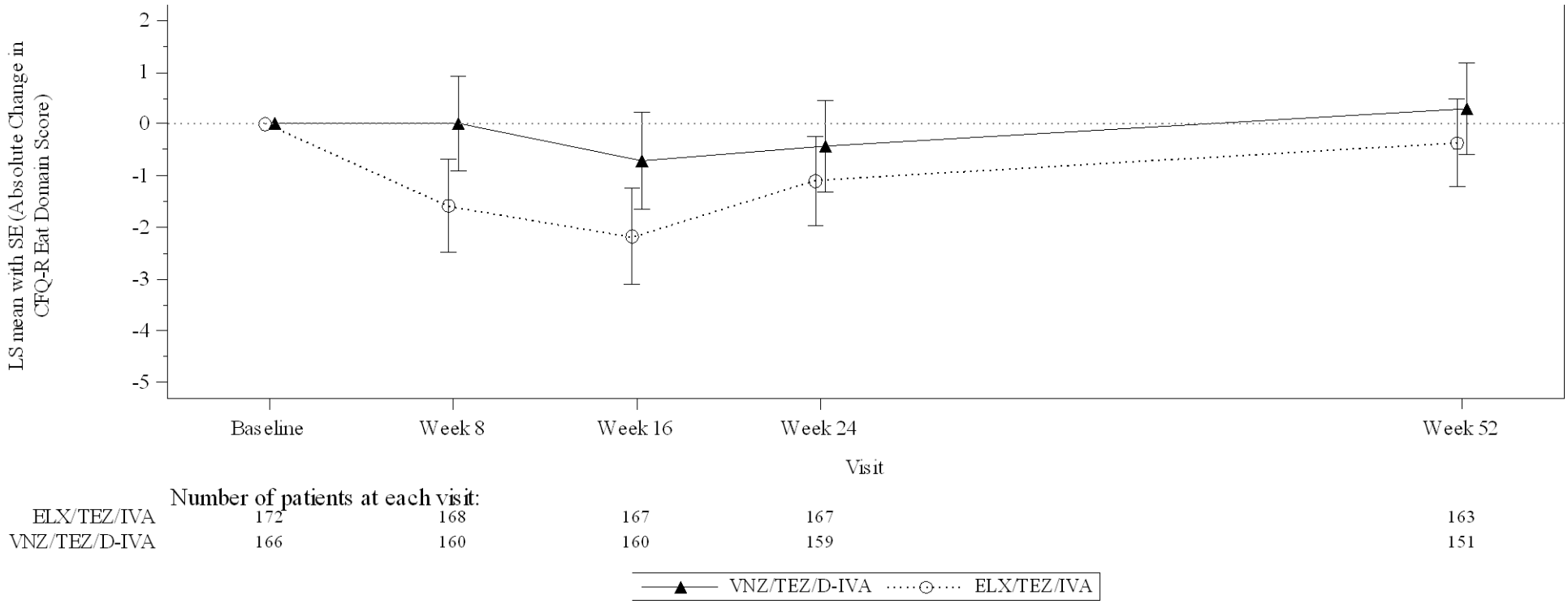
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

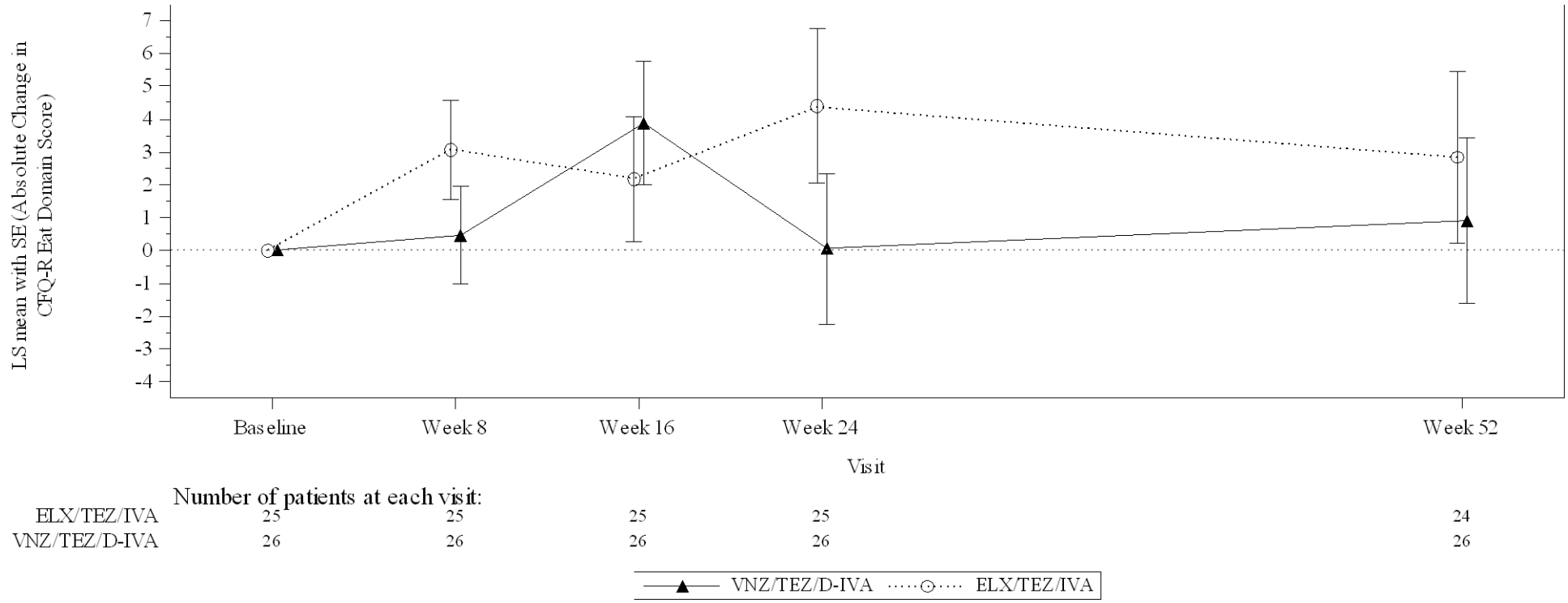
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

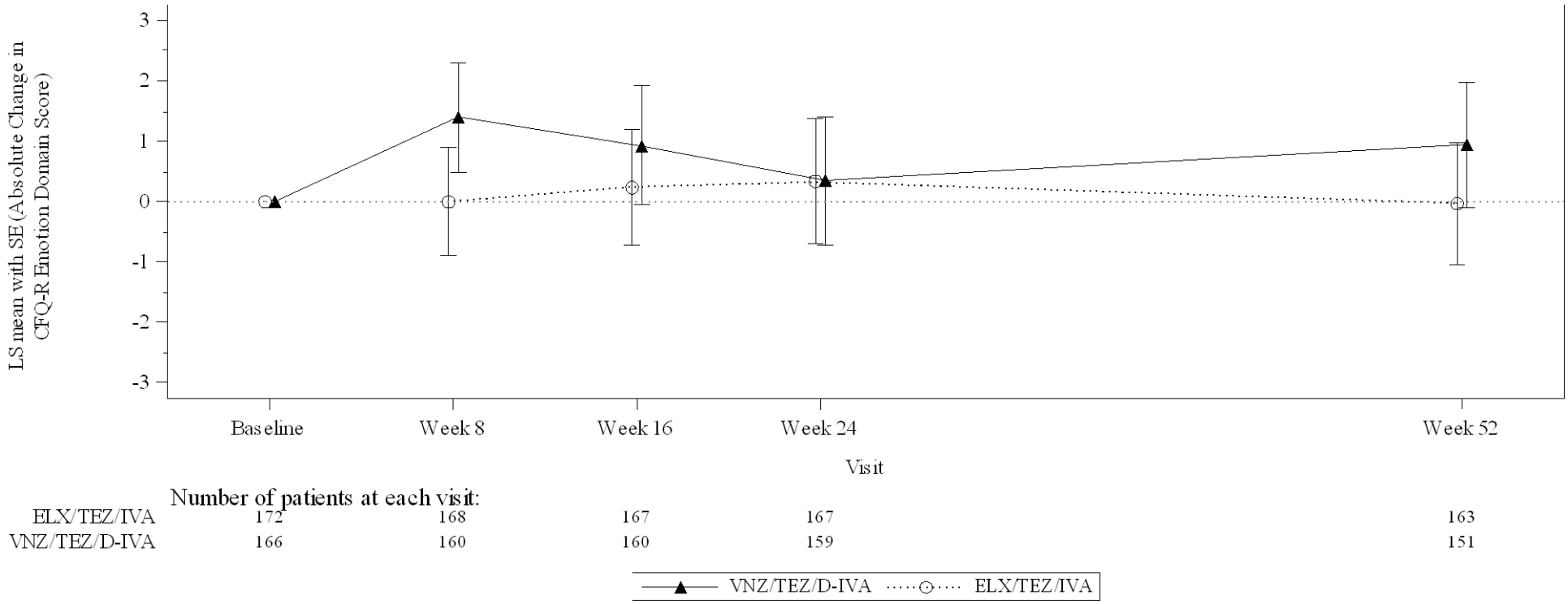
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

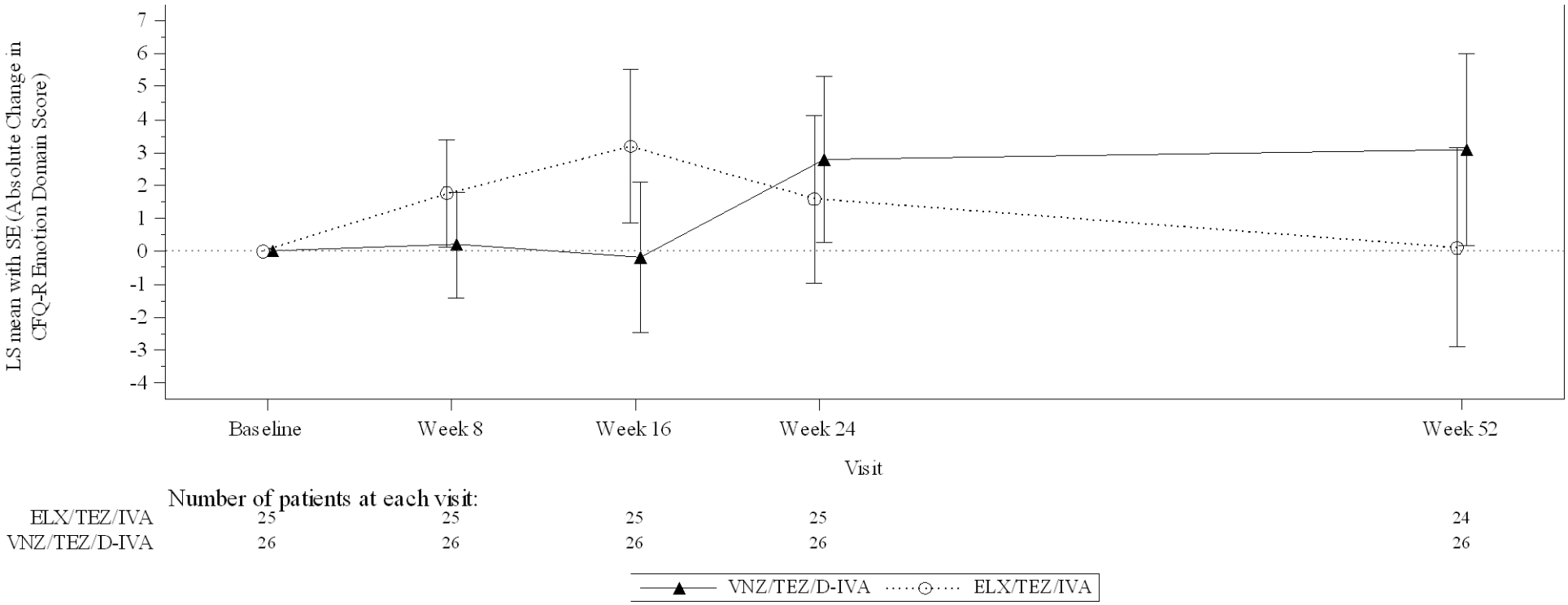
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

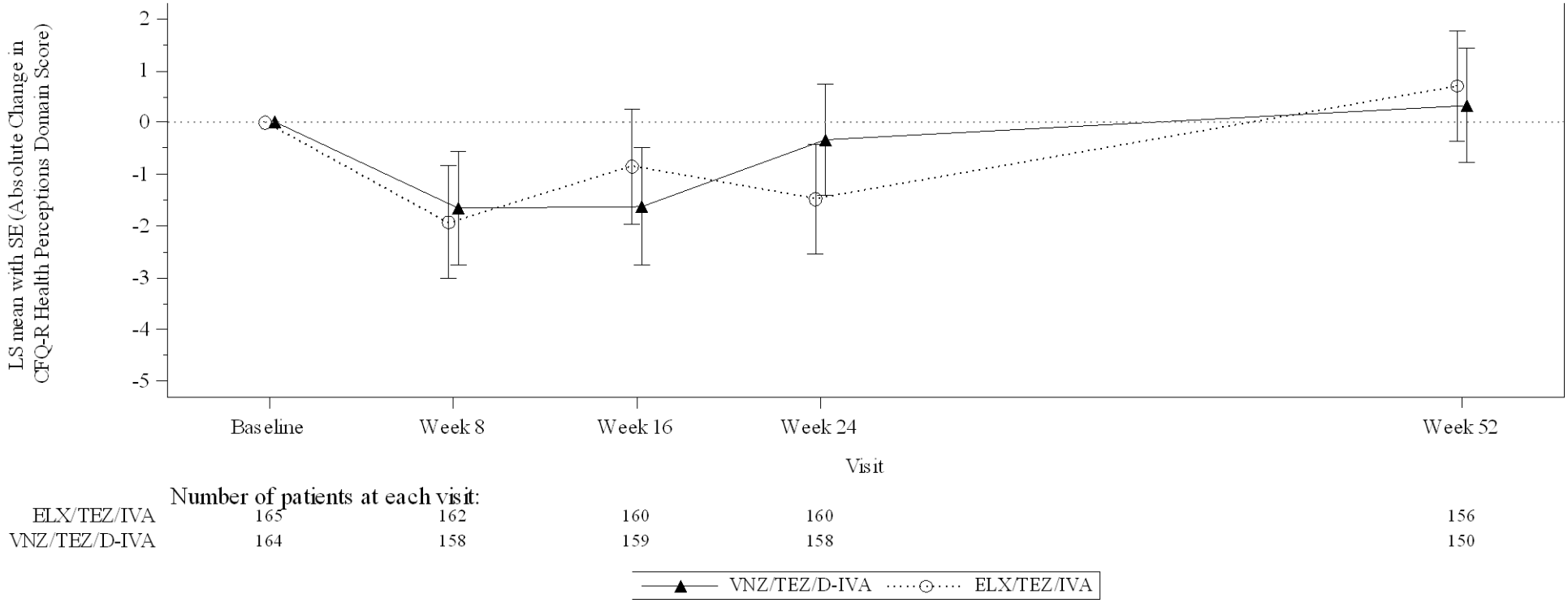
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

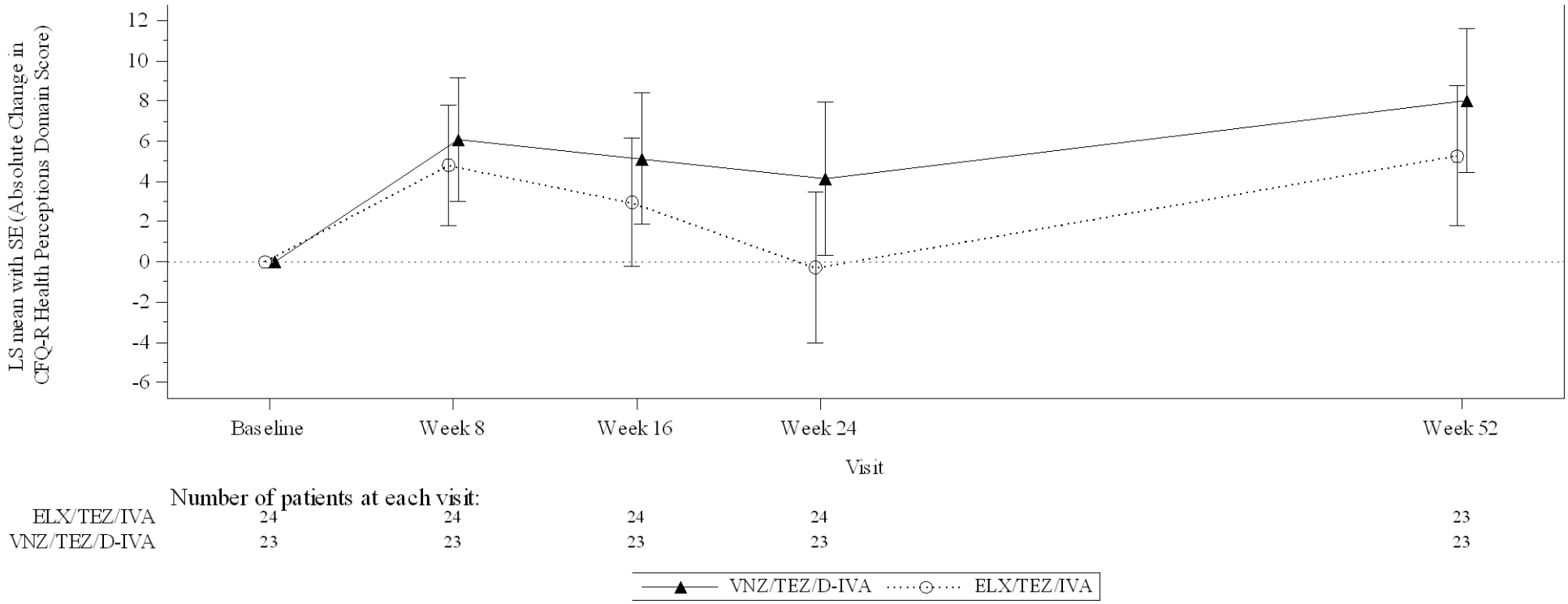
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

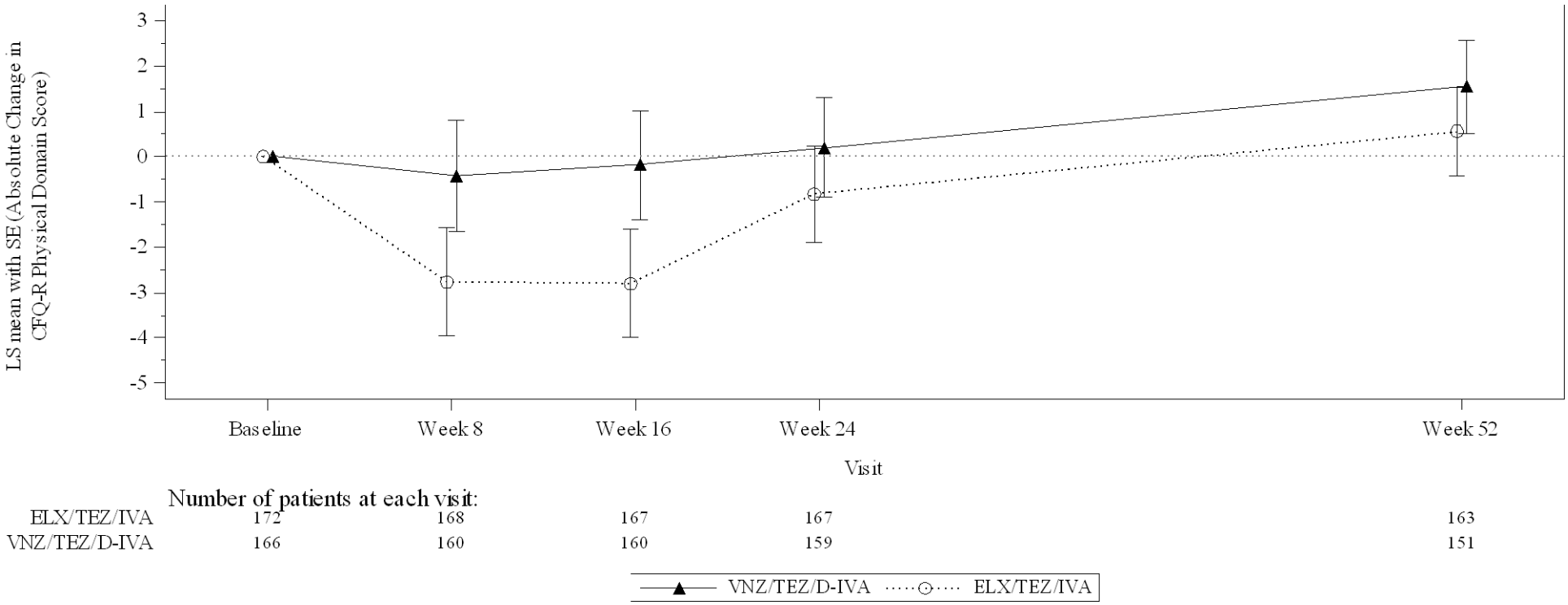
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

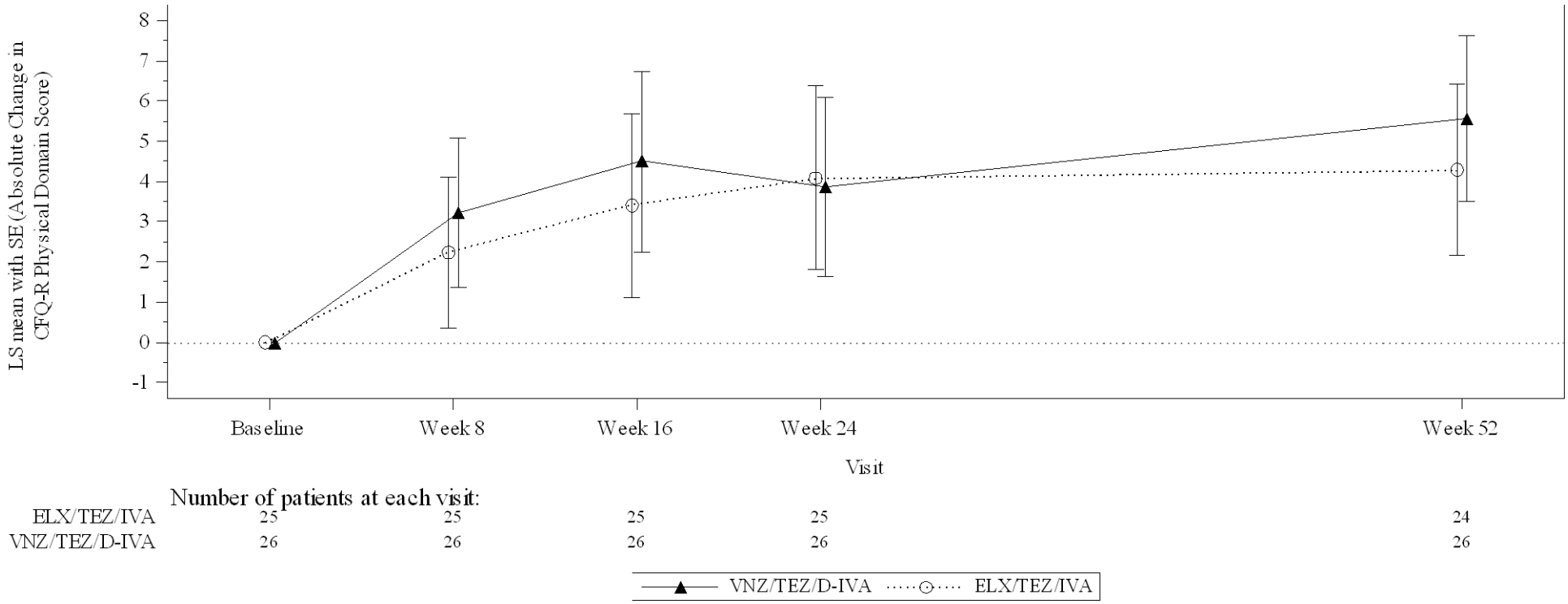
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

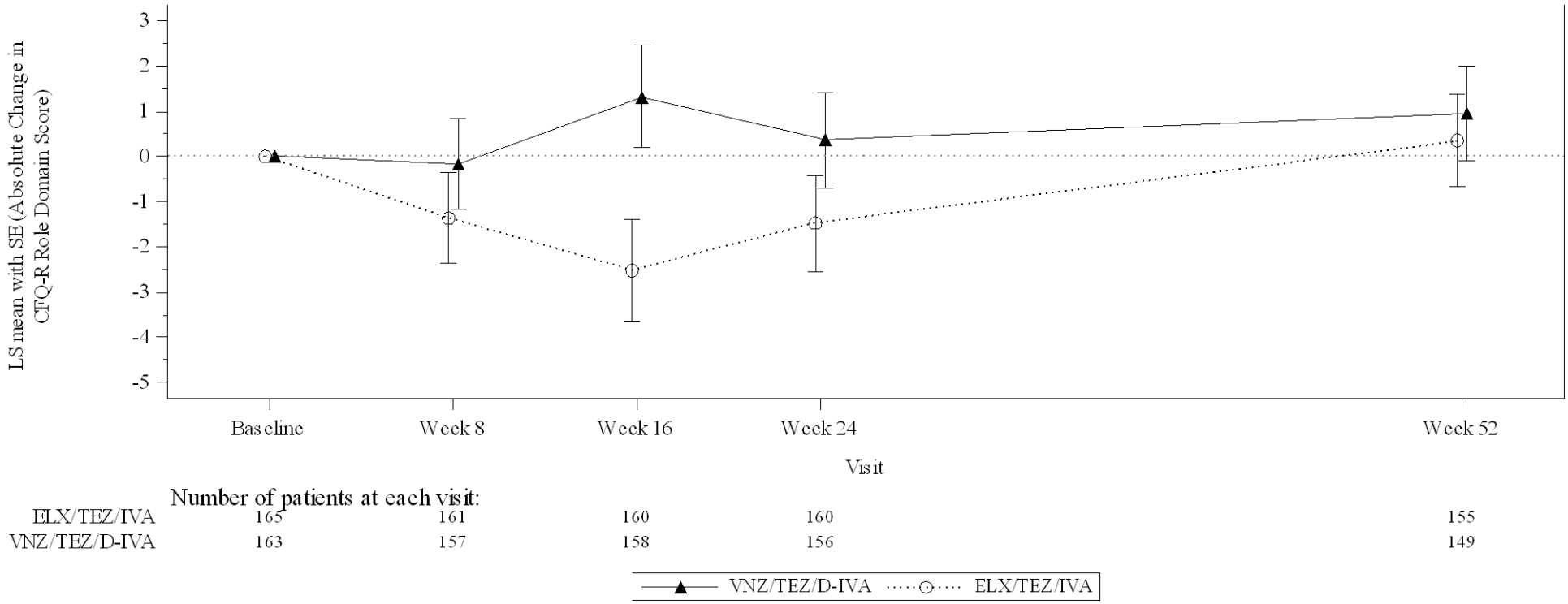
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

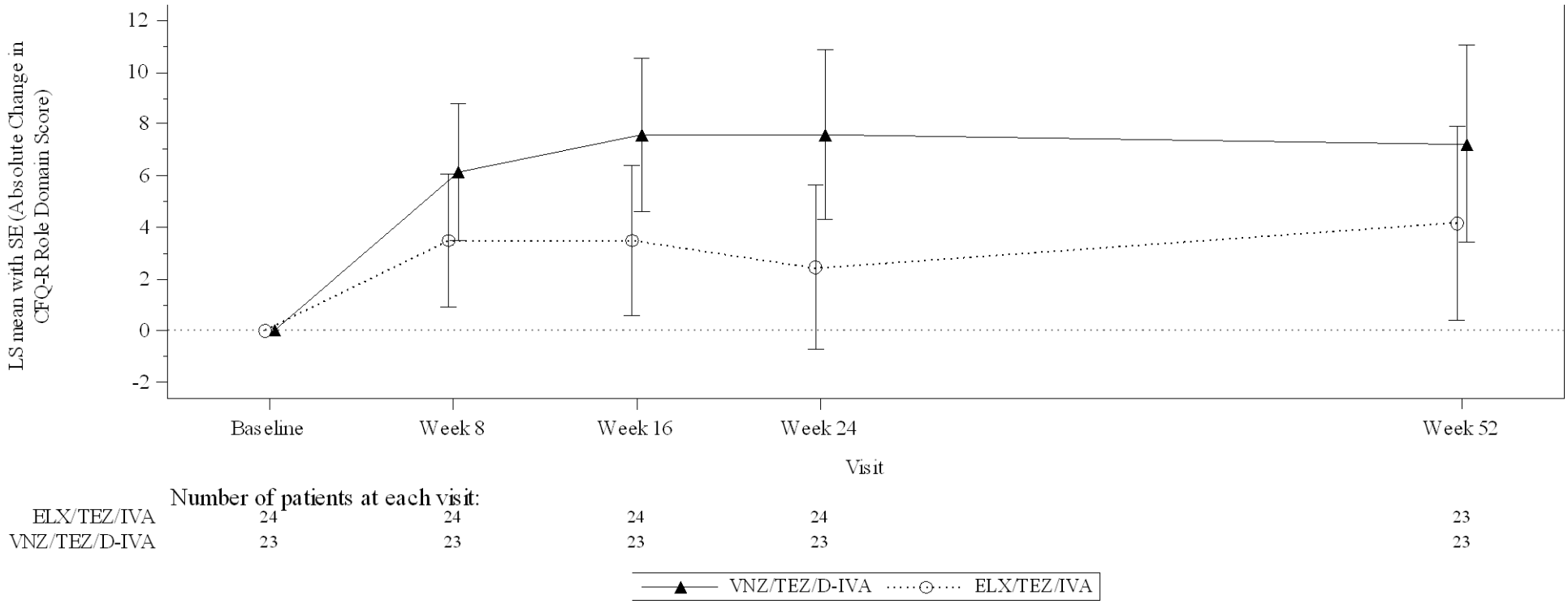
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

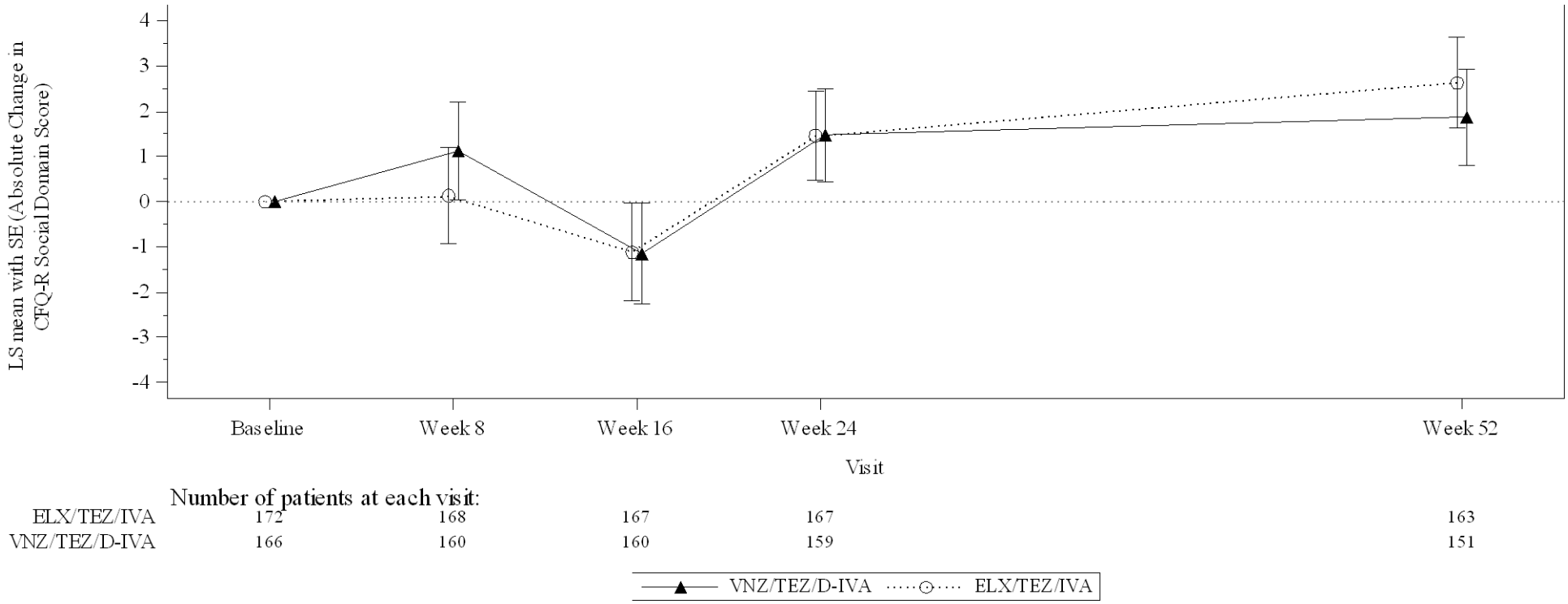
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

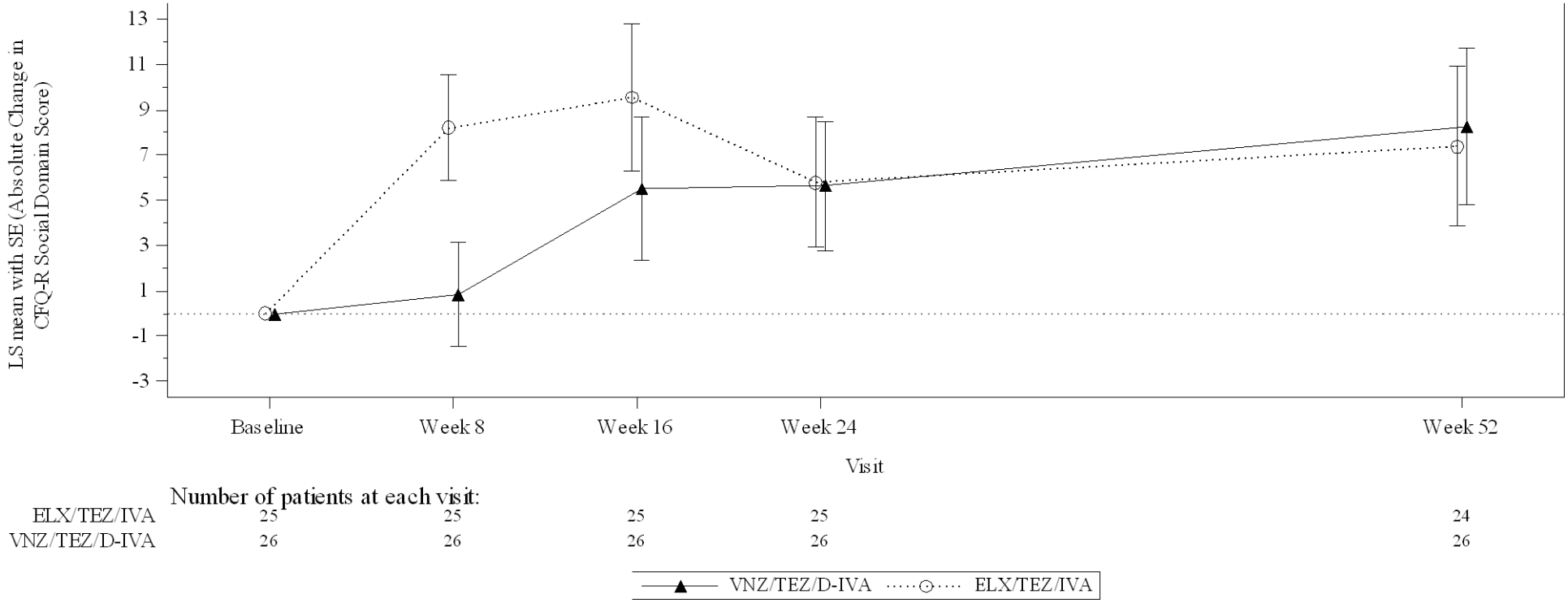
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

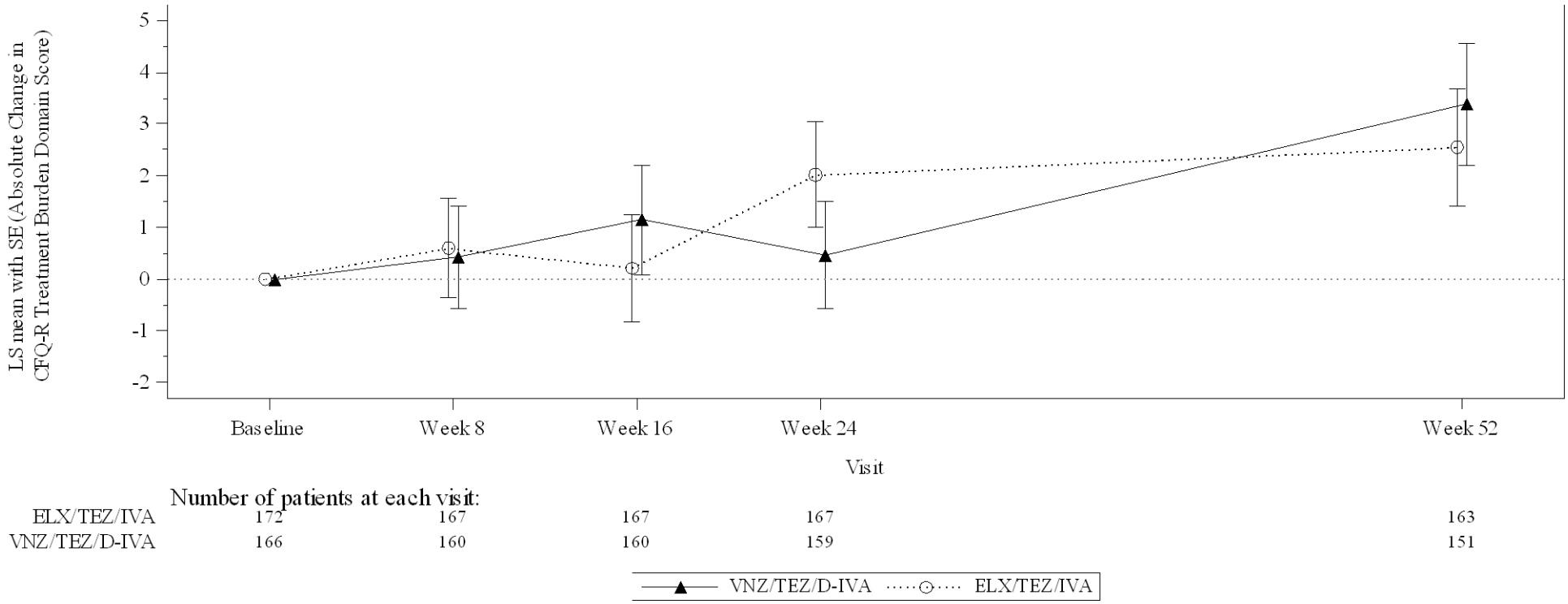
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

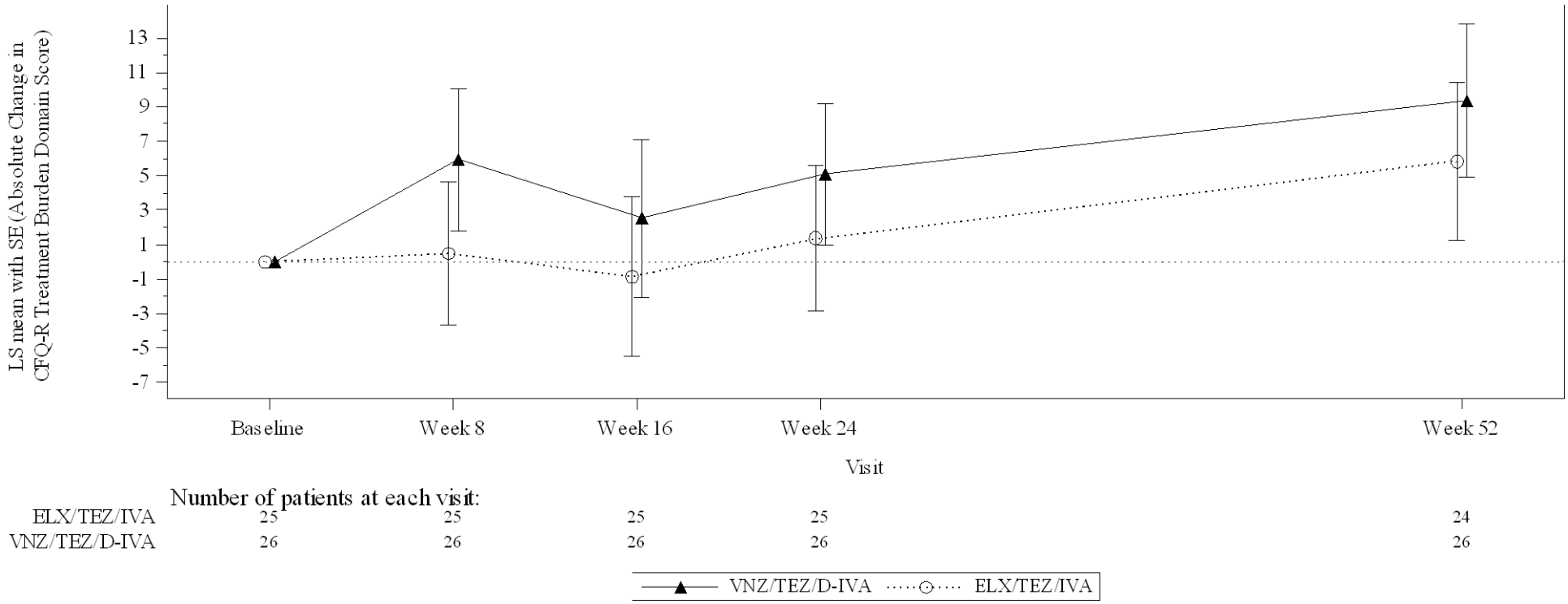
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

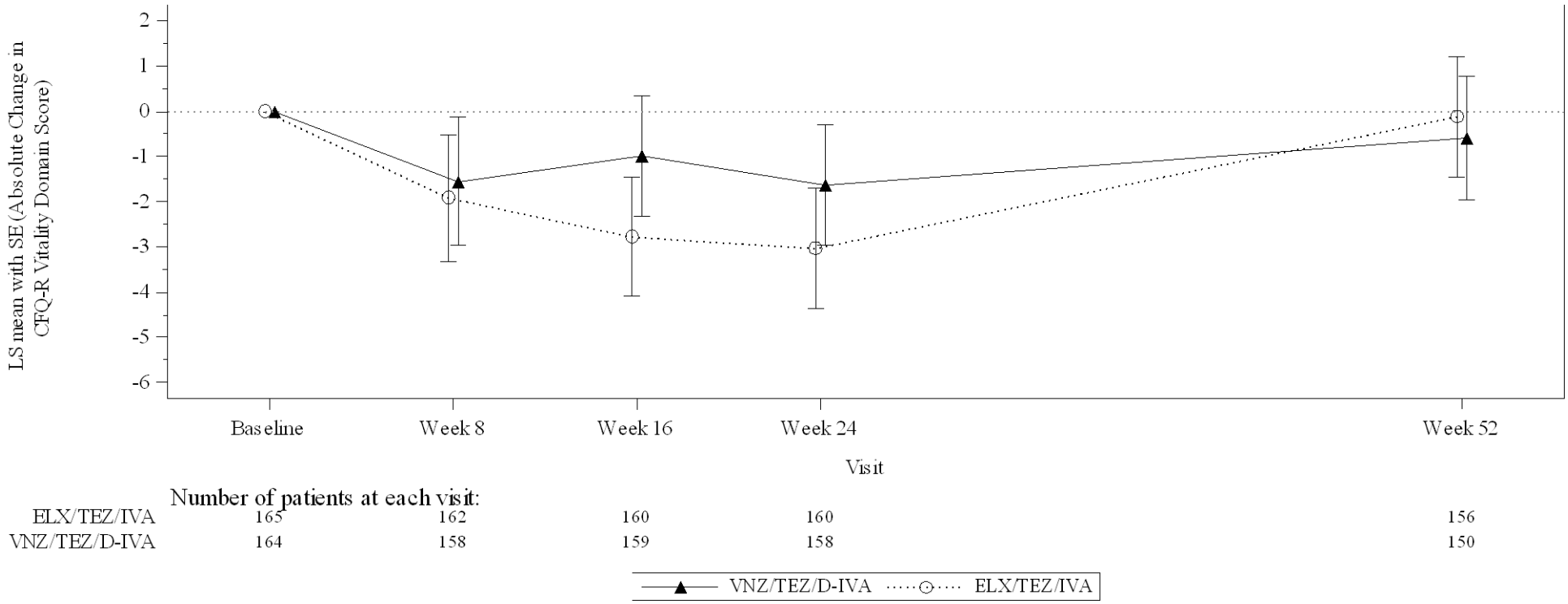
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

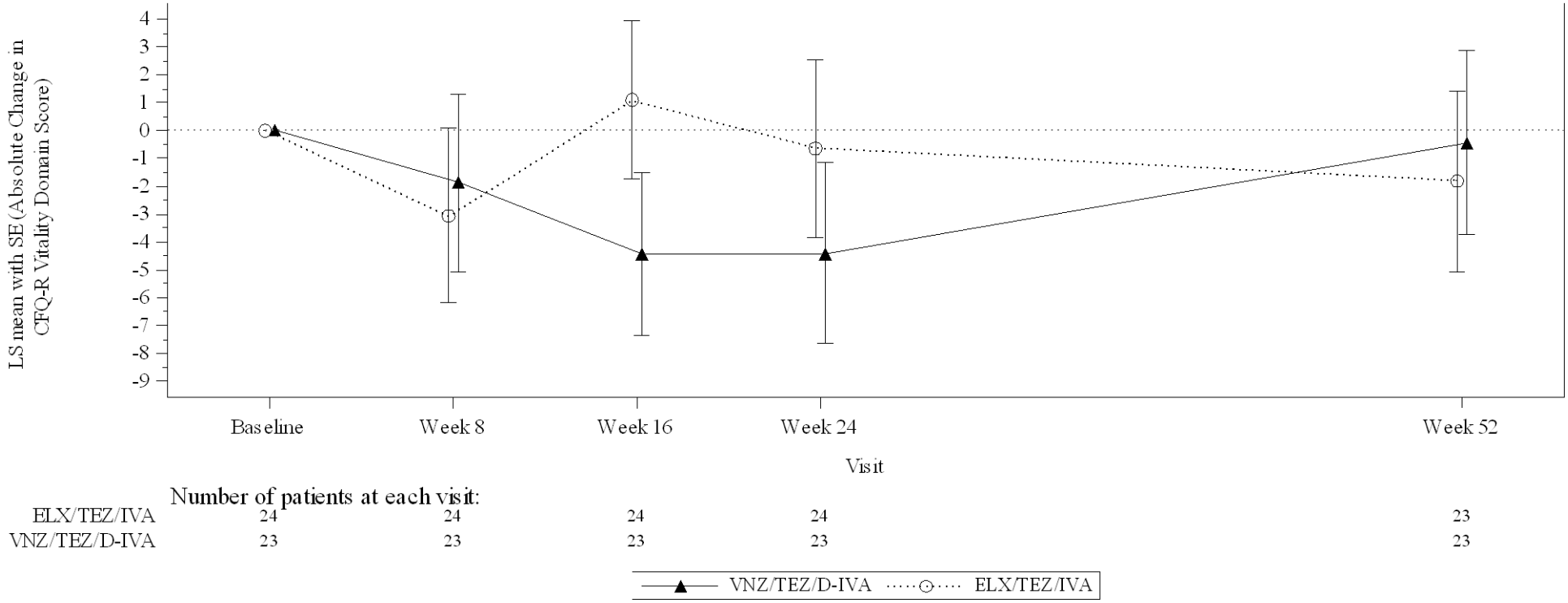
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

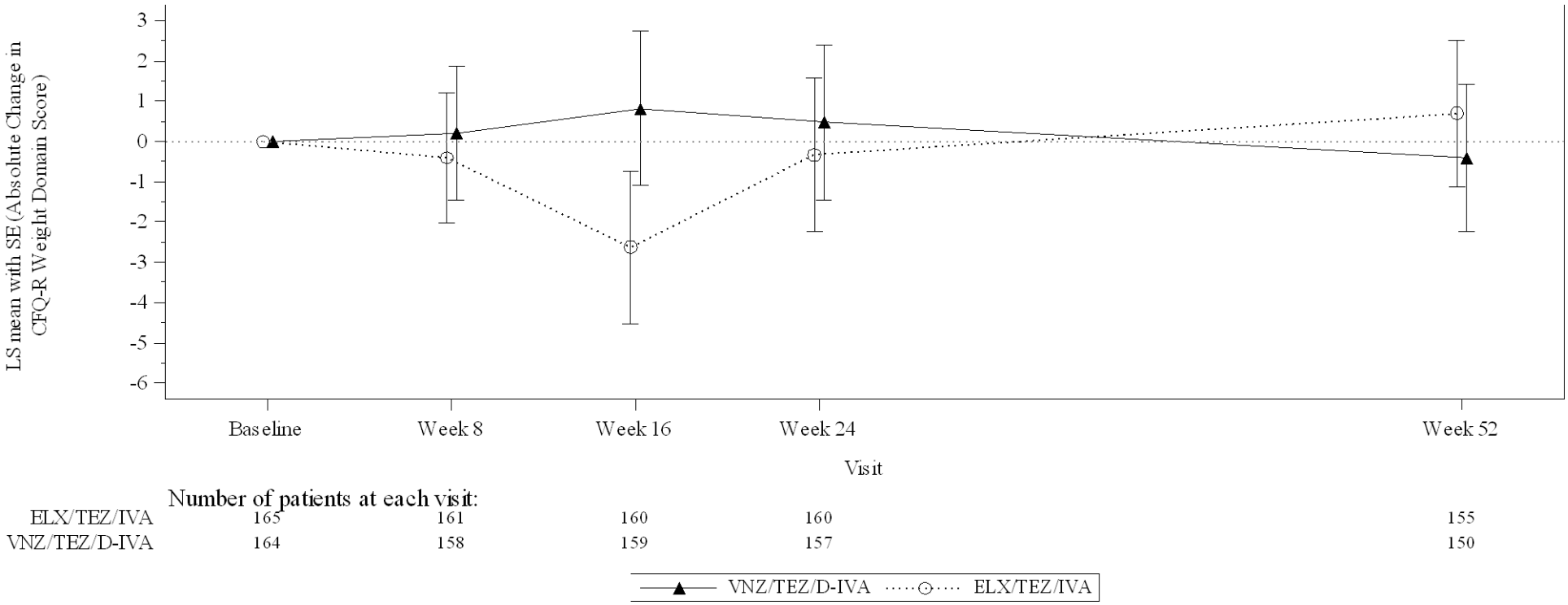
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.9.5.1
Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

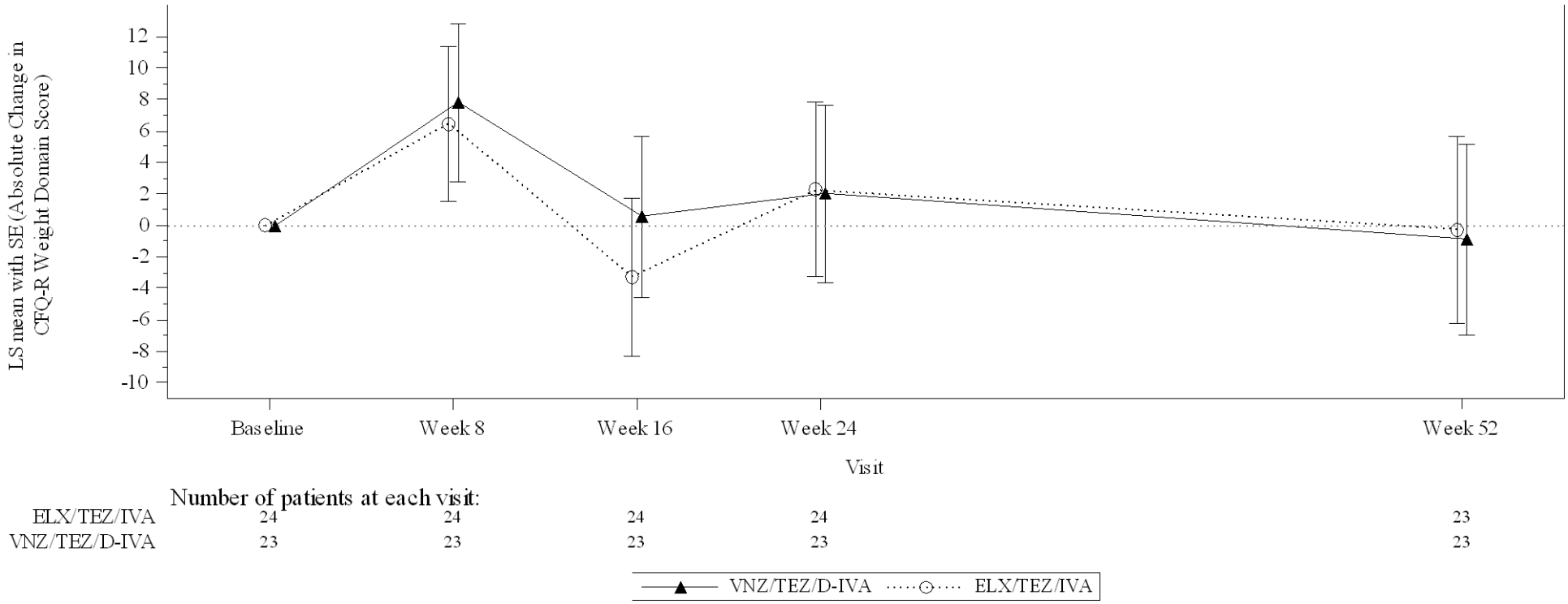
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-102: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 for Subgroup Prior CFTR Modulator Use
Full Analysis Set

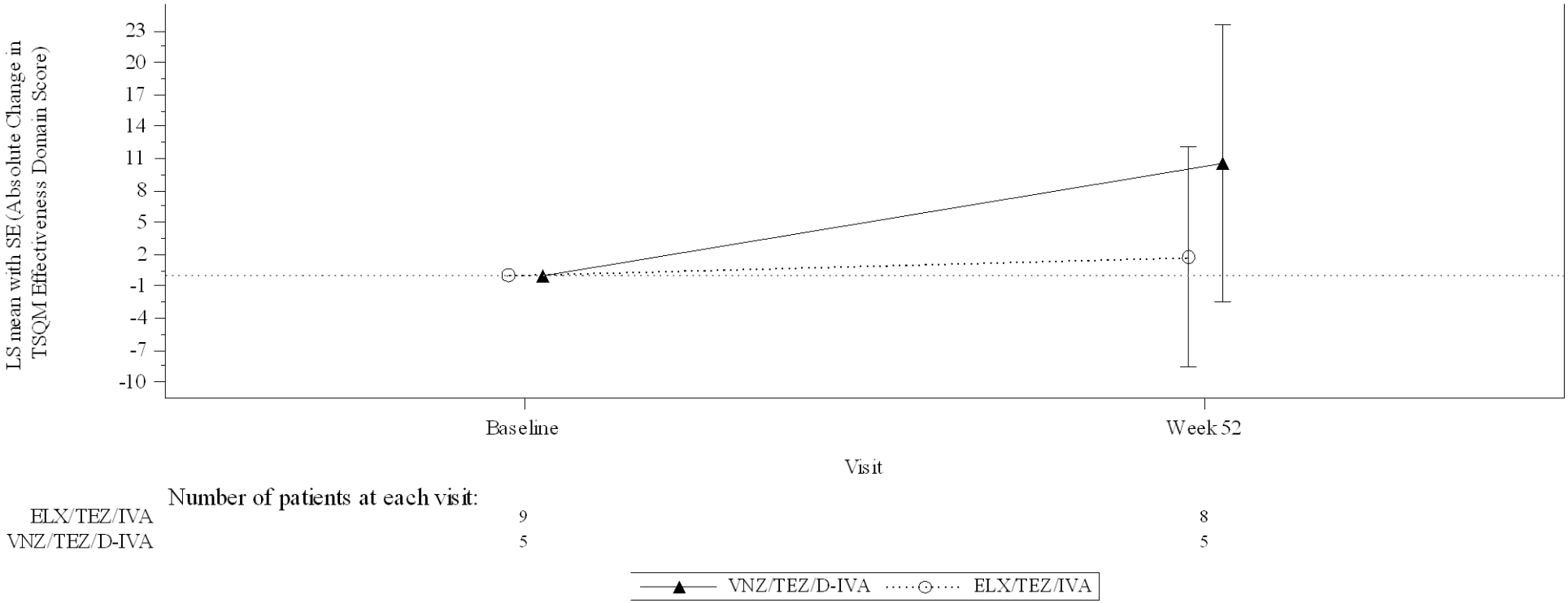
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

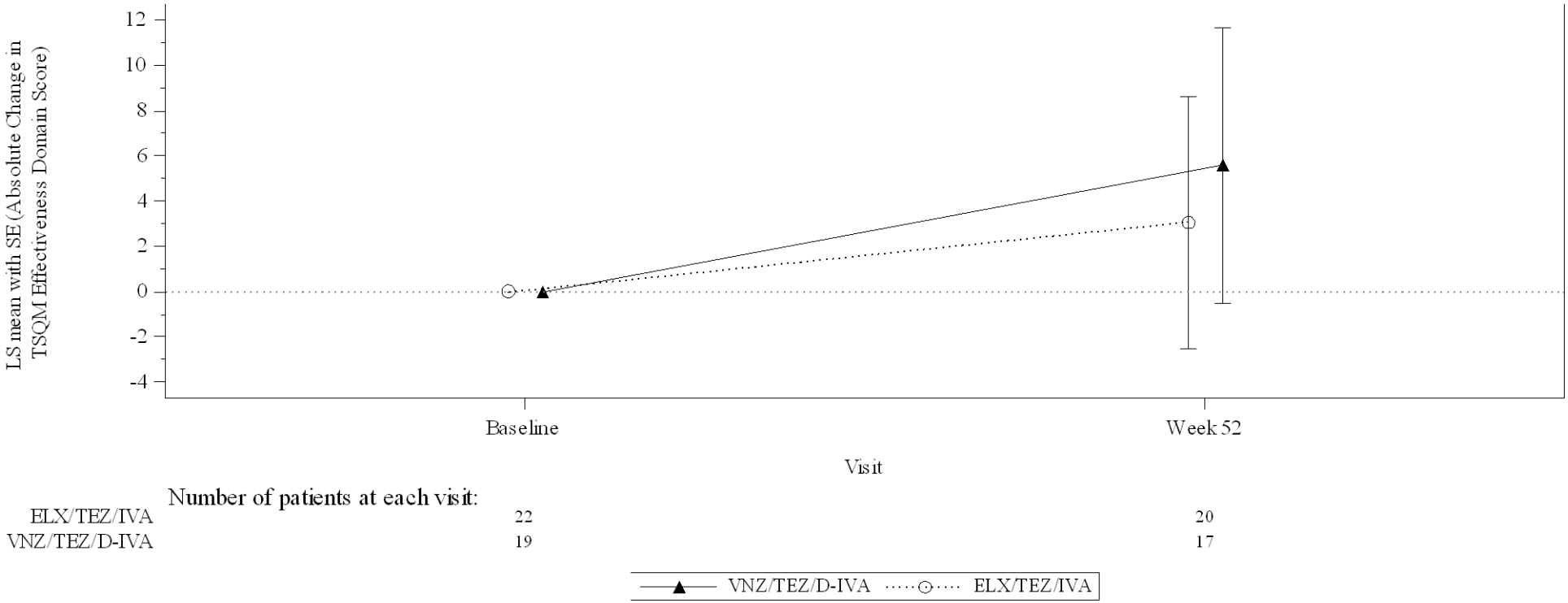
Domain: Effectiveness
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

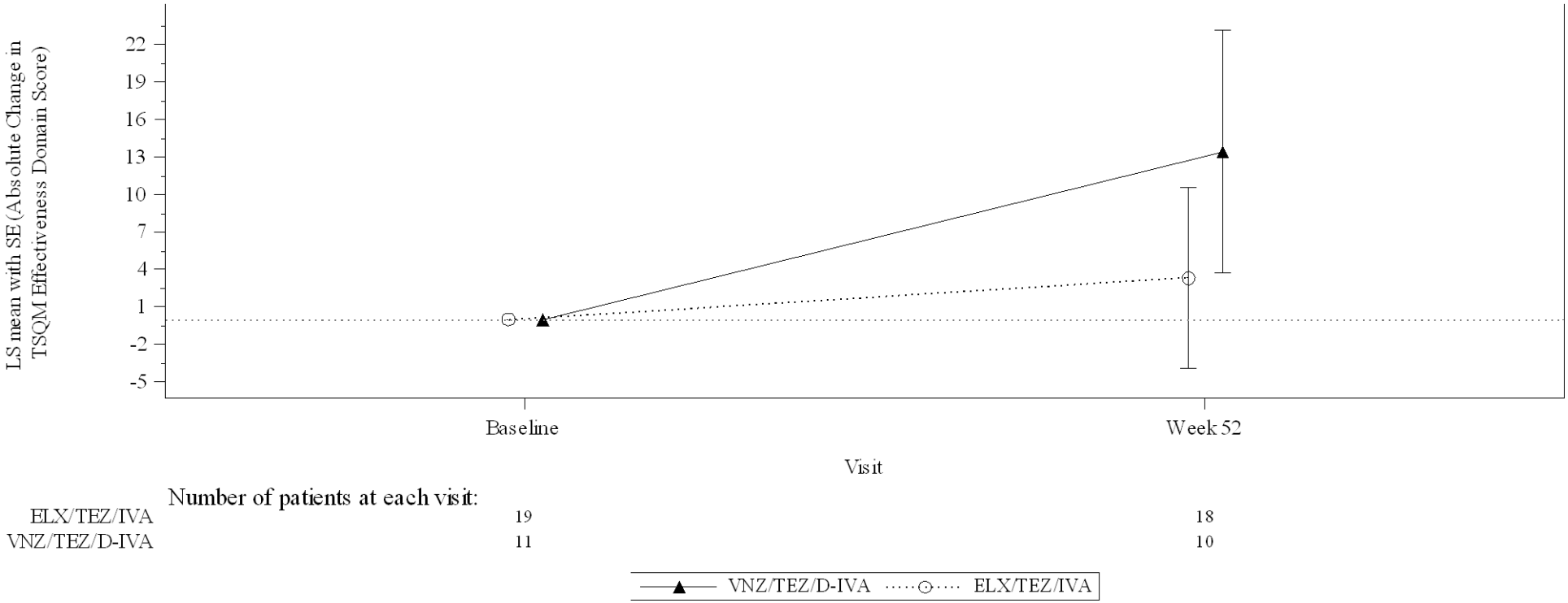
Domain: Effectiveness
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

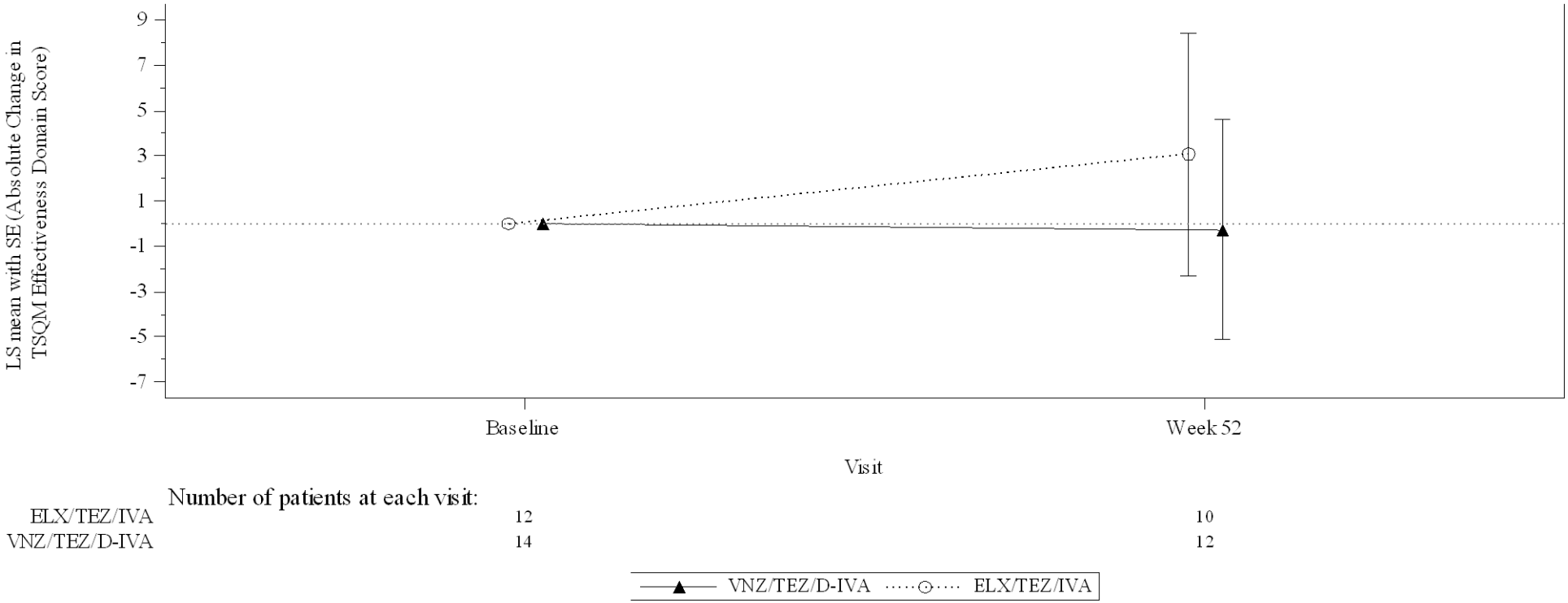
Domain: Effectiveness
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

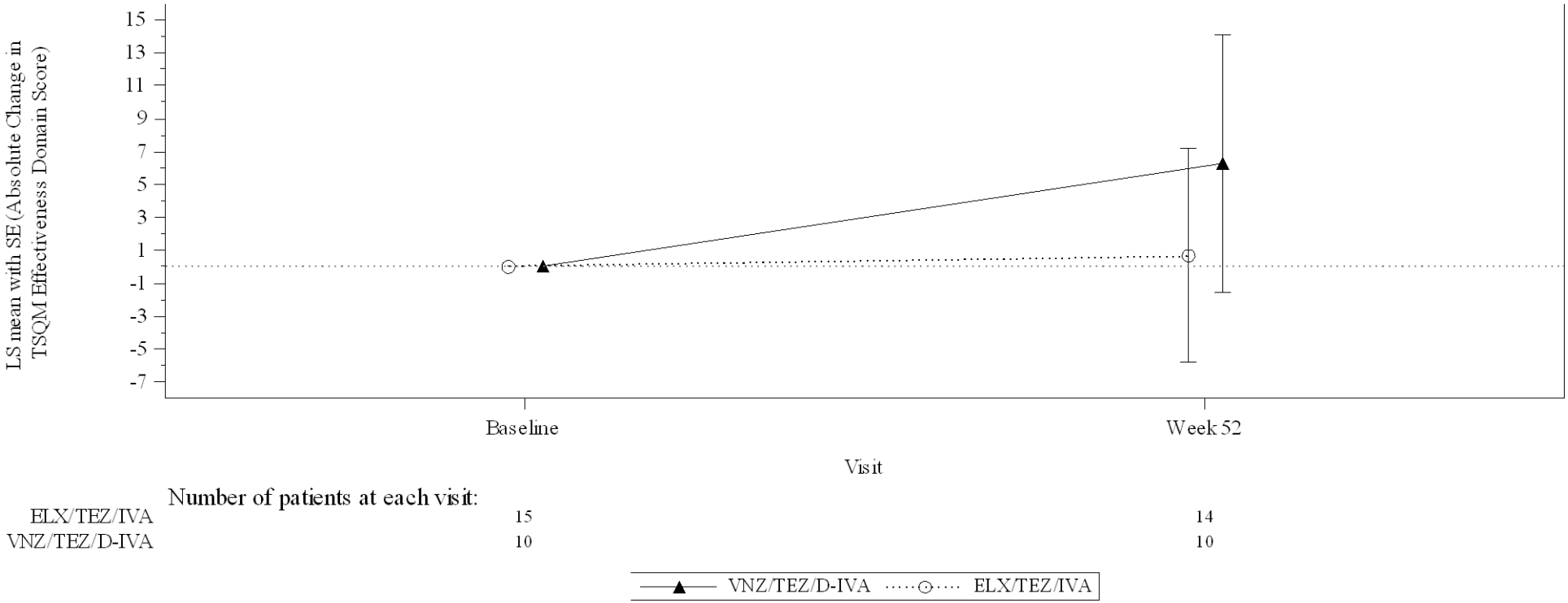
Domain: Effectiveness
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

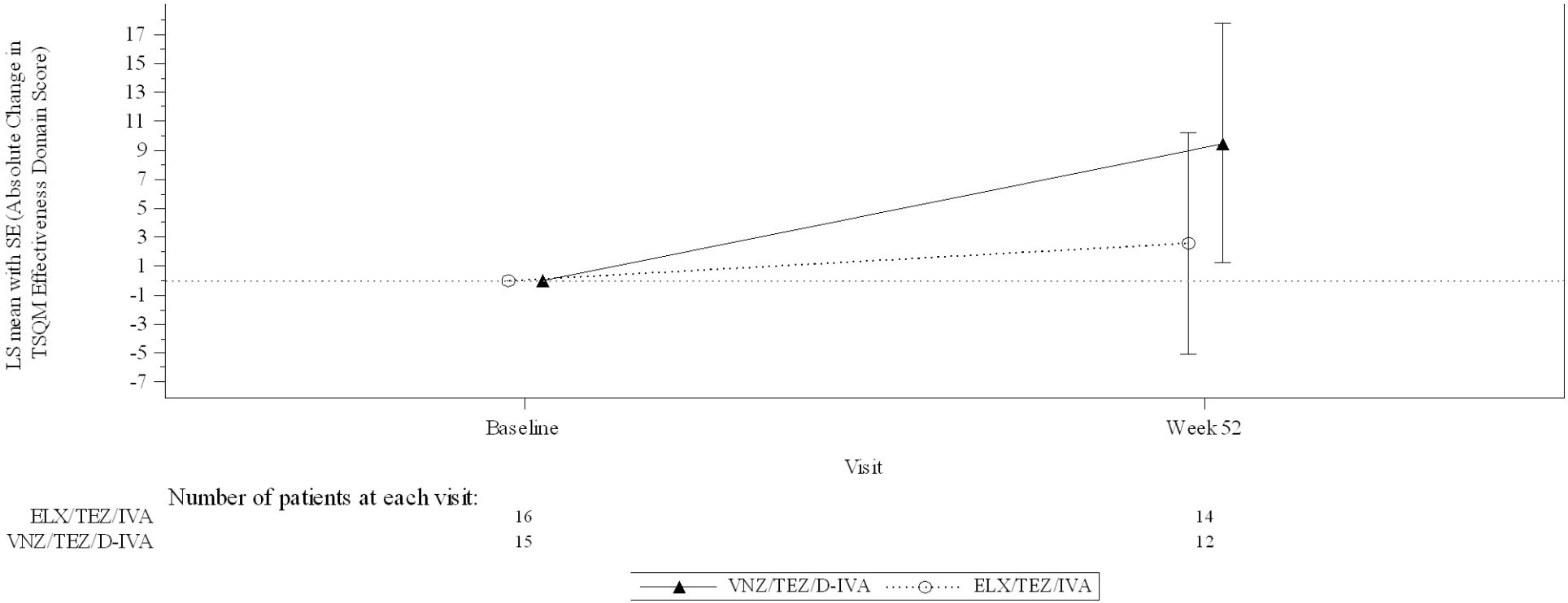
Domain: Effectiveness
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

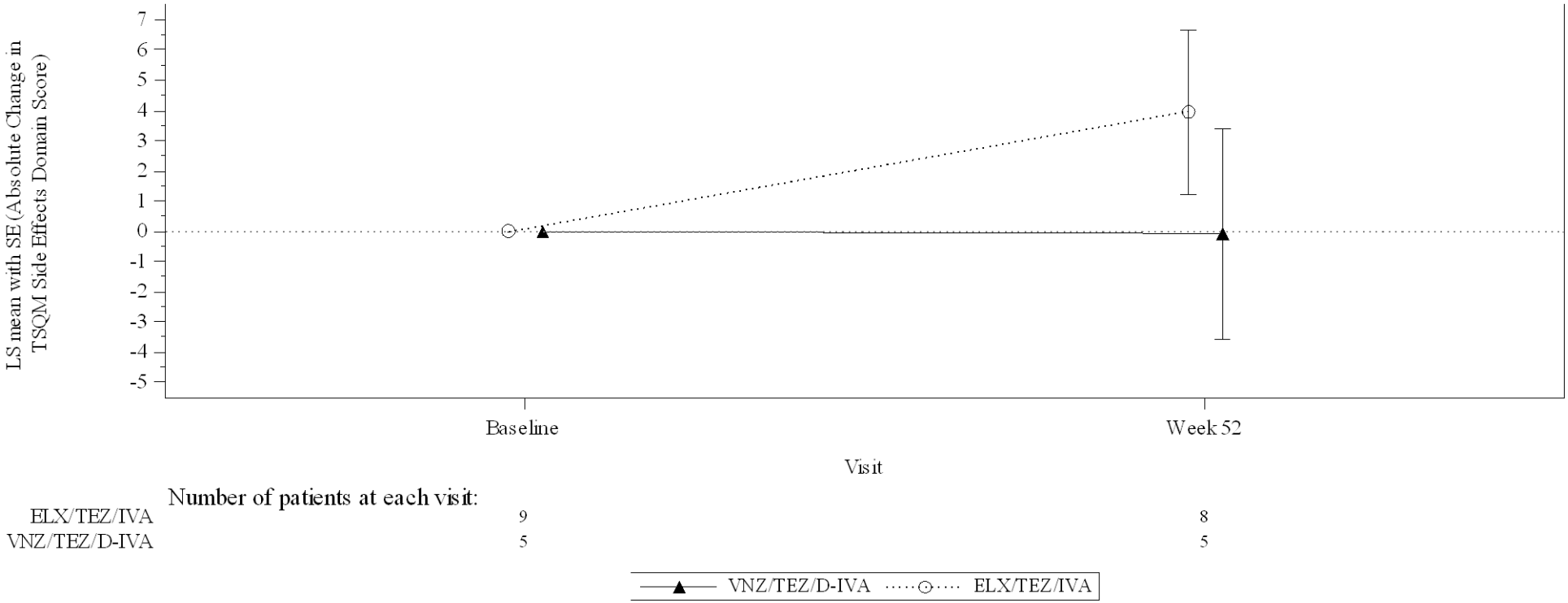
Domain: Effectiveness
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

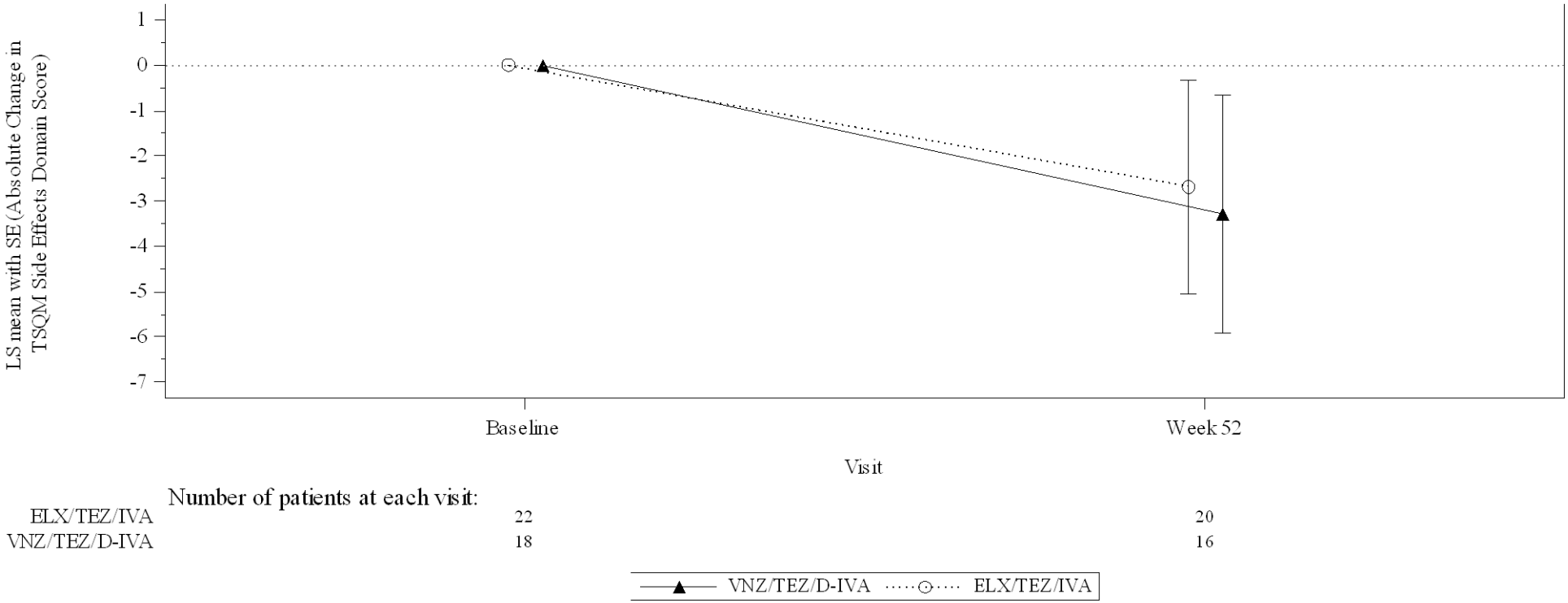
Domain: Side Effects
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

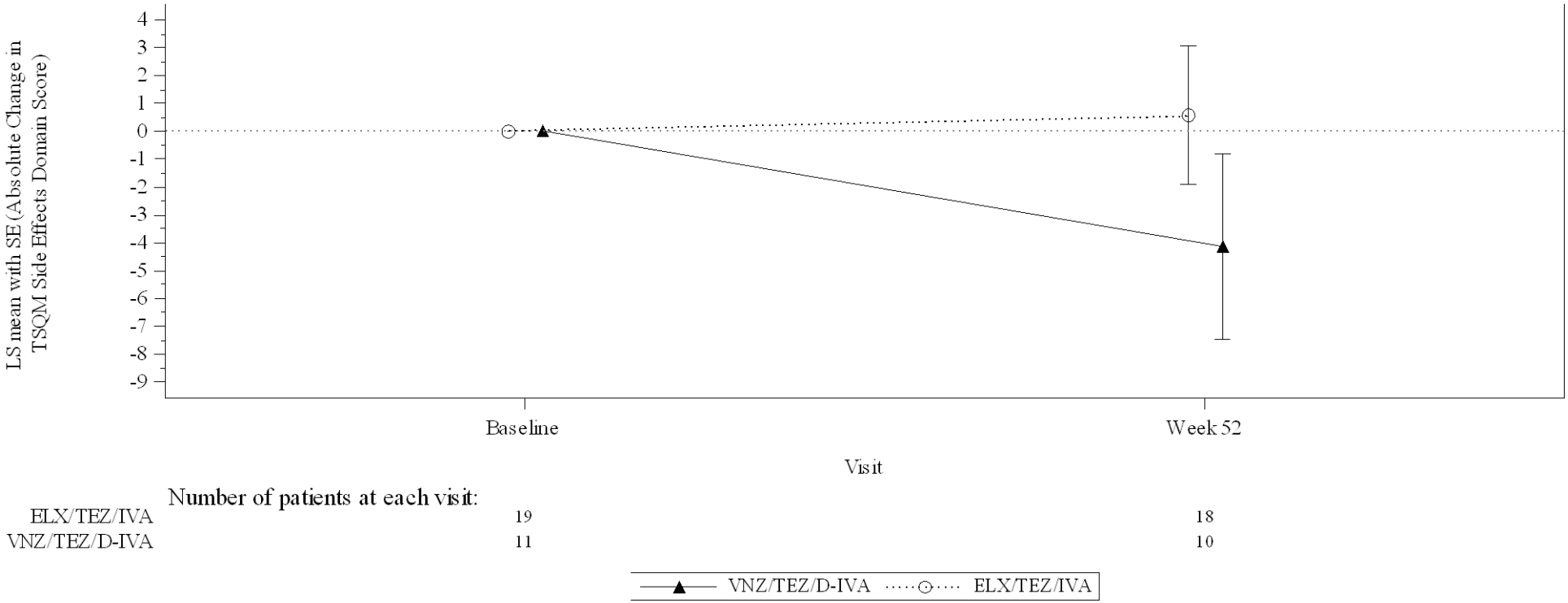
Domain: Side Effects
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

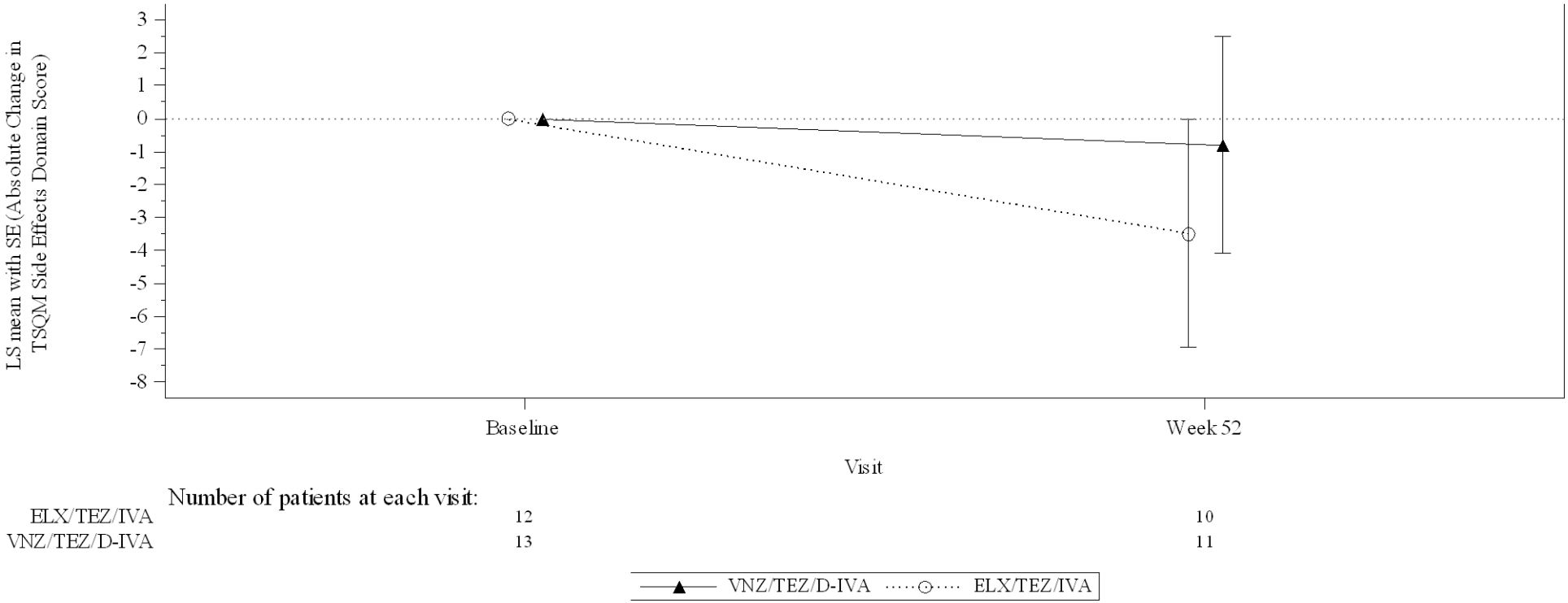
Domain: Side Effects
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

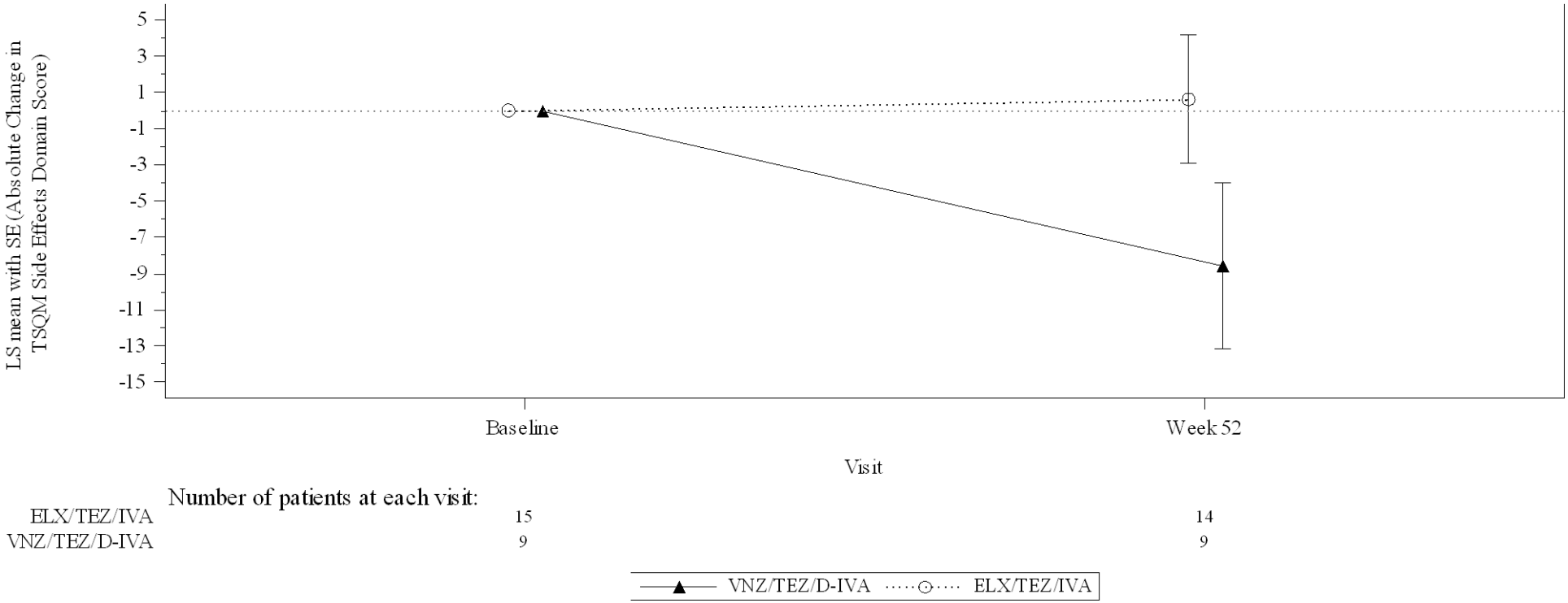
Domain: Side Effects
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

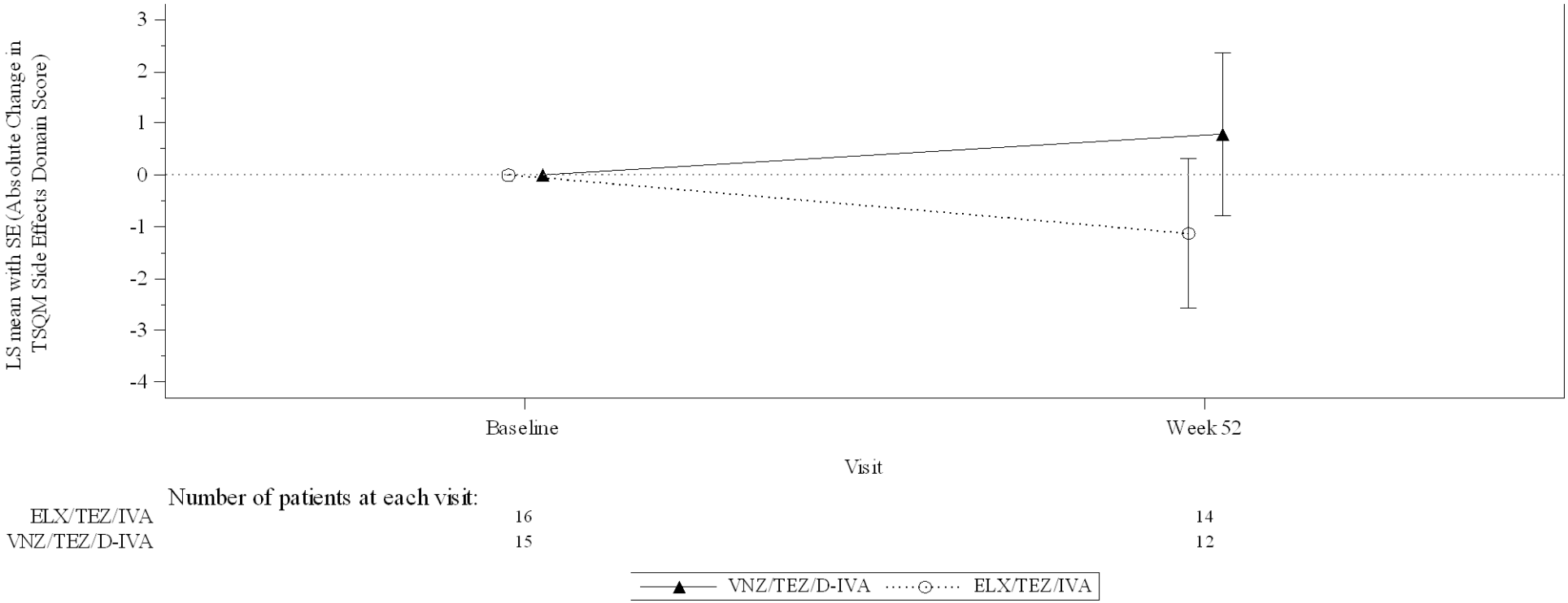
Domain: Side Effects
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

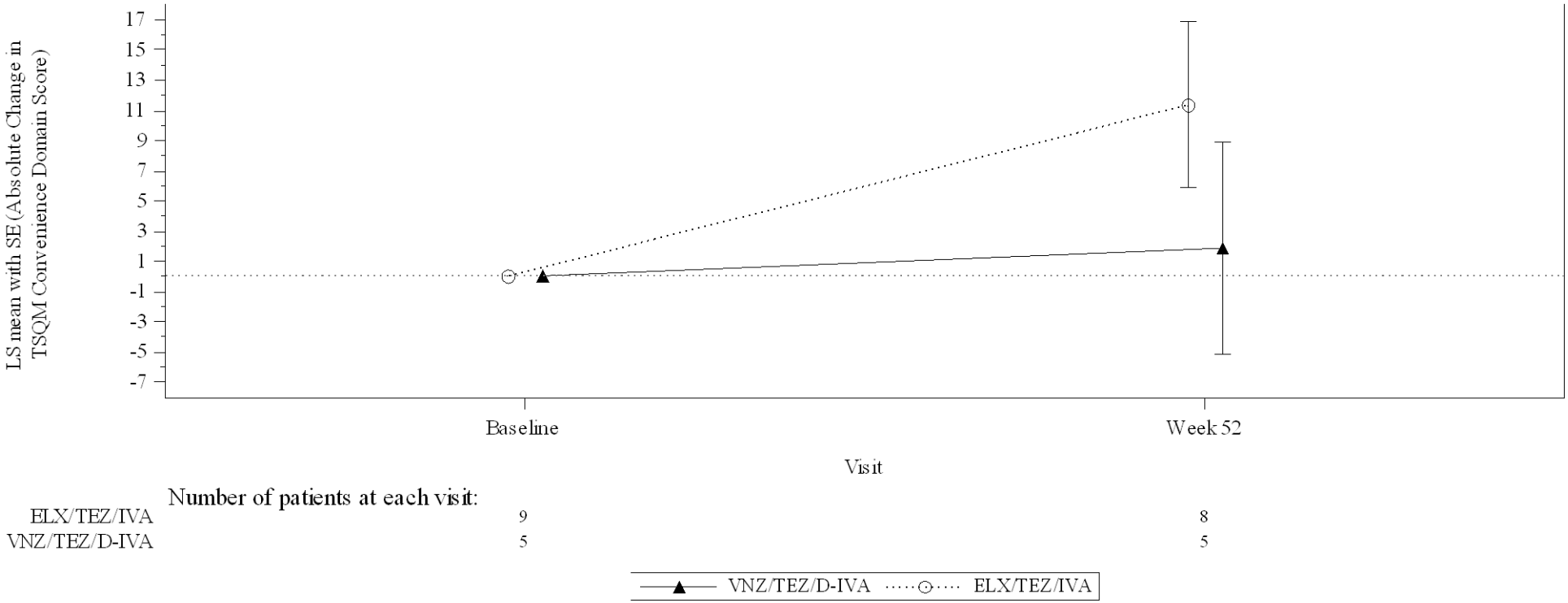
Domain: Side Effects
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

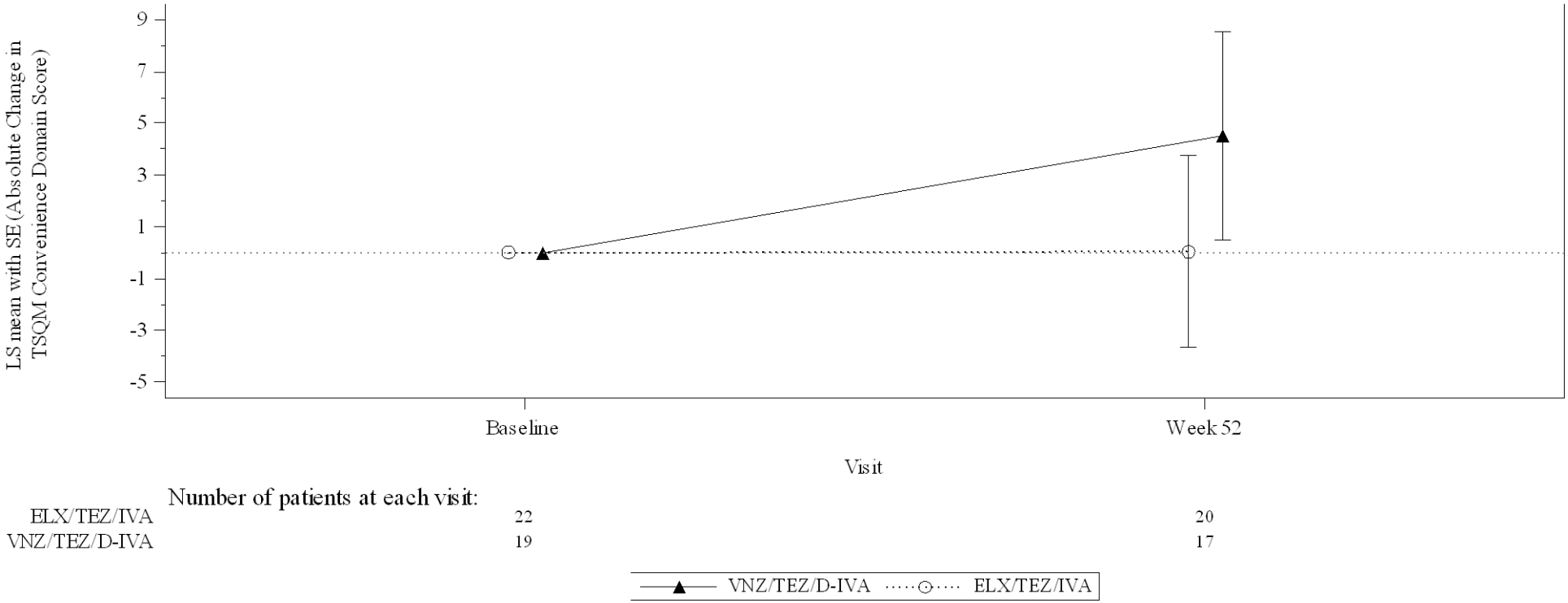
Domain: Convenience
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

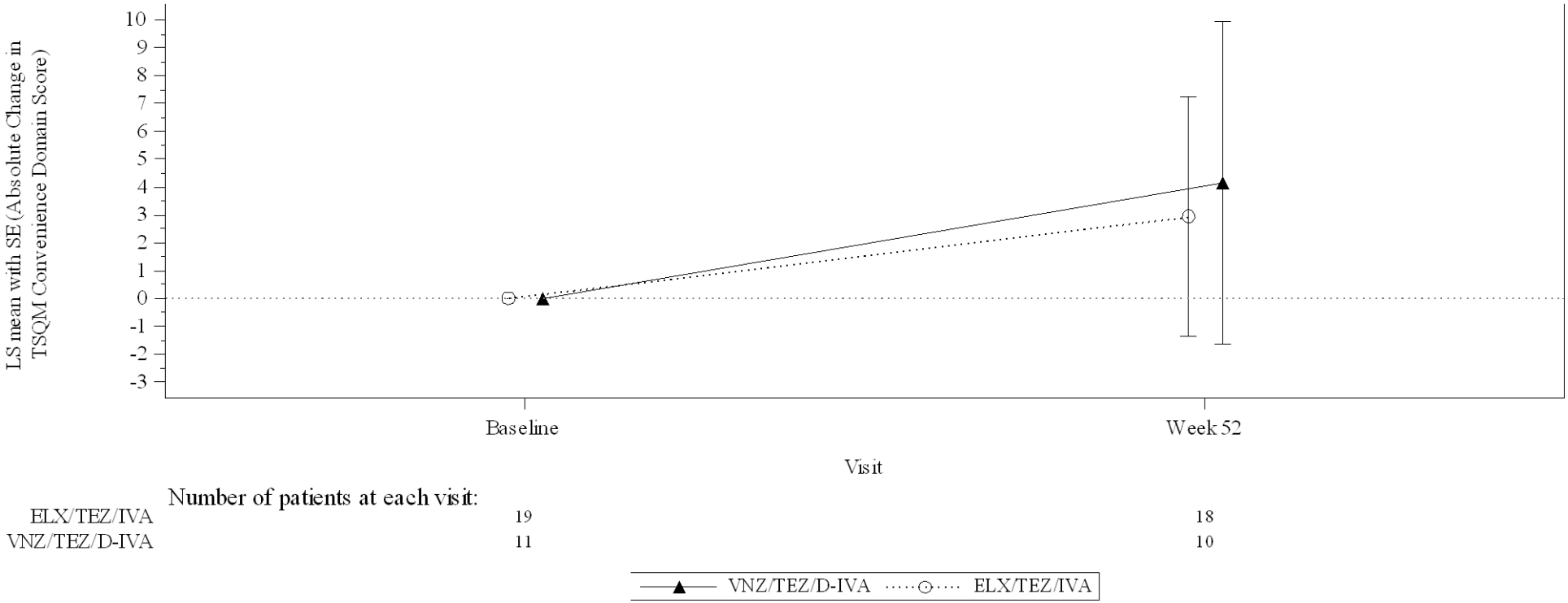
Domain: Convenience
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

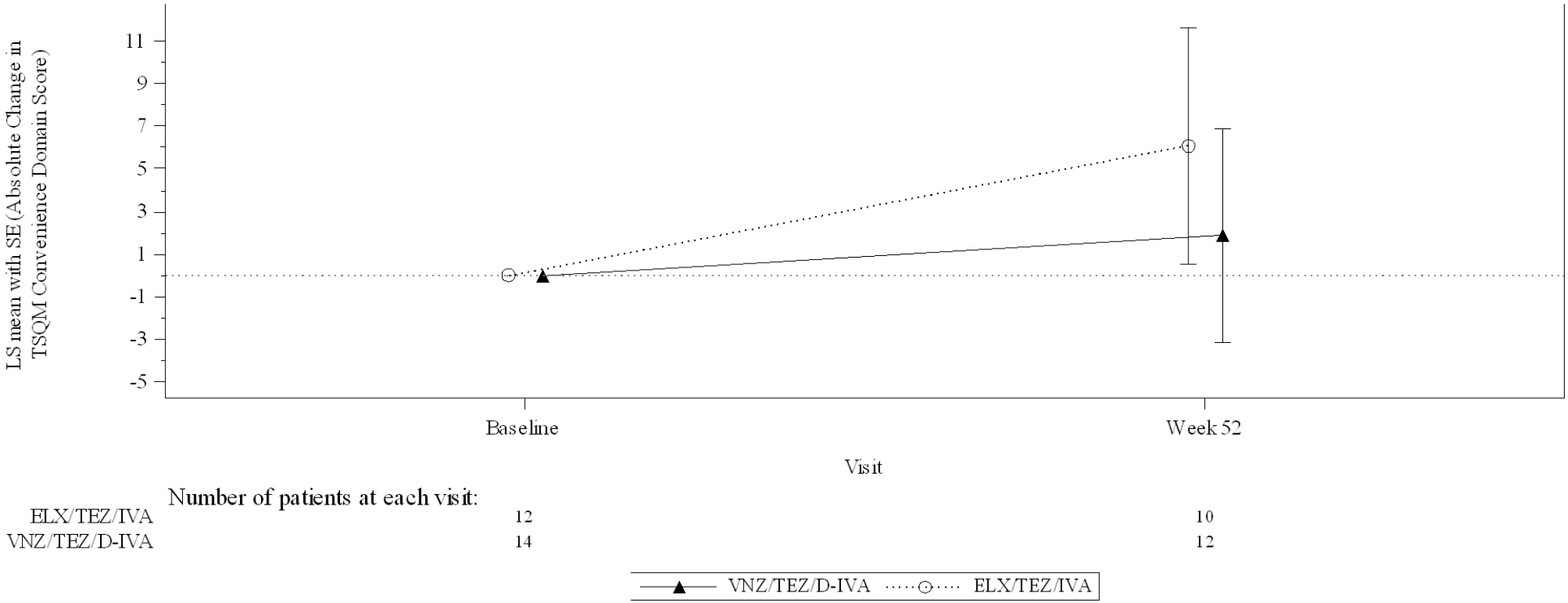
Domain: Convenience
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

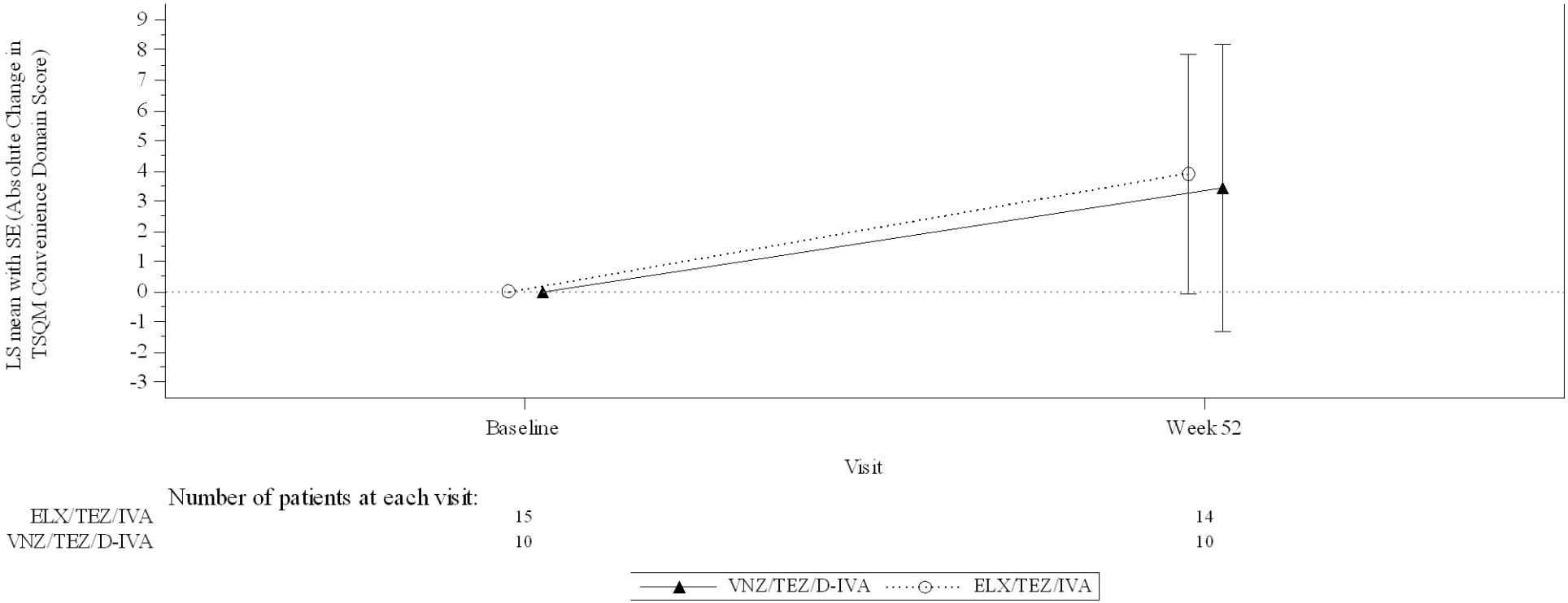
Domain: Convenience
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

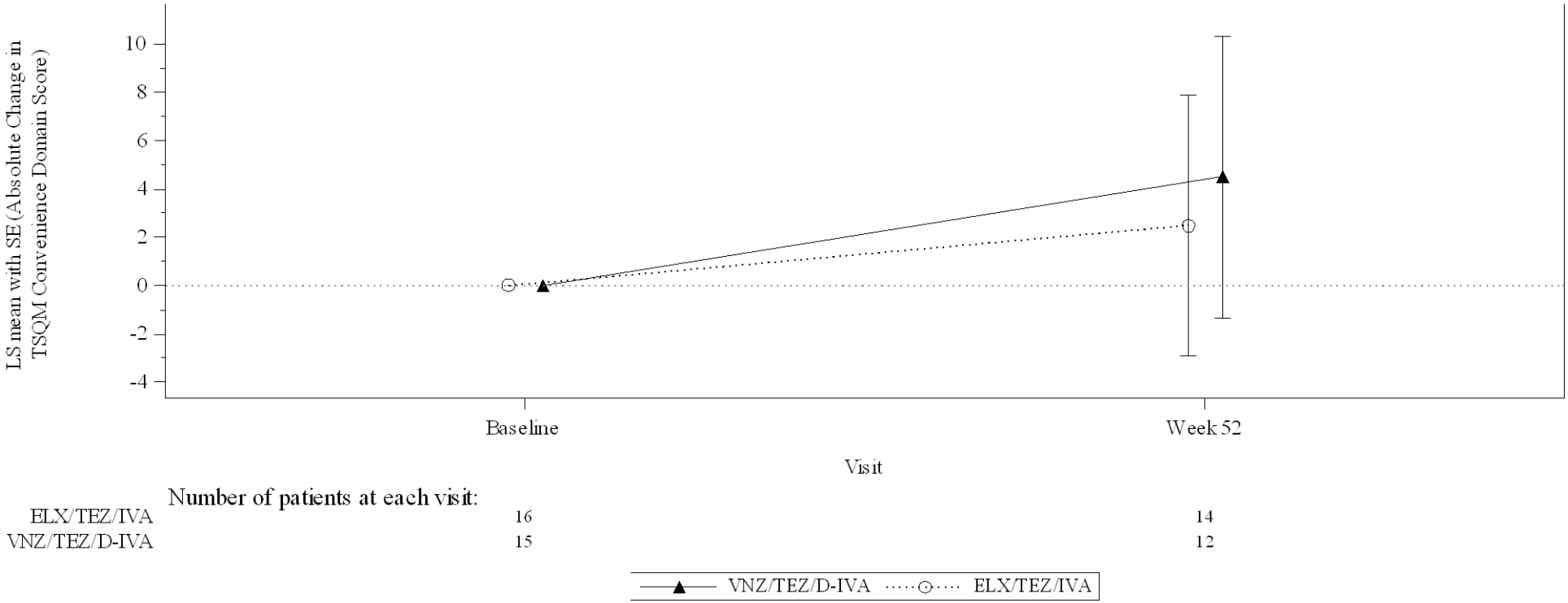
Domain: Convenience
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

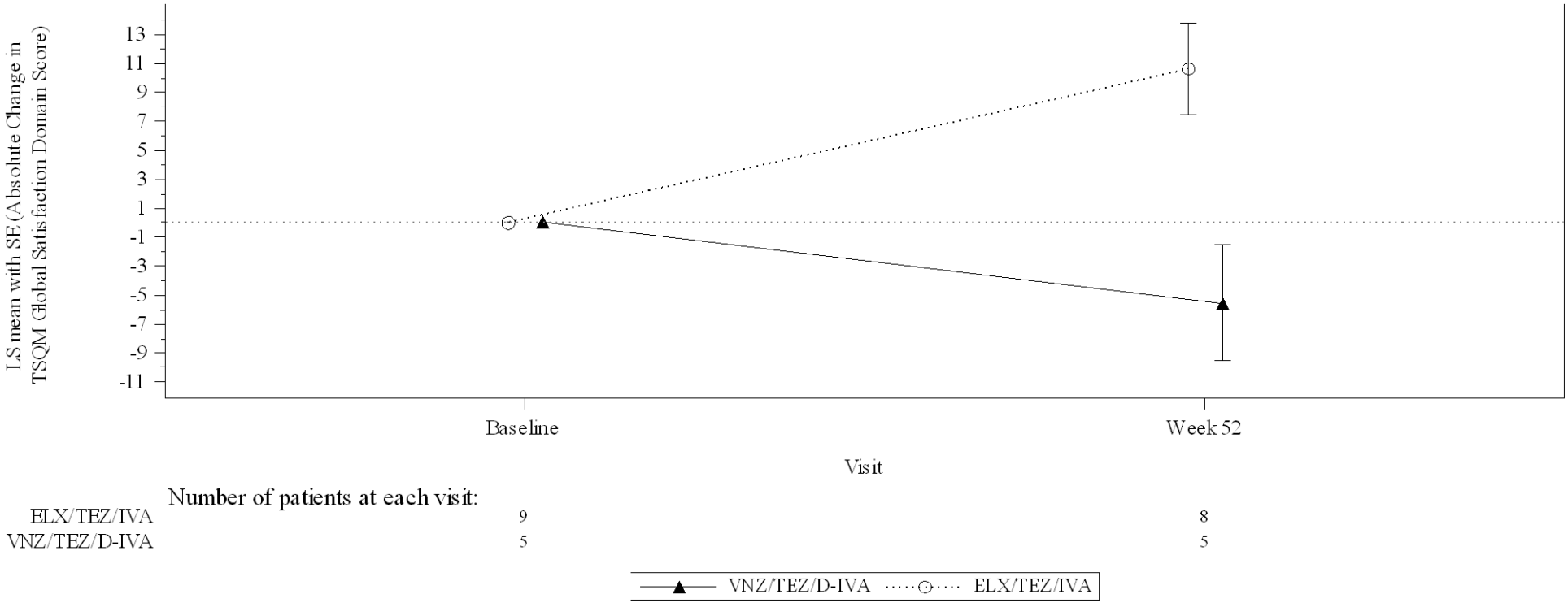
Domain: Convenience
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

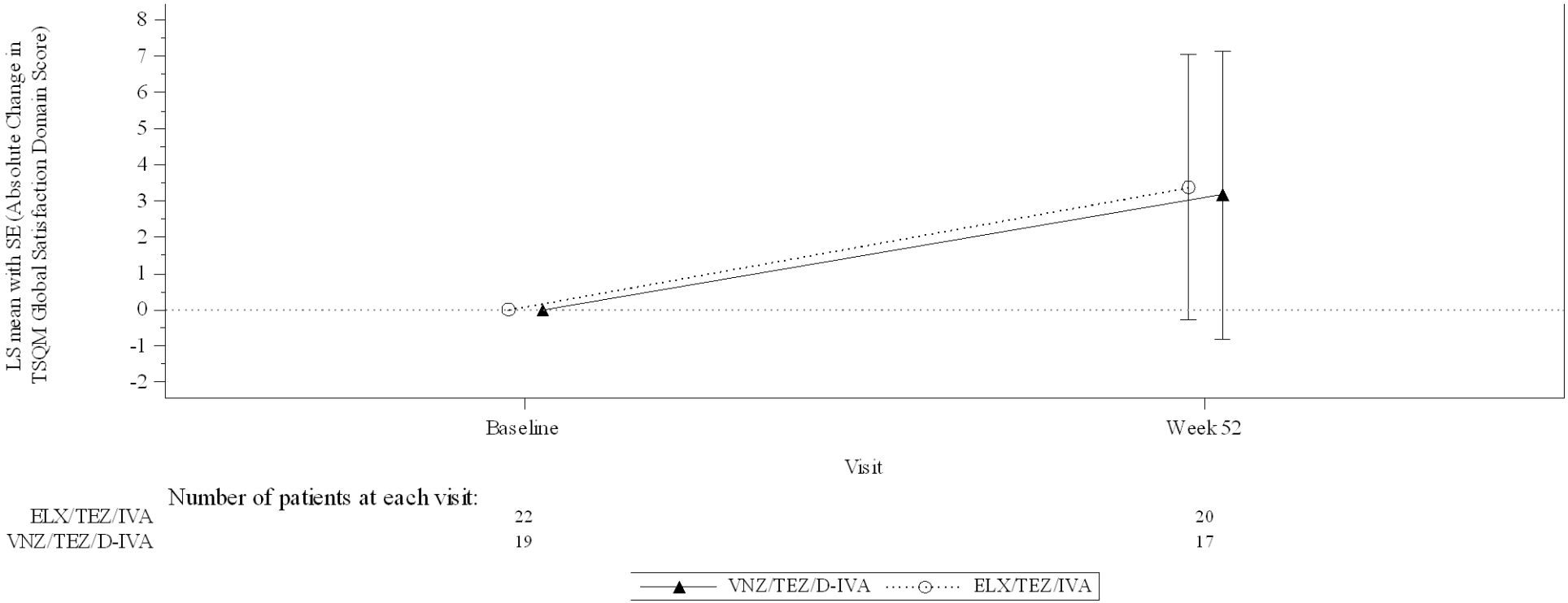
Domain: Global Satisfaction
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

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Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

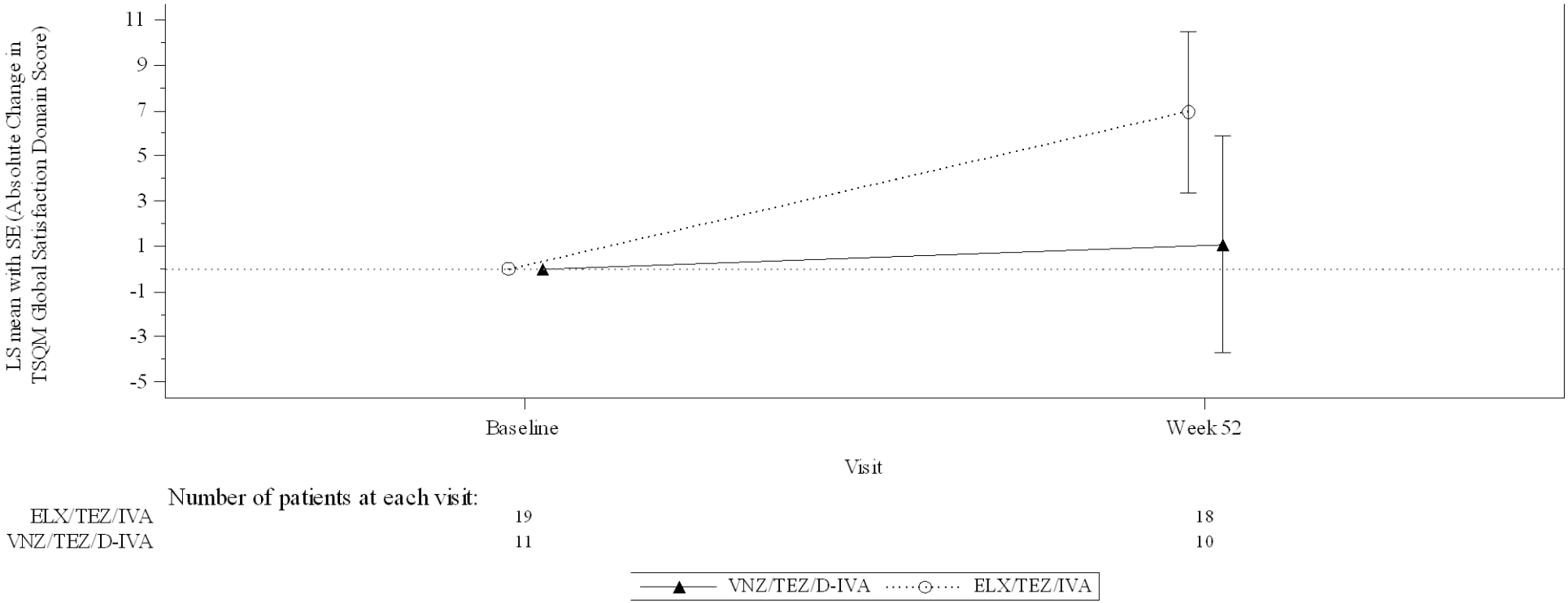
Domain: Global Satisfaction
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Full Analysis Set

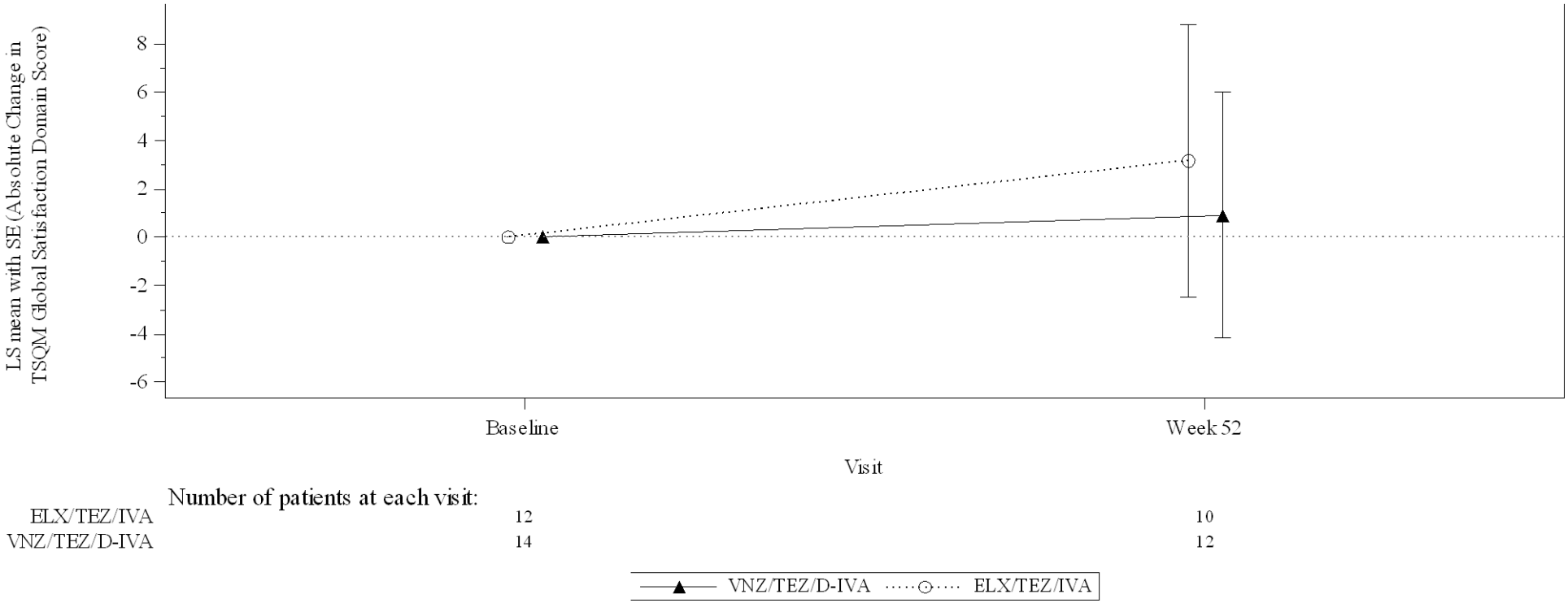
Domain: Global Satisfaction
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

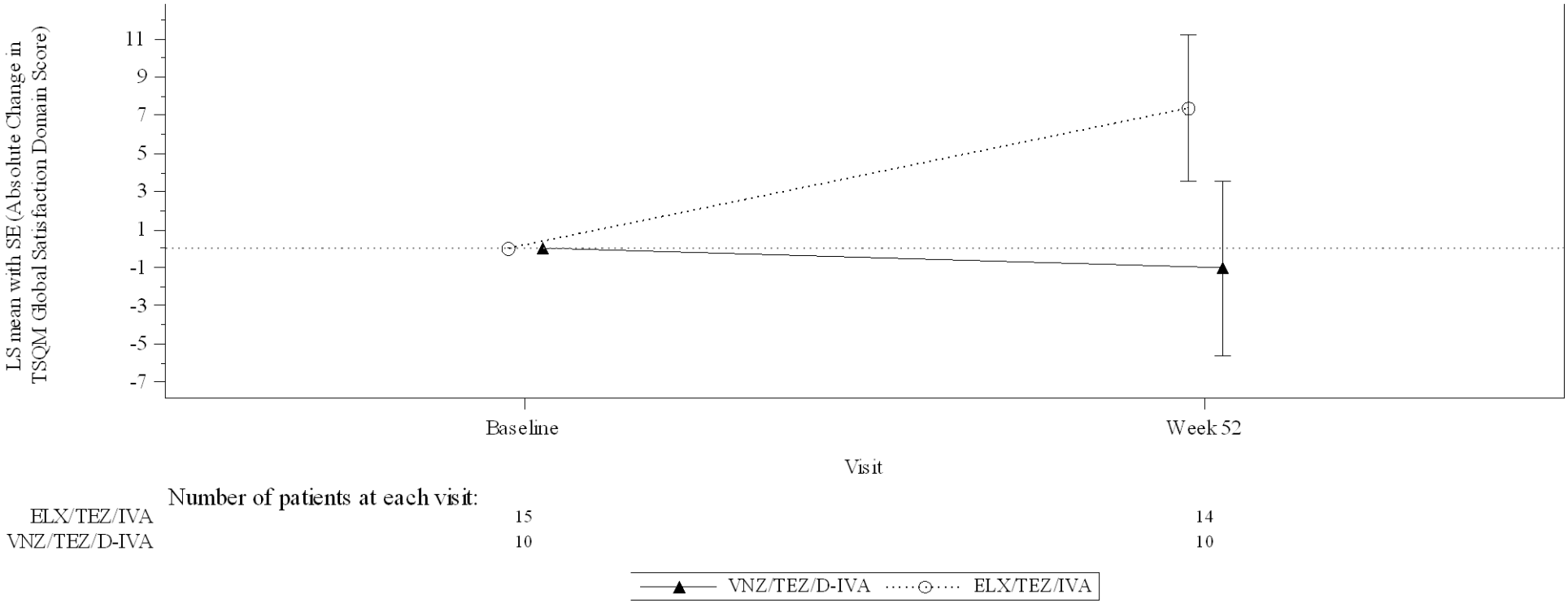
Domain: Global Satisfaction
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

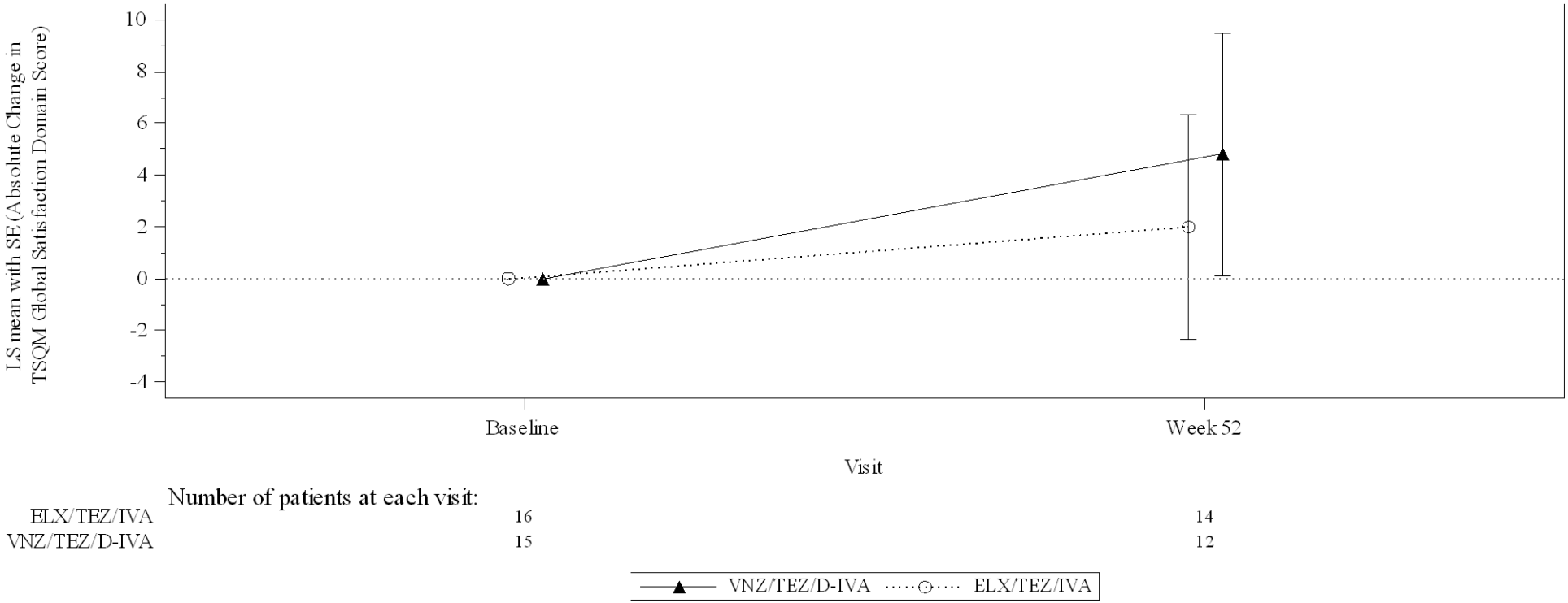
Domain: Global Satisfaction
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

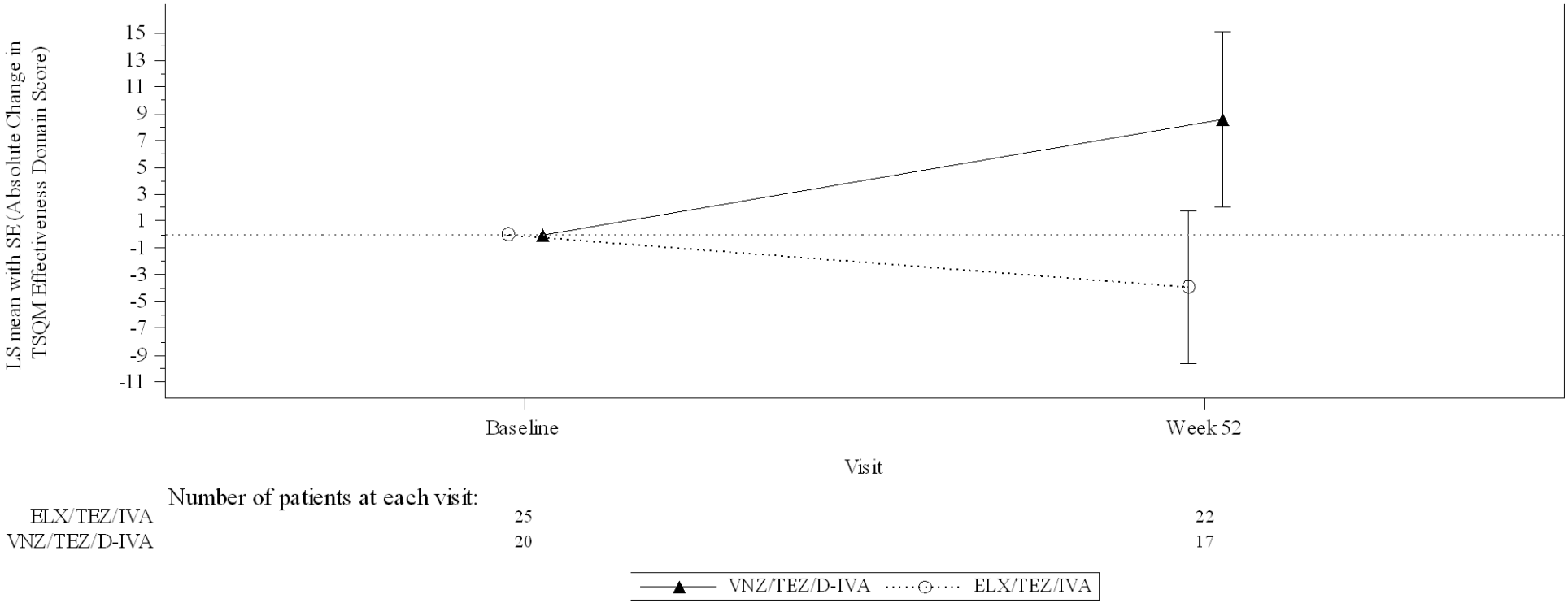
Domain: Global Satisfaction
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2.1
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

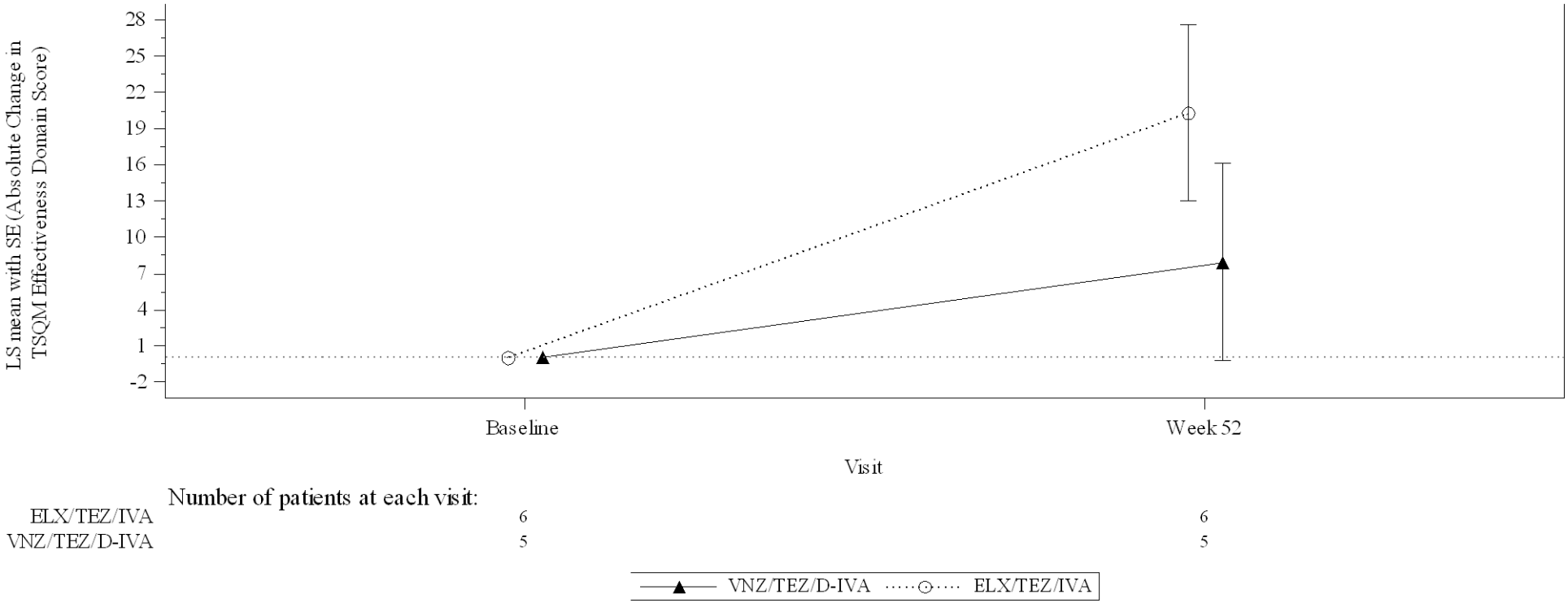
Domain: Effectiveness
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.12.2.1
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

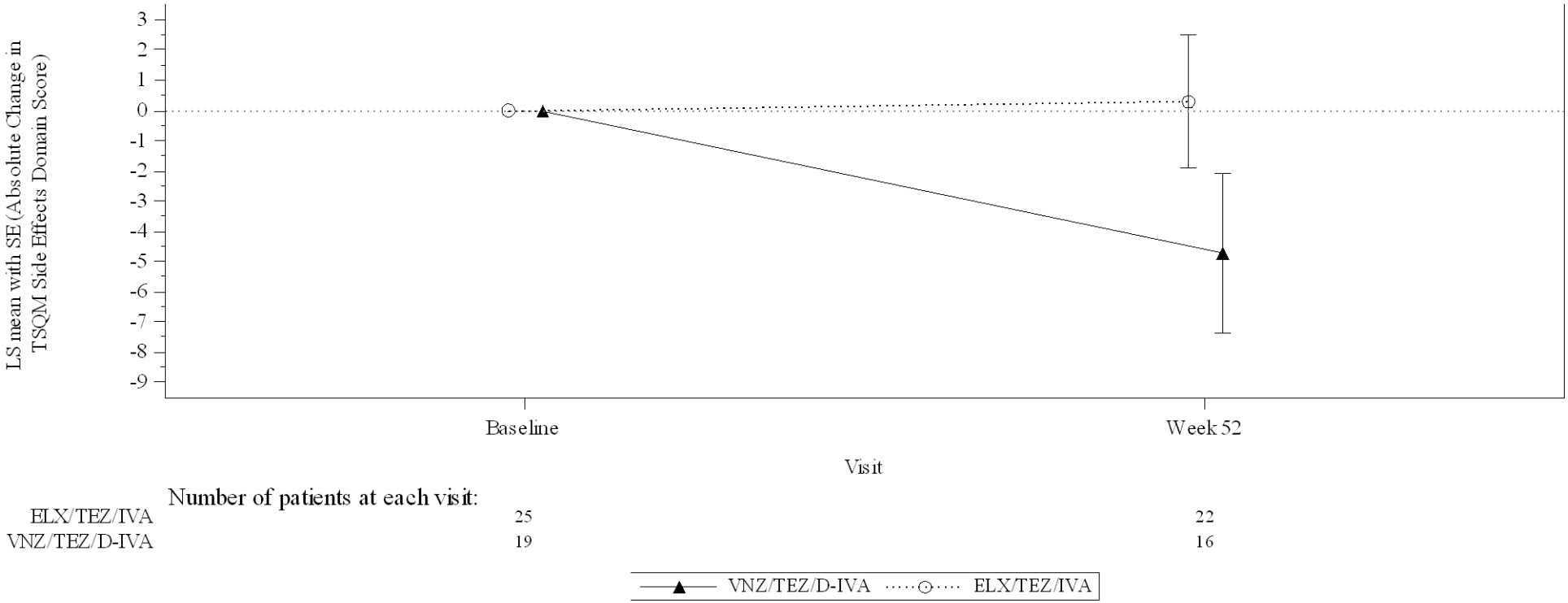
Domain: Effectiveness
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Full Analysis Set

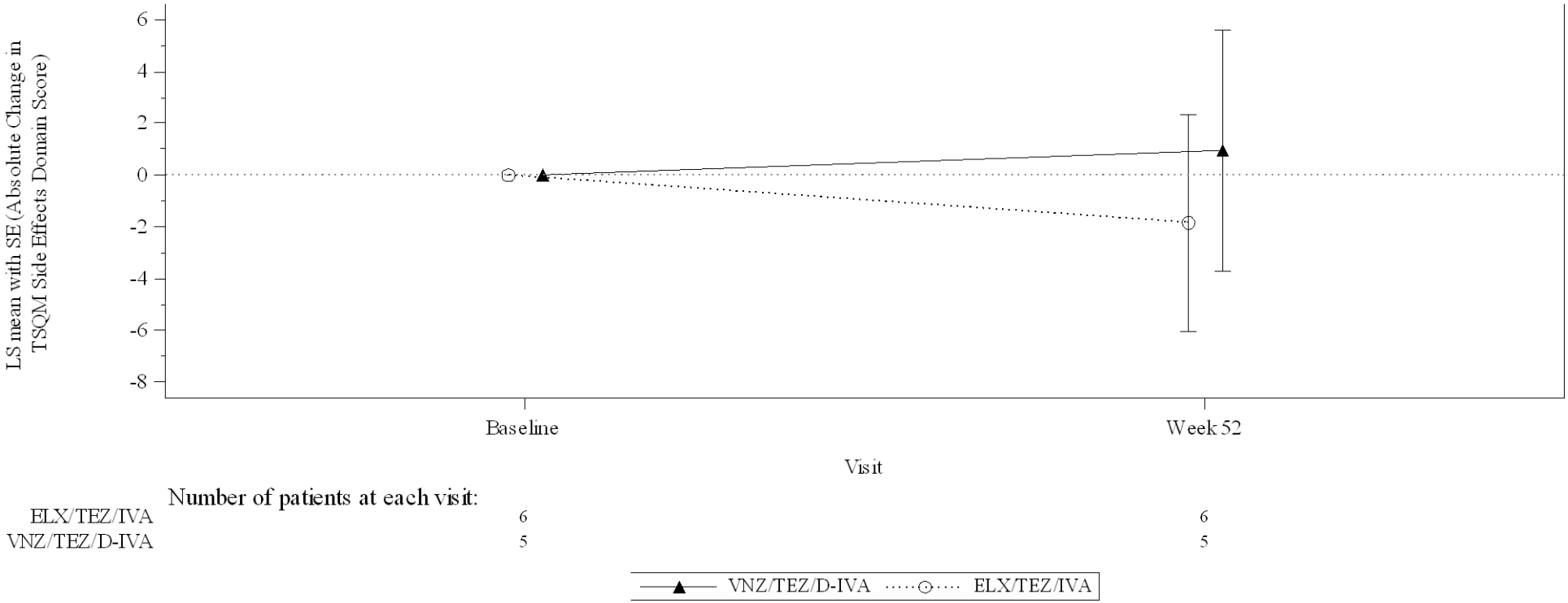
Domain: Side Effects
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 1.2.2.12.2.1
Study VX20-121-102: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Subgroup Prior CFTR Modulator Use
Full Analysis Set

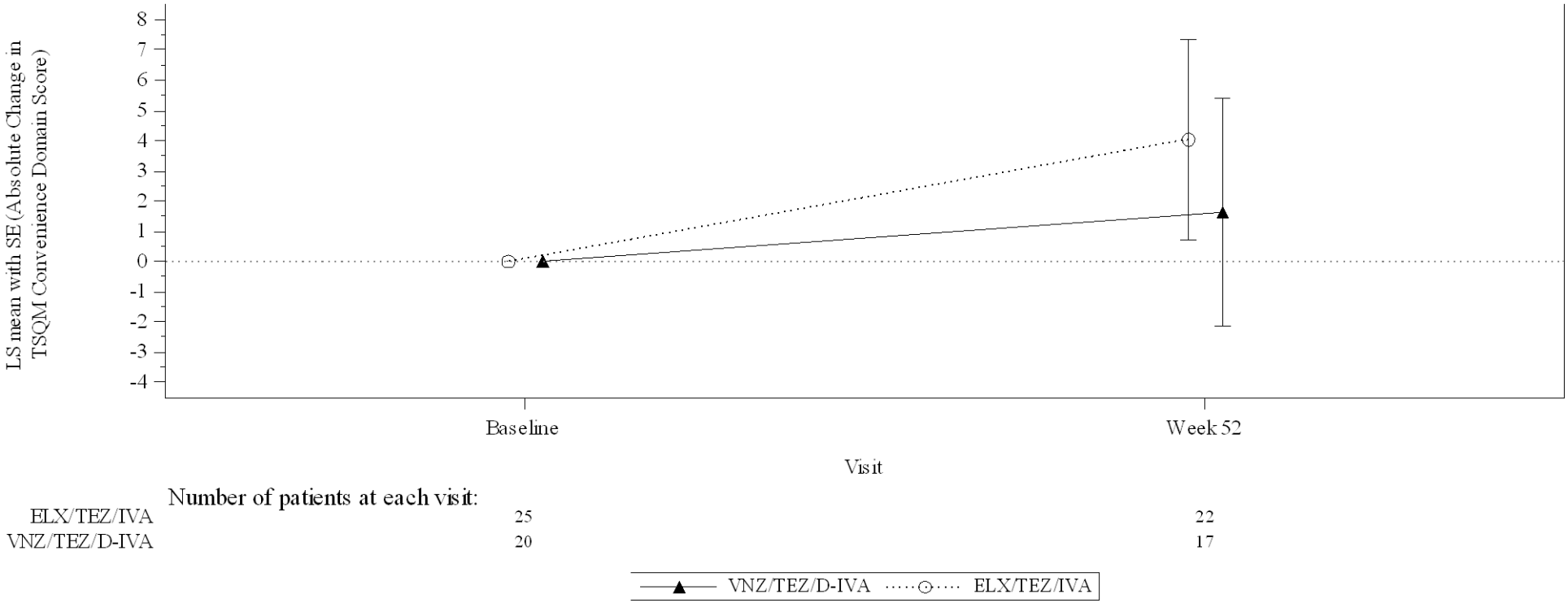
Domain: Side Effects
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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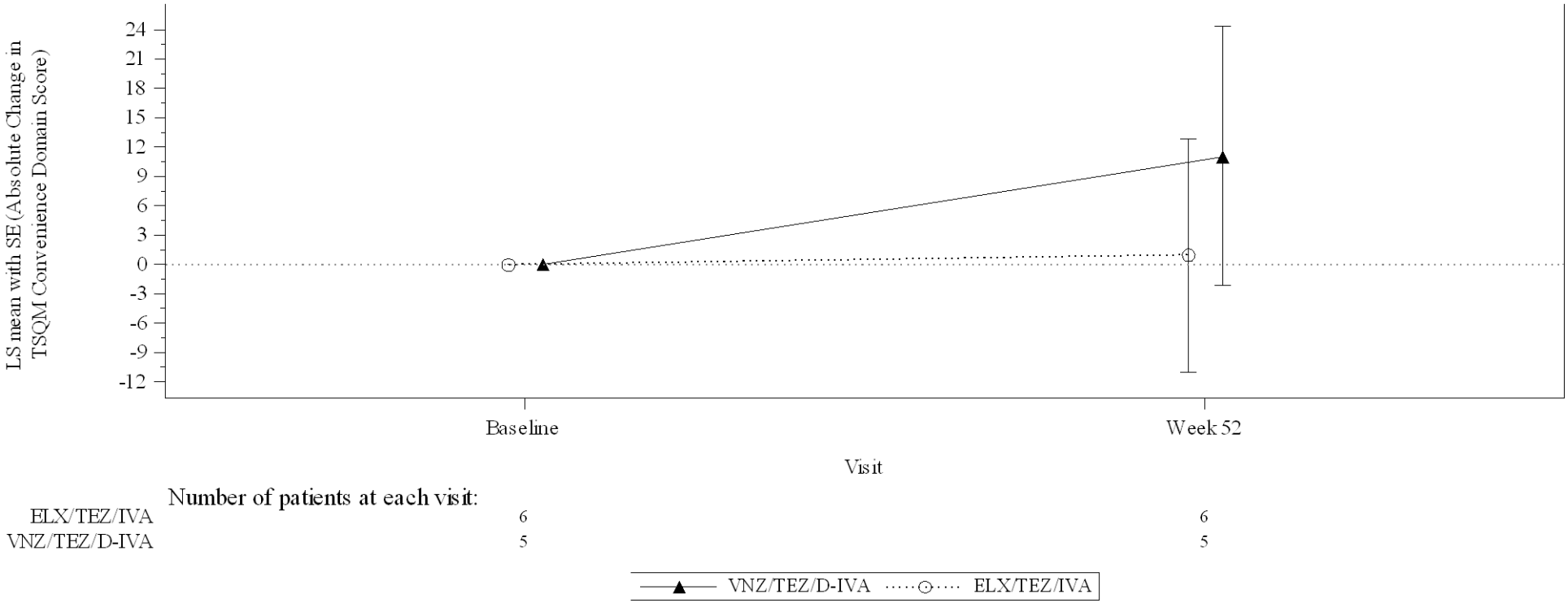
Domain: Convenience
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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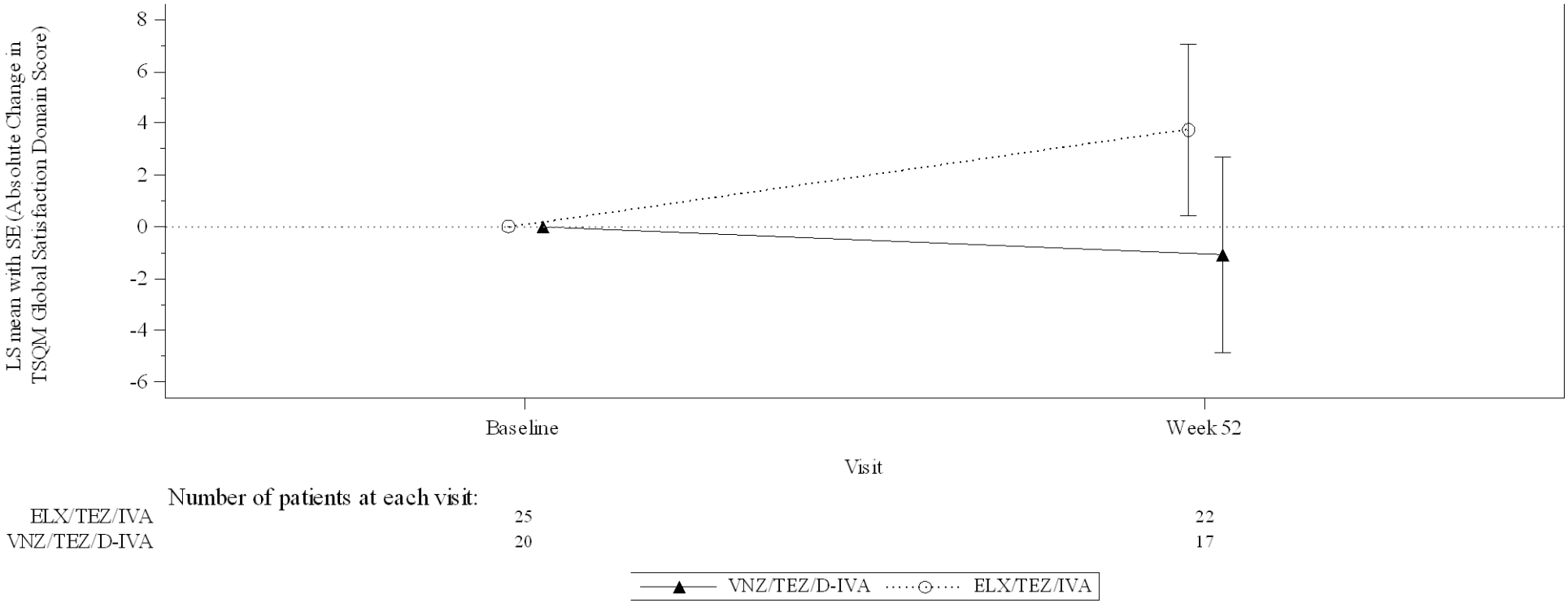
Domain: Convenience
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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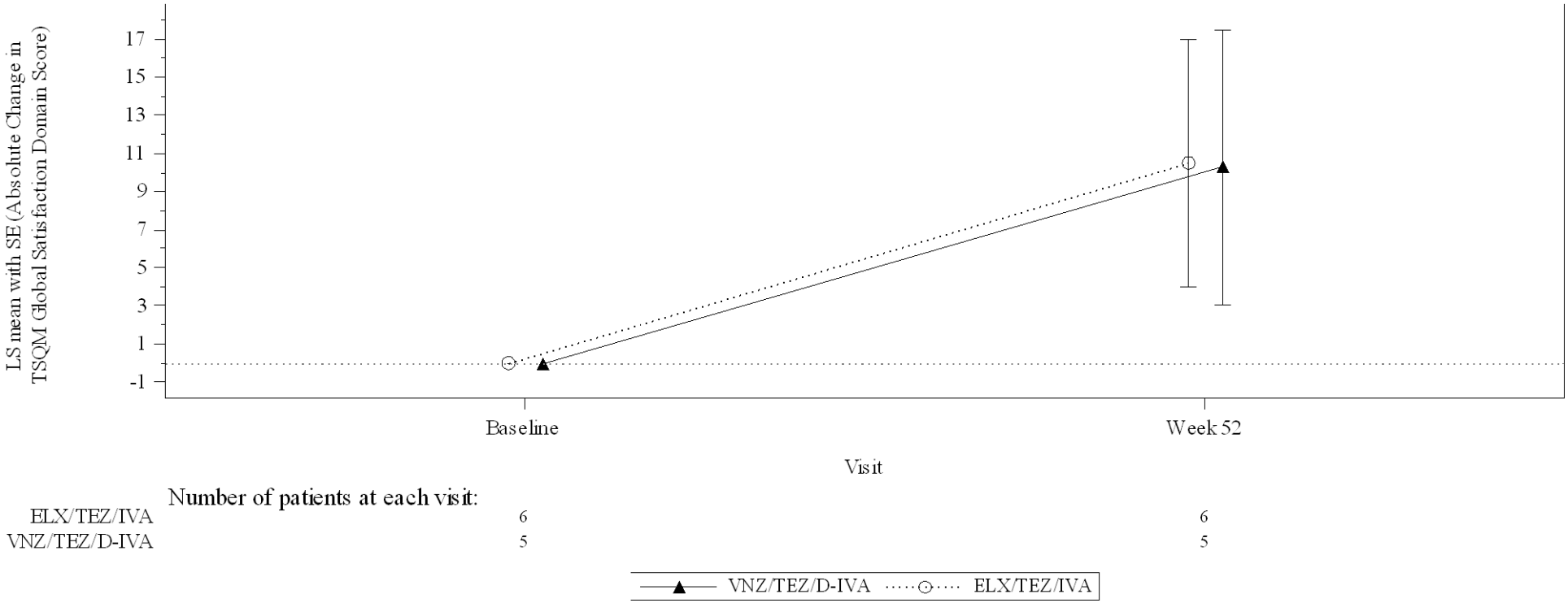
Domain: Global Satisfaction
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effect for treatment, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 1.2.2.12.2.1
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Full Analysis Set

Domain: Global Satisfaction
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Table 2.1.1.1
Study VX20-121-103: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Overall Study Observation Time		
n	289	284
Mean (SD)	51.26 (5.63)	50.42 (7.77)
Median	52.14	52.14
Min, Max	4.29, 56.86	4.57, 56.14
$ppFEV_1$ (percentage points)		
n	289	284
Mean (SD)	50.69 (6.46)	49.73 (8.84)
Median	52.14	52.14
Min, Max	4.29, 56.86	2.00, 56.14
BMI (kg/m^2)		
n	289	284
Mean (SD)	50.92 (6.17)	49.81 (8.69)
Median	52.14	52.14
Min, Max	4.29, 56.86	4.43, 56.00
BMI z-score		
n	42	53
Mean (SD)	48.21 (11.70)	45.76 (13.32)
Median	52.00	52.14
Min, Max	4.29, 56.86	4.43, 53.00
Sweat Chloride (mmol/L)		
n	286	283
Mean (SD)	50.54 (6.74)	48.62 (10.80)
Median	52.14	52.14
Min, Max	4.29, 53.71	0.14, 55.86

- Observation duration [weeks] is defined as (date of last observation - date of randomization +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results.

Table 2.1.1.1
Study VX20-121-103: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Weight (kg)		
n	289	284
Mean (SD)	51.20 (5.86)	50.19 (8.43)
Median	52.14	52.14
Min, Max	4.29, 56.86	4.43, 56.00
Pulmonary Exacerbation		
n	289	284
Mean (SD)	51.17 (5.59)	50.35 (7.75)
Median	52.14	52.14
Min, Max	4.29, 53.71	4.57, 53.86
CFQ-R		
n	289	284
Mean (SD)	50.80 (6.59)	49.88 (9.08)
Median	52.14	52.14
Min, Max	4.29, 53.71	0.14, 55.86
TSQM		
n	148	138
Mean (SD)	24.47 (25.58)	26.54 (25.45)
Median	0.71	26.43
Min, Max	0.00, 53.14	0.14, 53.86
CF-IQ		
n	288	284
Mean (SD)	50.39 (7.82)	48.70 (11.54)
Median	52.14	52.14
Min, Max	3.57, 53.71	0.14, 53.86

- Observation duration [weeks] is defined as (date of last observation - date of randomization +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results.

Table 2.1.1.1
Study VX20-121-103: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Safety		
n	289	284
Mean (SD)	50.72 (6.85)	49.70 (9.15)
Median	52.14	52.14
Min, Max	4.14, 56.71	4.57, 56.00

- Observation duration [weeks] is defined as (date of last observation - date of randomization +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results.

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Table 2.1.2.1
Study VX20-121-103: Summary of Patients with Ongoing Antibiotic Medications at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline, N1	289	284
Subjects with 0 ongoing AB	121 (41.87)	128 (45.07)
Subjects with 1 ongoing AB	104 (35.99)	88 (30.99)
Subjects with ≥ 2 ongoing AB	64 (22.15)	68 (23.94)
Subjects with ≥ 1 ongoing IV AB	1 (0.35)	1 (0.35)
Week 52, N1	278	264
Subjects with 0 ongoing AB	122 (43.88)	116 (43.94)
Subjects with 1 ongoing AB	94 (33.81)	95 (35.98)
Subjects with ≥ 2 ongoing AB	62 (22.30)	53 (20.08)
Subjects with ≥ 1 ongoing IV AB	5 (1.80)	2 (0.76)

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- Ongoing antibiotic medications at baseline refer to those with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing antibiotic medications at Week 52 refer to those with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

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Table 2.1.2.2
Study VX20-121-103: Summary of Patients with Antibiotic Medications during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
All subjects	289	284
Subjects with 0 AB	32 (11.07)	37 (13.03)
Subjects with 1-3 AB	127 (43.94)	129 (45.42)
Subjects with ≥ 4 AB	130 (44.98)	118 (41.55)
Subjects with 0 IV AB	238 (82.35)	240 (84.51)
Subjects with 1 IV AB	9 (3.11)	11 (3.87)
Subjects with ≥ 2 IV AB	42 (14.53)	33 (11.62)
Subjects with 0 ongoing antibiotic medications at baseline	121	128
Subjects with 0 AB	32 (26.45)	37 (28.91)
Subjects with 1-3 AB	60 (49.59)	65 (50.78)
Subjects with ≥ 4 AB	29 (23.97)	26 (20.31)
Subjects with 0 IV AB	105 (86.78)	114 (89.06)
Subjects with 1 IV AB	4 (3.31)	4 (3.13)
Subjects with ≥ 2 IV AB	12 (9.92)	10 (7.81)

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- Antibiotic medications during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX20-121-103

Table 2.1.3.1
Study VX20-121-103: Summary of Patients with Ongoing Physiotherapies at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline, N1	289	284
Subjects with 0 ongoing PT	155 (53.63)	162 (57.04)
Subjects with 1 ongoing PT	121 (41.87)	104 (36.62)
Subjects with ≥ 2 ongoing PT	13 (4.50)	18 (6.34)
Week 52, N1	278	264
Subjects with 0 ongoing PT	148 (53.24)	150 (56.82)
Subjects with 1 ongoing PT	117 (42.09)	96 (36.36)
Subjects with ≥ 2 ongoing PT	13 (4.68)	18 (6.82)

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- The ongoing physiotherapy at baseline is defined as a physiotherapy whose start date is prior to first dose date of study drug in the Treatment Period and the end date is ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing physiotherapy at Week 52 is defined as a physiotherapy whose start date is prior to Week 52 visit date and the end date is ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX20-121-103

Table 2.1.3.2
Study VX20-121-103: Summary of Patients with Physiotherapies during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
All subjects	289	284
Subjects with 0 PT	154 (53.29)	160 (56.34)
Subjects with 1 PT	120 (41.52)	104 (36.62)
Subjects with ≥ 2 PT	15 (5.19)	20 (7.04)
Subjects with 0 ongoing physiotherapies at baseline	155	162
Subjects with 0 PT	154 (99.35)	160 (98.77)
Subjects with 1 PT	1 (0.65)	1 (0.62)
Subjects with ≥ 2 PT	0	1 (0.62)

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- Physiotherapies during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

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Table 2.1.4.1
Study VX20-121-103: Summary of Patients with Ongoing Inhaled Medications at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline, N1	289	284
Subjects with 0 ongoing IM	25 (8.65)	15 (5.28)
Subjects with 1 ongoing IM	30 (10.38)	40 (14.08)
Subjects with ≥ 2 ongoing IM	234 (80.97)	229 (80.63)
Week 52, N1	278	264
Subjects with 0 ongoing IM	24 (8.63)	11 (4.17)
Subjects with 1 ongoing IM	31 (11.15)	39 (14.77)
Subjects with ≥ 2 ongoing IM	223 (80.22)	214 (81.06)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 52 refer to those IMs with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX20-121-103

Table 2.1.4.2
Study VX20-121-103: Summary of Patients with Inhaled Medications during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
All subjects	289	284
Subjects with 0 IM	21 (7.27)	10 (3.52)
Subjects with 1 IM	27 (9.34)	35 (12.32)
Subjects with ≥ 2 IM	241 (83.39)	239 (84.15)
Subjects with 0 ongoing inhaled medications at baseline	25	15
Subjects with 0 IM	21 (84.00)	10 (66.67)
Subjects with 1 IM	2 (8.00)	2 (13.33)
Subjects with ≥ 2 IM	2 (8.00)	3 (20.00)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

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Table 2.1.4.3
Study VX20-121-103: Summary of Patients with Ongoing Inhaled Medications for Mucolytics at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline, N1	289	284
Subjects with 0 ongoing IM	59 (20.42)	71 (25.00)
Subjects with 1 ongoing IM	107 (37.02)	102 (35.92)
Subjects with ≥ 2 ongoing IM	123 (42.56)	111 (39.08)
Week 52, N1	278	264
Subjects with 0 ongoing IM	64 (23.02)	70 (26.52)
Subjects with 1 ongoing IM	102 (36.69)	93 (35.23)
Subjects with ≥ 2 ongoing IM	112 (40.29)	101 (38.26)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 52 refer to those IMs with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX20-121-103

Table 2.1.4.4
Study VX20-121-103: Summary of Patients with Inhaled Medications for Mucolytics during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
All subjects	289	284
Subjects with 0 IM	54 (18.69)	64 (22.54)
Subjects with 1 IM	103 (35.64)	102 (35.92)
Subjects with ≥ 2 IM	132 (45.67)	118 (41.55)
Subjects with 0 ongoing inhaled medications at baseline	59	71
Subjects with 0 IM	54 (91.53)	64 (90.14)
Subjects with 1 IM	5 (8.47)	3 (4.23)
Subjects with ≥ 2 IM	0	4 (5.63)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

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Table 2.1.4.5
Study VX20-121-103: Summary of Patients with Ongoing Inhaled Medications for Obstructive Airway Disease at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline, N1	289	284
Subjects with 0 ongoing IM	48 (16.61)	30 (10.56)
Subjects with 1 ongoing IM	88 (30.45)	109 (38.38)
Subjects with ≥ 2 ongoing IM	153 (52.94)	145 (51.06)
Week 52, N1	278	264
Subjects with 0 ongoing IM	45 (16.19)	23 (8.71)
Subjects with 1 ongoing IM	89 (32.01)	102 (38.64)
Subjects with ≥ 2 ongoing IM	144 (51.80)	139 (52.65)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 52 refer to those IMs with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

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Table 2.1.4.6
Study VX20-121-103: Summary of Patients with Inhaled Medications for Obstructive Airway Disease during the Study Treatment Period
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
All subjects	289	284
Subjects with 0 IM	42 (14.53)	23 (8.10)
Subjects with 1 IM	84 (29.07)	101 (35.56)
Subjects with ≥ 2 IM	163 (56.40)	160 (56.34)
Subjects with 0 ongoing inhaled medications at baseline	48	30
Subjects with 0 IM	42 (87.50)	23 (76.67)
Subjects with 1 IM	4 (8.33)	2 (6.67)
Subjects with ≥ 2 IM	2 (4.17)	5 (16.67)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX20-121-103

Table 2.1.5.1
Study VX20-121-103: Summary of Patients with Ongoing CF-related Medications at Baseline or at Week 52
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline, N1	289	284
Subjects with 0 ongoing CF-related medications	2 (0.69)	3 (1.06)
Subjects with 1 ongoing CF-related medications	8 (2.77)	6 (2.11)
Subjects with 2 ongoing CF-related medications	18 (6.23)	14 (4.93)
Subjects with 3 ongoing CF-related medications	19 (6.57)	23 (8.10)
Subjects with 4 ongoing CF-related medications	37 (12.80)	36 (12.68)
Subjects with ≥5 ongoing CF-related medications	205 (70.93)	202 (71.13)
Week 52, N1	278	264
Subjects with 0 ongoing CF-related medications	2 (0.72)	3 (1.14)
Subjects with 1 ongoing CF-related medications	8 (2.88)	5 (1.89)
Subjects with 2 ongoing CF-related medications	16 (5.76)	8 (3.03)
Subjects with 3 ongoing CF-related medications	19 (6.83)	29 (10.98)
Subjects with 4 ongoing CF-related medications	36 (12.95)	31 (11.74)
Subjects with ≥5 ongoing CF-related medications	197 (70.86)	188 (71.21)

- CF-related medications: CF co-medications are defined as those medications with
o ATC level 2 names of "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES", "DIGESTIVES, INCL. ENZYMES", "ANTIBACTERIALS FOR SYSTEMIC USE", "DRUGS USED IN DIABETES", "BILE AND LIVER THERAPY", "GENERAL NUTRIENTS";
o or ATC level 3 names of "DRUGS FOR CONSTIPATION", "PROPULSIVES";
o or ATC level 4 names of "MUCOLYTICS".
In addition, the route of administration for "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES" and "MUCOLYTICS" requires to be "RESPIRATORY (INHALATION)" and the route for "ANTIBACTERIALS FOR SYSTEMIC USE" requires to be "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- The ongoing CF-related medications at baseline refer to those CF-related medications with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing CF-related medications at Week 52 refer to those CF-related medications with start date < Week 52 visit date and the end date ≥ Week 52 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 52 visit, respectively. The percentages in this table are calculated based on N1.

Table 2.1.6
Study VX20-121-103: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

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ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 25 n (%)	Total N = 41 n (%)
Subjects with any concomitant medications during the Treatment Period	14 (87.5)	16 (64.0)	30 (73.2)
RESPIRATORY SYSTEM	11 (68.8)	12 (48.0)	23 (56.1)
OTHER RESPIRATORY SYSTEM PRODUCTS	8 (50.0)	9 (36.0)	17 (41.5)
ELEXACAFTOR;IVACAFTOR;TEZACAFTOR	6 (37.5)	9 (36.0)	15 (36.6)
IVACAFTOR	2 (12.5)	2 (8.0)	4 (9.8)
IVACAFTOR;LUMACAFTOR	1 (6.3)	1 (4.0)	2 (4.9)
IVACAFTOR;TEZACAFTOR	1 (6.3)	0	1 (2.4)
NASAL PREPARATIONS	2 (12.5)	3 (12.0)	5 (12.2)
PREDNISOLONE	0	2 (8.0)	2 (4.9)
SODIUM CHLORIDE	1 (6.3)	1 (4.0)	2 (4.9)
ACETYLCYSTEINE	1 (6.3)	0	1 (2.4)
DEXAMETHASONE	1 (6.3)	0	1 (2.4)
SODIUM BICARBONATE	0	1 (4.0)	1 (2.4)
COUGH AND COLD PREPARATIONS	3 (18.8)	1 (4.0)	4 (9.8)
SODIUM CHLORIDE	1 (6.3)	1 (4.0)	2 (4.9)
ACETYLCYSTEINE	1 (6.3)	0	1 (2.4)
CODEINE PHOSPHATE	1 (6.3)	0	1 (2.4)
DORNASE ALFA	1 (6.3)	0	1 (2.4)
THROAT PREPARATIONS	3 (18.8)	1 (4.0)	4 (9.8)
IBUPROFEN	2 (12.5)	0	2 (4.9)
TRANEXAMIC ACID	1 (6.3)	1 (4.0)	2 (4.9)
LIDOCAINE	1 (6.3)	0	1 (2.4)
ANTIHISTAMINES FOR SYSTEMIC USE	1 (6.3)	1 (4.0)	2 (4.9)
DIPHENHYDRAMINE HYDROCHLORIDE	1 (6.3)	0	1 (2.4)
MECLOZINE	0	1 (4.0)	1 (2.4)
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	1 (6.3)	0	1 (2.4)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 2.1.6
Study VX20-121-103: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-103

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 25 n (%)	Total N = 41 n (%)
DEXAMETHASONE	1 (6.3)	0	1 (2.4)
ALIMENTARY TRACT AND METABOLISM	5 (31.3)	9 (36.0)	14 (34.1)
ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	2 (12.5)	5 (20.0)	7 (17.1)
PREDNISONE	1 (6.3)	2 (8.0)	3 (7.3)
COLISTIMETHATE SODIUM	1 (6.3)	1 (4.0)	2 (4.9)
PREDNISOLONE	0	2 (8.0)	2 (4.9)
MESALAZINE	1 (6.3)	0	1 (2.4)
NYSTATIN	0	1 (4.0)	1 (2.4)
DRUGS FOR CONSTIPATION	3 (18.8)	3 (12.0)	6 (14.6)
SODIUM CHLORIDE	1 (6.3)	1 (4.0)	2 (4.9)
BISACODYL	1 (6.3)	0	1 (2.4)
DOCUSATE SODIUM;SENNOSIDE A+B	1 (6.3)	0	1 (2.4)
LACTULOSE	0	1 (4.0)	1 (2.4)
MACROGOL	1 (6.3)	0	1 (2.4)
MACROGOL 3350;POTASSIUM CHLORIDE;SODIUM BICARBONATE;SODIUM CHLORIDE	0	1 (4.0)	1 (2.4)
PARAFFIN, LIQUID	1 (6.3)	0	1 (2.4)
SENNOSIDE A+B	1 (6.3)	0	1 (2.4)
STOMATOLOGICAL PREPARATIONS	1 (6.3)	4 (16.0)	5 (12.2)
DOXYCYCLINE	0	2 (8.0)	2 (4.9)
PREDNISOLONE	0	2 (8.0)	2 (4.9)
SODIUM CHLORIDE	1 (6.3)	1 (4.0)	2 (4.9)
TRANEXAMIC ACID	1 (6.3)	1 (4.0)	2 (4.9)
DEXAMETHASONE	1 (6.3)	0	1 (2.4)
LIDOCAINE	1 (6.3)	0	1 (2.4)
NYSTATIN	0	1 (4.0)	1 (2.4)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 2.1.6
Study VX20-121-103: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-103

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 25 n (%)	Total N = 41 n (%)
SODIUM BICARBONATE	0	1 (4.0)	1 (2.4)
ANTIEMETICS AND ANTINAUSEANTS	1 (6.3)	2 (8.0)	3 (7.3)
ONDANSETRON	1 (6.3)	1 (4.0)	2 (4.9)
DIPHENHYDRAMINE HYDROCHLORIDE	1 (6.3)	0	1 (2.4)
MECLOZINE	0	1 (4.0)	1 (2.4)
MINERAL SUPPLEMENTS	2 (12.5)	1 (4.0)	3 (7.3)
SODIUM CHLORIDE	1 (6.3)	1 (4.0)	2 (4.9)
MINERALS NOS;VITAMINS NOS	1 (6.3)	0	1 (2.4)
BILE AND LIVER THERAPY	1 (6.3)	1 (4.0)	2 (4.9)
ACETYLCYSTEINE	1 (6.3)	0	1 (2.4)
LACTULOSE	0	1 (4.0)	1 (2.4)
DRUGS FOR ACID RELATED DISORDERS	1 (6.3)	1 (4.0)	2 (4.9)
OMEPRAZOLE	1 (6.3)	0	1 (2.4)
SODIUM BICARBONATE	0	1 (4.0)	1 (2.4)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	2 (12.5)	0	2 (4.9)
PHLOROGLUCINOL;TRIMETHYLPHLOROGLUCINOL	1 (6.3)	0	1 (2.4)
SIMETICONE	1 (6.3)	0	1 (2.4)
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS	1 (6.3)	1 (4.0)	2 (4.9)
ACETYLCYSTEINE	1 (6.3)	0	1 (2.4)
SODIUM BICARBONATE	0	1 (4.0)	1 (2.4)
VITAMINS	2 (12.5)	0	2 (4.9)
COLECALCIFEROL;MENADIOL;RETINOL PALMITATE;TOCOPHERYL ACETATE	1 (6.3)	0	1 (2.4)
MINERALS NOS;VITAMINS NOS	1 (6.3)	0	1 (2.4)
DIGESTIVES, INCL. ENZYMES	1 (6.3)	0	1 (2.4)
PANCREATIN	1 (6.3)	0	1 (2.4)
PANCRELIPASE	1 (6.3)	0	1 (2.4)
DRUGS USED IN DIABETES	1 (6.3)	0	1 (2.4)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 2.1.6
Study VX20-121-103: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-103

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 25 n (%)	Total N = 41 n (%)
INSULIN ASPART	1 (6.3)	0	1 (2.4)
INSULIN GLARGINE	1 (6.3)	0	1 (2.4)
INSULIN LISPRO	1 (6.3)	0	1 (2.4)
TONICS	1 (6.3)	0	1 (2.4)
MINERALS NOS;VITAMINS NOS	1 (6.3)	0	1 (2.4)
ANTIINFECTIVES FOR SYSTEMIC USE	6 (37.5)	8 (32.0)	14 (34.1)
ANTIBACTERIALS FOR SYSTEMIC USE	6 (37.5)	6 (24.0)	12 (29.3)
CIPROFLOXACIN	1 (6.3)	3 (12.0)	4 (9.8)
TOBRAMYCIN	1 (6.3)	3 (12.0)	4 (9.8)
COLISTIMETHATE SODIUM	1 (6.3)	1 (4.0)	2 (4.9)
DOXYCYCLINE	0	2 (8.0)	2 (4.9)
AMOXICILLIN	1 (6.3)	0	1 (2.4)
AMOXICILLIN;CLAVULANATE POTASSIUM	1 (6.3)	0	1 (2.4)
AZITHROMYCIN	1 (6.3)	0	1 (2.4)
AZTREONAM	1 (6.3)	0	1 (2.4)
AZTREONAM LYSINE	1 (6.3)	0	1 (2.4)
CEFEPIME	0	1 (4.0)	1 (2.4)
CEFTAZIDIME	1 (6.3)	0	1 (2.4)
CEFTRIAXONE	1 (6.3)	0	1 (2.4)
LEVOFLOXACIN	1 (6.3)	0	1 (2.4)
PIPERACILLIN	1 (6.3)	0	1 (2.4)
PIPERACILLIN SODIUM;TAZOBACTAM SODIUM	1 (6.3)	0	1 (2.4)
SULFAMETHOXAZOLE;TRIMETHOPRIM	0	1 (4.0)	1 (2.4)
TAZOBACTAM	1 (6.3)	0	1 (2.4)
ANTIVIRALS FOR SYSTEMIC USE	1 (6.3)	2 (8.0)	3 (7.3)
OSELTAMIVIR PHOSPHATE	1 (6.3)	1 (4.0)	2 (4.9)
MOLNUPIRAVIR	1 (6.3)	0	1 (2.4)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 2.1.6
Study VX20-121-103: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-103

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 25 n (%)	Total N = 41 n (%)
VALACICLOVIR	0	1 (4.0)	1 (2.4)
VALACICLOVIR HYDROCHLORIDE	0	1 (4.0)	1 (2.4)
VACCINES	2 (12.5)	1 (4.0)	3 (7.3)
COVID-19 VACCINE	1 (6.3)	1 (4.0)	2 (4.9)
INFLUENZA VACCINE INACT SPLIT 3V	1 (6.3)	0	1 (2.4)
TETANUS VACCINE	1 (6.3)	0	1 (2.4)
TICK-BORNE ENCEPHALITIS VACCINE	1 (6.3)	0	1 (2.4)
ANTIMYCOTICS FOR SYSTEMIC USE	0	2 (8.0)	2 (4.9)
FLUCONAZOLE	0	2 (8.0)	2 (4.9)
NYSTATIN	0	1 (4.0)	1 (2.4)
SENSORY ORGANS	4 (25.0)	9 (36.0)	13 (31.7)
OPHTHALMOLOGICALS	4 (25.0)	9 (36.0)	13 (31.7)
CIPROFLOXACIN	1 (6.3)	3 (12.0)	4 (9.8)
TOBRAMYCIN	1 (6.3)	3 (12.0)	4 (9.8)
PREDNISONE	1 (6.3)	2 (8.0)	3 (7.3)
COLISTIMETHATE SODIUM	1 (6.3)	1 (4.0)	2 (4.9)
FLUCONAZOLE	0	2 (8.0)	2 (4.9)
KETOROLAC TROMETHAMINE	2 (12.5)	0	2 (4.9)
PREDNISOLONE	0	2 (8.0)	2 (4.9)
SODIUM CHLORIDE	1 (6.3)	1 (4.0)	2 (4.9)
ACETYLCYSTEINE	1 (6.3)	0	1 (2.4)
AZITHROMYCIN	1 (6.3)	0	1 (2.4)
DEXAMETHASONE	1 (6.3)	0	1 (2.4)
INDOMETACIN	1 (6.3)	0	1 (2.4)
LEVOFLOXACIN	1 (6.3)	0	1 (2.4)
LIDOCAINE	1 (6.3)	0	1 (2.4)
MACROGOL	1 (6.3)	0	1 (2.4)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 2.1.6
Study VX20-121-103: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-103

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 25 n (%)	Total N = 41 n (%)
MINERALS NOS;VITAMINS NOS	1 (6.3)	0	1 (2.4)
PANCREATIN	1 (6.3)	0	1 (2.4)
PARAFFIN, LIQUID	1 (6.3)	0	1 (2.4)
OTOLOGICALS	3 (18.8)	5 (20.0)	8 (19.5)
CIPROFLOXACIN	1 (6.3)	3 (12.0)	4 (9.8)
PREDNISOLONE	0	2 (8.0)	2 (4.9)
SODIUM CHLORIDE	1 (6.3)	1 (4.0)	2 (4.9)
DEXAMETHASONE	1 (6.3)	0	1 (2.4)
LEVOFLOXACIN	1 (6.3)	0	1 (2.4)
LIDOCAINE	1 (6.3)	0	1 (2.4)
PARAFFIN, LIQUID	1 (6.3)	0	1 (2.4)
SODIUM BICARBONATE	0	1 (4.0)	1 (2.4)
OPHTHALMOLOGICAL AND OTOLOGICAL PREPARATIONS	2 (12.5)	4 (16.0)	6 (14.6)
CIPROFLOXACIN	1 (6.3)	3 (12.0)	4 (9.8)
PREDNISOLONE	0	2 (8.0)	2 (4.9)
DEXAMETHASONE	1 (6.3)	0	1 (2.4)
LEVOFLOXACIN	1 (6.3)	0	1 (2.4)
DERMATOLOGICALS	5 (31.3)	7 (28.0)	12 (29.3)
OTHER DERMATOLOGICAL PREPARATIONS	4 (25.0)	3 (12.0)	7 (17.1)
IBUPROFEN	2 (12.5)	0	2 (4.9)
TRANEXAMIC ACID	1 (6.3)	1 (4.0)	2 (4.9)
ESTRADIOL	0	1 (4.0)	1 (2.4)
MINERALS NOS;VITAMINS NOS	1 (6.3)	0	1 (2.4)
SODIUM BICARBONATE	0	1 (4.0)	1 (2.4)
ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE	2 (12.5)	4 (16.0)	6 (14.6)
CIPROFLOXACIN	1 (6.3)	3 (12.0)	4 (9.8)
DOXYCYCLINE	0	2 (8.0)	2 (4.9)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 2.1.6
Study VX20-121-103: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-103

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 25 n (%)	Total N = 41 n (%)
LEVOFLOXACIN	1 (6.3)	0	1 (2.4)
CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	2 (12.5)	4 (16.0)	6 (14.6)
PREDNISONE	1 (6.3)	2 (8.0)	3 (7.3)
PREDNISOLONE	0	2 (8.0)	2 (4.9)
DEXAMETHASONE	1 (6.3)	0	1 (2.4)
ANTI-ACNE PREPARATIONS	3 (18.8)	2 (8.0)	5 (12.2)
DOXYCYCLINE	0	2 (8.0)	2 (4.9)
IBUPROFEN	2 (12.5)	0	2 (4.9)
AZITHROMYCIN	1 (6.3)	0	1 (2.4)
ANTIFUNGALS FOR DERMATOLOGICAL USE	0	2 (8.0)	2 (4.9)
FLUCONAZOLE	0	2 (8.0)	2 (4.9)
NYSTATIN	0	1 (4.0)	1 (2.4)
MEDICATED DRESSINGS	1 (6.3)	1 (4.0)	2 (4.9)
SODIUM CHLORIDE	1 (6.3)	1 (4.0)	2 (4.9)
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS	1 (6.3)	1 (4.0)	2 (4.9)
SODIUM CHLORIDE	1 (6.3)	1 (4.0)	2 (4.9)
FISH OIL	1 (6.3)	0	1 (2.4)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	1 (6.3)	0	1 (2.4)
DIPHENHYDRAMINE HYDROCHLORIDE	1 (6.3)	0	1 (2.4)
LIDOCAINE	1 (6.3)	0	1 (2.4)
EMOLLIENTS AND PROTECTIVES	1 (6.3)	0	1 (2.4)
PARAFFIN, LIQUID	1 (6.3)	0	1 (2.4)
NERVOUS SYSTEM	7 (43.8)	4 (16.0)	11 (26.8)
ANALGESICS	6 (37.5)	2 (8.0)	8 (19.5)
PARACETAMOL	5 (31.3)	1 (4.0)	6 (14.6)
ANALGESICS	0	1 (4.0)	1 (2.4)
CODEINE PHOSPHATE	1 (6.3)	0	1 (2.4)

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- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 2.1.6
Study VX20-121-103: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 25 n (%)	Total N = 41 n (%)
CODEINE PHOSPHATE;PARACETAMOL	0	1 (4.0)	1 (2.4)
FENTANYL	1 (6.3)	0	1 (2.4)
GABAPENTIN	1 (6.3)	0	1 (2.4)
HYDROMORPHONE HYDROCHLORIDE	1 (6.3)	0	1 (2.4)
MORPHINE	1 (6.3)	0	1 (2.4)
MORPHINE SULFATE	1 (6.3)	0	1 (2.4)
TRAMADOL	1 (6.3)	0	1 (2.4)
TRAMADOL HYDROCHLORIDE	1 (6.3)	0	1 (2.4)
ANTIEPILEPTICS	3 (18.8)	0	3 (7.3)
GABAPENTIN	1 (6.3)	0	1 (2.4)
LEVETIRACETAM	1 (6.3)	0	1 (2.4)
MIDAZOLAM	1 (6.3)	0	1 (2.4)
OTHER NERVOUS SYSTEM DRUGS	1 (6.3)	1 (4.0)	2 (4.9)
GABAPENTIN	1 (6.3)	0	1 (2.4)
MECLOZINE	0	1 (4.0)	1 (2.4)
ANESTHETICS	1 (6.3)	0	1 (2.4)
FENTANYL	1 (6.3)	0	1 (2.4)
LIDOCAINE	1 (6.3)	0	1 (2.4)
PROPOFOL	1 (6.3)	0	1 (2.4)
ANTI-PARKINSON DRUGS	1 (6.3)	0	1 (2.4)
DIPHENHYDRAMINE HYDROCHLORIDE	1 (6.3)	0	1 (2.4)
PSYCHOANALEPTICS	0	1 (4.0)	1 (2.4)
TRAZODONE	0	1 (4.0)	1 (2.4)
PSYCHOLEPTICS	1 (6.3)	0	1 (2.4)
DIPHENHYDRAMINE HYDROCHLORIDE	1 (6.3)	0	1 (2.4)
MIDAZOLAM	1 (6.3)	0	1 (2.4)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 2.1.6
Study VX20-121-103: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-103

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 25 n (%)	Total N = 41 n (%)
VARIOUS	6 (37.5)	2 (8.0)	8 (19.5)
DIAGNOSTIC AGENTS	2 (12.5)	1 (4.0)	3 (7.3)
FOLIC ACID	1 (6.3)	1 (4.0)	2 (4.9)
TUBERCULIN	1 (6.3)	0	1 (2.4)
GENERAL NUTRIENTS	3 (18.8)	0	3 (7.3)
FISH OIL	1 (6.3)	0	1 (2.4)
MINERALS NOS;VITAMINS NOS	1 (6.3)	0	1 (2.4)
NUTRIENTS NOS	1 (6.3)	0	1 (2.4)
HOMEOPATHIC PREPARATION	2 (12.5)	1 (4.0)	3 (7.3)
SODIUM CHLORIDE	1 (6.3)	1 (4.0)	2 (4.9)
PARAFFIN, LIQUID	1 (6.3)	0	1 (2.4)
ALL OTHER NON-THERAPEUTIC PRODUCTS	1 (6.3)	1 (4.0)	2 (4.9)
SODIUM CHLORIDE	1 (6.3)	1 (4.0)	2 (4.9)
CONTRAST MEDIA	2 (12.5)	0	2 (4.9)
IOHEXOL	1 (6.3)	0	1 (2.4)
MEGLUMINE AMIDOTRIZOATE;SODIUM AMIDOTRIZOATE	1 (6.3)	0	1 (2.4)
ALL OTHER THERAPEUTIC PRODUCTS	1 (6.3)	0	1 (2.4)
ACETYLCYSTEINE	1 (6.3)	0	1 (2.4)
BLOOD AND BLOOD FORMING ORGANS	4 (25.0)	3 (12.0)	7 (17.1)
ANTIANEMIC PREPARATIONS	2 (12.5)	2 (8.0)	4 (9.8)
FOLIC ACID	1 (6.3)	1 (4.0)	2 (4.9)
FERROUS FUMARATE	0	1 (4.0)	1 (2.4)
FERROUS SULFATE	0	1 (4.0)	1 (2.4)
MINERALS NOS;VITAMINS NOS	1 (6.3)	0	1 (2.4)
BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS	3 (18.8)	1 (4.0)	4 (9.8)
SODIUM CHLORIDE	1 (6.3)	1 (4.0)	2 (4.9)
MINERALS NOS;VITAMINS NOS	1 (6.3)	0	1 (2.4)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 2.1.6
Study VX20-121-103: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Zusatzanalysen zur Studie VX20-121-103

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 25 n (%)	Total N = 41 n (%)
NUTRIENTS NOS	1 (6.3)	0	1 (2.4)
SODIUM BICARBONATE	0	1 (4.0)	1 (2.4)
ANTIHEMORRHAGICS	1 (6.3)	1 (4.0)	2 (4.9)
TRANEXAMIC ACID	1 (6.3)	1 (4.0)	2 (4.9)
ANTITHROMBOTIC AGENTS	0	1 (4.0)	1 (2.4)
ENOXAPARIN SODIUM	0	1 (4.0)	1 (2.4)
OTHER HEMATOLOGICAL AGENTS	1 (6.3)	0	1 (2.4)
DORNASE ALFA	1 (6.3)	0	1 (2.4)
GENITO URINARY SYSTEM AND SEX HORMONES	3 (18.8)	4 (16.0)	7 (17.1)
GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS	1 (6.3)	3 (12.0)	4 (9.8)
CIPROFLOXACIN	1 (6.3)	3 (12.0)	4 (9.8)
NYSTATIN	0	1 (4.0)	1 (2.4)
OTHER GYNECOLOGICALS	2 (12.5)	1 (4.0)	3 (7.3)
IBUPROFEN	2 (12.5)	0	2 (4.9)
SODIUM BICARBONATE	0	1 (4.0)	1 (2.4)
UROLOGICALS	1 (6.3)	1 (4.0)	2 (4.9)
LIDOCAINE	1 (6.3)	0	1 (2.4)
SODIUM BICARBONATE	0	1 (4.0)	1 (2.4)
SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	0	1 (4.0)	1 (2.4)
ESTRADIOL	0	1 (4.0)	1 (2.4)
CARDIOVASCULAR SYSTEM	4 (25.0)	2 (8.0)	6 (14.6)
CARDIAC THERAPY	3 (18.8)	0	3 (7.3)
IBUPROFEN	2 (12.5)	0	2 (4.9)
INDOMETACIN	1 (6.3)	0	1 (2.4)
LIDOCAINE	1 (6.3)	0	1 (2.4)
VASOPROTECTIVES	1 (6.3)	2 (8.0)	3 (7.3)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 2.1.6
Study VX20-121-103: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 25 n (%)	Total N = 41 n (%)
PREDNISOLONE	0	2 (8.0)	2 (4.9)
DEXAMETHASONE	1 (6.3)	0	1 (2.4)
LIDOCAINE	1 (6.3)	0	1 (2.4)
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	1 (6.3)	0	1 (2.4)
LISINOPRIL DIHYDRATE	1 (6.3)	0	1 (2.4)
BETA BLOCKING AGENTS	1 (6.3)	0	1 (2.4)
CARVEDILOL	1 (6.3)	0	1 (2.4)
LIPID MODIFYING AGENTS	1 (6.3)	0	1 (2.4)
FISH OIL	1 (6.3)	0	1 (2.4)
MUSCULO-SKELETAL SYSTEM	5 (31.3)	1 (4.0)	6 (14.6)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	5 (31.3)	1 (4.0)	6 (14.6)
FOLIC ACID	1 (6.3)	1 (4.0)	2 (4.9)
IBUPROFEN	2 (12.5)	0	2 (4.9)
KETOROLAC TROMETHAMINE	2 (12.5)	0	2 (4.9)
INDOMETACIN	1 (6.3)	0	1 (2.4)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	4 (25.0)	0	4 (9.8)
IBUPROFEN	2 (12.5)	0	2 (4.9)
KETOROLAC TROMETHAMINE	2 (12.5)	0	2 (4.9)
FISH OIL	1 (6.3)	0	1 (2.4)
INDOMETACIN	1 (6.3)	0	1 (2.4)
DRUGS FOR TREATMENT OF BONE DISEASES	1 (6.3)	0	1 (2.4)
ALENDRONATE SODIUM	1 (6.3)	0	1 (2.4)
MUSCLE RELAXANTS	1 (6.3)	0	1 (2.4)
SUXAMETHONIUM	1 (6.3)	0	1 (2.4)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 2.1.6
Study VX20-121-103: Follow-up Medications after Treatment Discontinuation by ATC Level 1, ATC Level 2, and Preferred Name for Patients that discontinued treatment
Full Analysis Set

ATC Level 1 ATC Level 2 Preferred Name	ELX/TEZ/IVA N = 16 n (%)	VNZ/TEZ/D-IVA N = 25 n (%)	Total N = 41 n (%)
SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS	2 (12.5)	4 (16.0)	6 (14.6)
CORTICOSTEROIDS FOR SYSTEMIC USE	2 (12.5)	4 (16.0)	6 (14.6)
PREDNISONE	1 (6.3)	2 (8.0)	3 (7.3)
PREDNISOLONE	0	2 (8.0)	2 (4.9)
DEXAMETHASONE	1 (6.3)	0	1 (2.4)
ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	0	1 (4.0)	1 (2.4)
ENDOCRINE THERAPY	0	1 (4.0)	1 (2.4)
ESTRADIOL	0	1 (4.0)	1 (2.4)

- Medications are coded using WHODD, version WHODrug Global March 2023 B3 Format.
- Anatomical therapeutic chemical (ATC) classes 1 and 2 and Preferred Names are sorted in descending order of frequency of the Total column.
- A subject with multiple medications within a category (Any, ATC Level, or Preferred Name) is counted only once within that category.
- Follow-up Medications after Treatment Discontinuation: medication initiated after treatment discontinuation
- Non-specific: medications without an ATC level 2 code are grouped under this category

Table 2.2.1.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	286	279
Mean (SD)	66.42 (14.85)	67.24 (14.63)
Week 52		
n	271	257
Mean (SD)	66.38 (15.28)	66.82 (14.85)
Absolute Change at Week 52		
n	269	254
Mean (SD)	-0.08 (5.39)	0.14 (4.87)
Absolute Change through Week 52 (MMRM)		
n	277	271
LS mean (SE)	-0.01 (0.24)	0.31 (0.24)
95% CI of LS mean	(-0.48, 0.47)	(-0.17, 0.79)
P-value within Treatment	0.9806	0.2061

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-0.36, 0.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3597
Hedges' G (SE)		0.08 (0.09)
Hedges' 95% CI		(-0.09, 0.25)
Hedges' P-value		0.3597

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52
Full Analysis Set

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	289	280
Mean (SD)	22.92 (3.27)	23.27 (4.02)
Week 52		
n	275	258
Mean (SD)	23.27 (3.45)	23.72 (4.15)
Absolute Change at Week 52		
n	275	254
Mean (SD)	0.27 (1.19)	0.37 (1.27)
Absolute Change at Week 52 (MMRM)		
n	266	248
LS mean (SE)	0.22 (0.07)	0.37 (0.08)
95% CI of LS mean	(0.07, 0.36)	(0.22, 0.52)
P-value within Treatment	0.0035	<0.0001
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-0.05, 0.36)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1442
Hedges' G (SE)		0.13 (0.09)
Hedges' 95% CI		(-0.04, 0.30)
Hedges' P-value		0.1447

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.1.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52
for Subjects ≤20 Years at Baseline
Full Analysis Set

- N is the number of subjects in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 42	VNZ/TEZ/D-IVA N = 53
Baseline		
n	42	53
Mean (SD)	-0.30 (0.98)	-0.17 (0.95)
Week 52		
n	37	42
Mean (SD)	-0.35 (1.01)	0.02 (0.96)
Absolute Change at Week 52		
n	37	42
Mean (SD)	-0.08 (0.48)	0.15 (0.37)
Absolute Change at Week 52 (MMRM)		
n	35	42
LS mean (SE)	-0.13 (0.07)	0.11 (0.06)
95% CI of LS mean	(-0.27, 0.01)	(-0.01, 0.23)
P-value within Treatment	0.0643	0.0729
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (0.06, 0.42)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0109
Hedges' G (SE)		0.59 (0.23)
Hedges' 95% CI		(0.13, 1.05)

- N is the number of subjects in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52
for Subjects ≤20 Years at Baseline
Full Analysis Set

	ELX/TEZ/IVA N = 42	VNZ/TEZ/D-IVA N = 53
Hedges' P-value		0.0125

- N is the number of subjects in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.4.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	282
Mean (SD)	42.07 (17.88)	43.43 (18.54)
Week 52		
n	269	254
Mean (SD)	40.06 (20.41)	38.16 (20.58)
Absolute Change at Week 52		
n	266	253
Mean (SD)	-2.38 (14.81)	-5.10 (14.03)
Absolute Change through Week 52 (MMRM)		
n	277	271
LS mean (SE)	-2.21 (0.64)	-4.98 (0.65)
95% CI of LS mean	(-3.46, -0.96)	(-6.25, -3.71)
P-value within Treatment	0.0006	<0.0001

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.4.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.77 (-4.55, -0.98)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0024
Hedges' G (SE)		-0.26 (0.09)
Hedges' 95% CI		(-0.43, -0.09)
Hedges' P-value		0.0025

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.4.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Non-missing value at Week 52, N1	269	254
Number of subjects with missing value at Week 52	20	30
SwCl <60 mmol/L at Week 52, n (%)	234 (80.97)	223 (78.52)
Relative Risk (RR) (95% CI)		0.9685 (0.8964, 1.0465)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4182*

- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.1.4.3
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Non-missing value at Week 52, N1	269	254
Number of subjects with missing value at Week 52	20	30
SwCl <30 mmol/L at Week 52, n (%)	93 (32.18)	100 (35.21)
Relative Risk (RR) (95% CI)		1.1124 (0.9223, 1.3416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2654*

- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- N/C: model does not converge.

Table 2.2.1.5
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52
Full Analysis Set

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	289	280
Mean (SD)	65.05 (13.35)	66.58 (13.98)
Week 52		
n	275	258
Mean (SD)	66.40 (13.22)	68.15 (14.01)
Absolute Change at Week 52		
n	275	254
Mean (SD)	0.97 (3.52)	1.33 (3.91)
Absolute Change at Week 52 (MMRM)		
n	266	248
LS mean (SE)	0.81 (0.22)	1.31 (0.23)
95% CI of LS mean	(0.38, 1.25)	(0.87, 1.76)
P-value within Treatment	0.0003	<0.0001
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-0.12, 1.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1140
Hedges' G (SE)		0.14 (0.09)
Hedges' 95% CI		(-0.03, 0.31)
Hedges' P-value		0.1145

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.1.6.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	59 (20.4)	61 (21.5)
Subjects Censored	230 (79.6)	223 (78.5)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9827 (0.9589, 0.9928)	0.9894 (0.9676, 0.9966)
4 Weeks	0.9689 (0.9410, 0.9837)	0.9789 (0.9536, 0.9905)
8 Weeks	0.9480 (0.9153, 0.9683)	0.9647 (0.9354, 0.9808)
12 Weeks	0.9272 (0.8905, 0.9519)	0.9255 (0.8880, 0.9508)
16 Weeks	0.9098 (0.8703, 0.9376)	0.8967 (0.8548, 0.9271)
24 Weeks	0.8817 (0.8384, 0.9140)	0.8567 (0.8098, 0.8928)
36 Weeks	0.8429 (0.7953, 0.8802)	0.8164 (0.7656, 0.8572)
52 Weeks	0.7916 (0.7392, 0.8346)	0.7829 (0.7295, 0.8271)
Hazard Ratio (95% CI)*	-	1.0762 (0.7494, 1.5456)
Two-sided P-value, superiority*	-	0.6909

-CI: Confidence interval.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.1.7.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	9 (3.1)	14 (4.9)
Subjects Censored	280 (96.9)	270 (95.1)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9965 (0.9753, 0.9995)
4 Weeks	0.9965 (0.9757, 0.9995)	0.9930 (0.9721, 0.9982)
8 Weeks	0.9965 (0.9757, 0.9995)	0.9930 (0.9721, 0.9982)
12 Weeks	0.9931 (0.9726, 0.9983)	0.9930 (0.9721, 0.9982)
16 Weeks	0.9931 (0.9726, 0.9983)	0.9858 (0.9626, 0.9946)
24 Weeks	0.9825 (0.9585, 0.9927)	0.9749 (0.9480, 0.9879)
36 Weeks	0.9755 (0.9493, 0.9882)	0.9529 (0.9203, 0.9724)
52 Weeks	0.9683 (0.9400, 0.9834)	0.9492 (0.9157, 0.9696)
Hazard Ratio (95% CI)*	-	1.4491 (0.6189, 3.3927)
Two-sided P-value, superiority*	-	0.3927

- CI: Confidence interval.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring hospitalization during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.1.8.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	17 (5.9)	19 (6.7)
Subjects Censored	272 (94.1)	265 (93.3)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9965 (0.9753, 0.9995)
4 Weeks	0.9931 (0.9726, 0.9983)	0.9930 (0.9721, 0.9982)
8 Weeks	0.9896 (0.9681, 0.9966)	0.9894 (0.9675, 0.9966)
12 Weeks	0.9792 (0.9543, 0.9906)	0.9858 (0.9627, 0.9947)
16 Weeks	0.9792 (0.9543, 0.9906)	0.9787 (0.9531, 0.9904)
24 Weeks	0.9616 (0.9318, 0.9786)	0.9605 (0.9298, 0.9779)
36 Weeks	0.9511 (0.9188, 0.9707)	0.9385 (0.9030, 0.9614)
52 Weeks	0.9403 (0.9058, 0.9625)	0.9311 (0.8942, 0.9555)
Hazard Ratio (95% CI)*	-	1.1021 (0.5609, 2.1653)
Two-sided P-value, superiority*	-	0.7779

- CI: Confidence interval.
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring IV Antibiotics during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).

Table 2.2.1.9.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	85.62 (13.21)	85.71 (13.19)
Week 8 (MMRM)		
n	277	274
LS mean (SE)	85.12 (0.94)	84.70 (0.95)
95% CI of LS mean	(83.26, 86.97)	(82.84, 86.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-3.05, 2.21)
Absolute Change at Week 8 (MMRM)		
n	270	271
LS mean (SE)	-0.56 (0.99)	-1.20 (0.98)
95% CI of LS mean	(-2.50, 1.38)	(-3.14, 0.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-3.38, 2.10)
Week 16 (MMRM)		
n	272	268
LS mean (SE)	85.20 (0.97)	85.20 (0.98)
95% CI of LS mean	(83.30, 87.11)	(83.28, 87.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-2.71, 2.70)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	265	265
LS mean (SE)	-0.41 (0.96)	-0.64 (0.96)
95% CI of LS mean	(-2.30, 1.48)	(-2.53, 1.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-2.90, 2.45)
Week 24 (MMRM)		
n	274	265
LS mean (SE)	83.63 (0.93)	83.78 (0.94)
95% CI of LS mean	(81.81, 85.46)	(81.93, 85.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-2.45, 2.75)
Absolute Change at Week 24 (MMRM)		
n	267	262
LS mean (SE)	-1.98 (0.91)	-1.87 (0.92)
95% CI of LS mean	(-3.77, -0.19)	(-3.67, -0.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-2.43, 2.64)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 52		
n	277	264
Mean (SD)	84.88 (16.92)	87.24 (13.15)
Absolute Change at Week 52		
n	270	260
Mean (SD)	-0.79 (17.30)	1.55 (13.41)
Week 52 (MMRM)		
n	269	258
LS mean (SE)	84.91 (0.89)	87.09 (0.91)
95% CI of LS mean	(83.15, 86.66)	(85.30, 88.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.18 (-0.32, 4.69)
Absolute Change at Week 52 (MMRM)		
n	262	254
LS mean (SE)	-0.76 (0.96)	1.33 (0.97)
95% CI of LS mean	(-2.64, 1.13)	(-0.57, 3.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.09 (-0.59, 4.77)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	-1.05 (0.74)	-0.39 (0.74)
95% CI of LS mean	(-2.50, 0.40)	(-1.85, 1.06)
P-value within Treatment	0.1545	0.5944
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.66 (-1.40, 2.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5303
Hedges' G (SE)		0.05 (0.09)
Hedges' 95% CI		(-0.12, 0.22)
Hedges' P-value		0.5302

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	287 (99.31)	280 (98.59)
Absolute Change at Week 8	280 (96.89)	277 (97.54)
Week 16	282 (97.58)	274 (96.48)
Absolute Change at Week 16	275 (95.16)	271 (95.42)
Week 24	283 (97.92)	271 (95.42)
Absolute Change at Week 24	276 (95.50)	268 (94.37)
Week 52	277 (95.85)	264 (92.96)
Absolute Change at Week 52	270 (93.43)	260 (91.55)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	287 (99.31)	279 (98.24)
Absolute Change at Week 8	280 (96.89)	276 (97.18)
Week 16	283 (97.92)	273 (96.13)
Absolute Change at Week 16	276 (95.50)	270 (95.07)
Week 24	283 (97.92)	271 (95.42)
Absolute Change at Week 24	276 (95.50)	268 (94.37)
Week 52	277 (95.85)	265 (93.31)
Absolute Change at Week 52	270 (93.43)	261 (91.90)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	287 (99.31)	279 (98.24)
Absolute Change at Week 8	280 (96.89)	276 (97.18)
Week 16	282 (97.58)	274 (96.48)
Absolute Change at Week 16	275 (95.16)	271 (95.42)
Week 24	282 (97.58)	271 (95.42)
Absolute Change at Week 24	275 (95.16)	268 (94.37)
Week 52	277 (95.85)	264 (92.96)
Absolute Change at Week 52	270 (93.43)	260 (91.55)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	287 (99.31)	280 (98.59)
Absolute Change at Week 8	280 (96.89)	277 (97.54)
Week 16	283 (97.92)	274 (96.48)
Absolute Change at Week 16	276 (95.50)	271 (95.42)
Week 24	283 (97.92)	271 (95.42)
Absolute Change at Week 24	276 (95.50)	268 (94.37)
Week 52	277 (95.85)	265 (93.31)
Absolute Change at Week 52	270 (93.43)	261 (91.90)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	286 (98.96)	280 (98.59)
Absolute Change at Week 8	280 (96.89)	277 (97.54)
Week 16	283 (97.92)	274 (96.48)
Absolute Change at Week 16	276 (95.50)	271 (95.42)
Week 24	282 (97.58)	271 (95.42)
Absolute Change at Week 24	275 (95.16)	268 (94.37)
Week 52	277 (95.85)	265 (93.31)
Absolute Change at Week 52	270 (93.43)	261 (91.90)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	286 (98.96)	280 (98.59)
Absolute Change at Week 8	280 (96.89)	277 (97.54)
Week 16	283 (97.92)	274 (96.48)
Absolute Change at Week 16	276 (95.50)	271 (95.42)
Week 24	282 (97.58)	271 (95.42)
Absolute Change at Week 24	275 (95.16)	268 (94.37)
Week 52	277 (95.85)	265 (93.31)
Absolute Change at Week 52	270 (93.43)	261 (91.90)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	287 (99.31)	279 (98.24)
Absolute Change at Week 8	280 (96.89)	276 (97.18)
Week 16	283 (97.92)	273 (96.13)
Absolute Change at Week 16	276 (95.50)	270 (95.07)
Week 24	283 (97.92)	271 (95.42)
Absolute Change at Week 24	276 (95.50)	268 (94.37)
Week 52	277 (95.85)	265 (93.31)
Absolute Change at Week 52	270 (93.43)	261 (91.90)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Baseline	282 (97.58)	280 (98.59)
Week 8	287 (99.31)	279 (98.24)
Absolute Change at Week 8	280 (96.89)	276 (97.18)
Week 16	283 (97.92)	274 (96.48)
Absolute Change at Week 16	276 (95.50)	271 (95.42)
Week 24	283 (97.92)	271 (95.42)
Absolute Change at Week 24	276 (95.50)	268 (94.37)
Week 52	277 (95.85)	265 (93.31)
Absolute Change at Week 52	270 (93.43)	261 (91.90)
Through Week 52	287 (99.31)	278 (97.89)
Absolute Change through Week 52	280 (96.89)	274 (96.48)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.2
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 275 n (%)	VNZ/TEZ/D-IVA N = 269 n (%)
Baseline	269 (97.82)	266 (98.88)
Week 8	275 (100.00)	266 (98.88)
Absolute Change at Week 8	269 (97.82)	263 (97.77)
Week 16	271 (98.55)	260 (96.65)
Absolute Change at Week 16	265 (96.36)	257 (95.54)
Week 24	269 (97.82)	257 (95.54)
Absolute Change at Week 24	263 (95.64)	255 (94.80)
Week 52	266 (96.73)	251 (93.31)
Absolute Change at Week 52	260 (94.55)	248 (92.19)
Through Week 52	273 (99.27)	263 (97.77)
Absolute Change through Week 52	267 (97.09)	260 (96.65)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.2
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 275 n (%)	VNZ/TEZ/D-IVA N = 269 n (%)
Baseline	269 (97.82)	266 (98.88)
Week 8	275 (100.00)	265 (98.51)
Absolute Change at Week 8	269 (97.82)	262 (97.40)
Week 16	269 (97.82)	261 (97.03)
Absolute Change at Week 16	263 (95.64)	258 (95.91)
Week 24	269 (97.82)	256 (95.17)
Absolute Change at Week 24	263 (95.64)	254 (94.42)
Week 52	266 (96.73)	250 (92.94)
Absolute Change at Week 52	260 (94.55)	247 (91.82)
Through Week 52	273 (99.27)	263 (97.77)
Absolute Change through Week 52	267 (97.09)	260 (96.65)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.2
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 275 n (%)	VNZ/TEZ/D-IVA N = 269 n (%)
Baseline	269 (97.82)	266 (98.88)
Week 8	274 (99.64)	267 (99.26)
Absolute Change at Week 8	269 (97.82)	264 (98.14)
Week 16	271 (98.55)	261 (97.03)
Absolute Change at Week 16	265 (96.36)	258 (95.91)
Week 24	268 (97.45)	257 (95.54)
Absolute Change at Week 24	262 (95.27)	255 (94.80)
Week 52	266 (96.73)	251 (93.31)
Absolute Change at Week 52	260 (94.55)	248 (92.19)
Through Week 52	273 (99.27)	263 (97.77)
Absolute Change through Week 52	267 (97.09)	260 (96.65)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.1.2
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 275 n (%)	VNZ/TEZ/D-IVA N = 269 n (%)
Baseline	266 (96.73)	266 (98.88)
Week 8	270 (98.18)	266 (98.88)
Absolute Change at Week 8	266 (96.73)	263 (97.77)
Week 16	264 (96.00)	261 (97.03)
Absolute Change at Week 16	260 (94.55)	258 (95.91)
Week 24	264 (96.00)	257 (95.54)
Absolute Change at Week 24	260 (94.55)	255 (94.80)
Week 52	266 (96.73)	250 (92.94)
Absolute Change at Week 52	257 (93.45)	247 (91.82)
Through Week 52	273 (99.27)	263 (97.77)
Absolute Change through Week 52	264 (96.00)	260 (96.65)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16, 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	94.81 (6.48)	90.65 (9.54)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	92.28 (2.77)	91.40 (2.54)
95% CI of LS mean	(86.50, 98.06)	(86.08, 96.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.88 (-8.79, 7.04)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	-0.89 (3.41)	-0.33 (2.94)
95% CI of LS mean	(-8.09, 6.31)	(-6.56, 5.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.56 (-8.99, 10.11)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	89.46 (4.78)	89.40 (4.37)
95% CI of LS mean	(79.50, 99.42)	(80.29, 98.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-13.59, 13.47)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	-3.41 (4.44)	-3.00 (3.63)
95% CI of LS mean	(-12.77, 5.94)	(-10.69, 4.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-11.77, 12.59)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	92.78 (5.42)	85.02 (5.14)
95% CI of LS mean	(81.59, 103.97)	(74.43, 95.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.75 (-23.20, 7.69)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	-0.86 (5.32)	-3.14 (5.10)
95% CI of LS mean	(-11.99, 10.27)	(-13.82, 7.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.28 (-17.74, 13.17)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Week 52		
n	11	13
Mean (SD)	96.26 (5.49)	94.87 (6.60)
Absolute Change at Week 52		
n	9	10
Mean (SD)	0.49 (6.90)	2.33 (7.56)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	96.26 (2.07)	95.20 (1.77)
95% CI of LS mean	(91.95, 100.56)	(91.50, 98.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.06 (-6.84, 4.72)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	1.83 (2.44)	1.47 (2.15)
95% CI of LS mean	(-3.31, 6.97)	(-3.06, 6.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-7.30, 6.58)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	-0.81 (2.44)	-1.56 (2.18)
95% CI of LS mean	(-5.95, 4.32)	(-6.17, 3.05)
P-value within Treatment	0.7427	0.4841
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.74 (-7.73, 6.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8249
Hedges' G (SE)		-0.09 (0.41)
Hedges' 95% CI		(-0.95, 0.77)
Hedges' P-value		0.8219

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.2.1
Study VX21-121-103: Compliance Rate for CFQ-R by Visit (All Domains)
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

	ELX/TEZ/IVA N = 14 n (%)	VNZ/TEZ/D-IVA N = 15 n (%)
Baseline	12 (85.71)	12 (80.00)
Week 8	12 (85.71)	12 (80.00)
Absolute Change at Week 8	10 (71.43)	11 (73.33)
Week 16	11 (78.57)	11 (73.33)
Absolute Change at Week 16	9 (64.29)	10 (66.67)
Week 24	14 (100.00)	13 (86.67)
Absolute Change at Week 24	12 (85.71)	11 (73.33)
Week 52	11 (78.57)	13 (86.67)
Absolute Change at Week 52	9 (64.29)	10 (66.67)
Through Week 52	14 (100.00)	15 (100.00)
Absolute Change through Week 52	12 (85.71)	12 (80.00)

- n (%): For "Through Week 52", n is the number of patients for whom the average between Week 16 , 24 and 52 can be calculated, i.e. for whom at least one of Week 16, 24 or 52 is non-missing. For "Change at Week X" or "Change through Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 52 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	75.81 (23.65)	78.61 (21.40)
Week 8 (MMRM)		
n	277	273
LS mean (SE)	78.47 (1.33)	79.34 (1.34)
95% CI of LS mean	(75.85, 81.08)	(76.71, 81.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.87 (-2.84, 4.58)
Absolute Change at Week 8 (MMRM)		
n	270	270
LS mean (SE)	2.45 (0.89)	0.55 (0.88)
95% CI of LS mean	(0.71, 4.18)	(-1.19, 2.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.90 (-4.36, 0.56)
Week 16 (MMRM)		
n	273	267
LS mean (SE)	78.36 (1.25)	79.61 (1.26)
95% CI of LS mean	(75.90, 80.81)	(77.13, 82.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.25 (-2.24, 4.74)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	266	264
LS mean (SE)	2.13 (0.86)	0.68 (0.86)
95% CI of LS mean	(0.45, 3.82)	(-1.01, 2.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.45 (-3.84, 0.94)
Week 24 (MMRM)		
n	274	265
LS mean (SE)	79.19 (1.31)	79.76 (1.32)
95% CI of LS mean	(76.63, 81.76)	(77.18, 82.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.57 (-3.07, 4.21)
Absolute Change at Week 24 (MMRM)		
n	267	262
LS mean (SE)	3.13 (0.93)	0.96 (0.94)
95% CI of LS mean	(1.30, 4.96)	(-0.88, 2.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.17 (-4.76, 0.42)
Week 52		
n	277	265
Mean (SD)	78.62 (21.08)	79.58 (21.84)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	261
Mean (SD)	2.51 (17.07)	1.32 (16.47)
Week 52 (MMRM)		
n	269	259
LS mean (SE)	78.42 (1.29)	80.13 (1.30)
95% CI of LS mean	(75.89, 80.94)	(77.58, 82.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-1.88, 5.30)
Absolute Change at Week 52 (MMRM)		
n	262	255
LS mean (SE)	2.22 (1.03)	1.37 (1.04)
95% CI of LS mean	(0.19, 4.26)	(-0.68, 3.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.85 (-3.74, 2.04)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	2.50 (0.79)	1.00 (0.80)
95% CI of LS mean	(0.94, 4.05)	(-0.56, 2.57)
P-value within Treatment	0.0017	0.2073
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.49 (-3.70, 0.72)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1848
Hedges' G (SE)		-0.11 (0.09)
Hedges' 95% CI		(-0.28, 0.05)
Hedges' P-value		0.1849

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	81.09 (17.14)	82.06 (18.39)
Week 8 (MMRM)		
n	277	273
LS mean (SE)	81.18 (1.11)	81.30 (1.12)
95% CI of LS mean	(78.99, 83.37)	(79.10, 83.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-2.99, 3.22)
Absolute Change at Week 8 (MMRM)		
n	270	270
LS mean (SE)	0.14 (0.89)	-0.70 (0.89)
95% CI of LS mean	(-1.60, 1.89)	(-2.44, 1.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.84 (-3.31, 1.62)
Week 16 (MMRM)		
n	272	268
LS mean (SE)	80.83 (1.11)	81.29 (1.12)
95% CI of LS mean	(78.64, 83.01)	(79.09, 83.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.46 (-2.64, 3.57)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	265	265
LS mean (SE)	-0.18 (0.92)	-0.82 (0.92)
95% CI of LS mean	(-1.99, 1.63)	(-2.63, 0.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-3.20, 1.92)
Week 24 (MMRM)		
n	273	265
LS mean (SE)	80.96 (1.16)	80.15 (1.17)
95% CI of LS mean	(78.67, 83.24)	(77.84, 82.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-4.05, 2.44)
Absolute Change at Week 24 (MMRM)		
n	266	262
LS mean (SE)	0.06 (0.92)	-1.97 (0.92)
95% CI of LS mean	(-1.74, 1.85)	(-3.78, -0.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.03 (-4.58, 0.52)
Week 52		
n	277	264
Mean (SD)	79.58 (20.30)	79.80 (19.08)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	260
Mean (SD)	-1.48 (15.73)	-2.44 (16.14)
Week 52 (MMRM)		
n	269	258
LS mean (SE)	79.10 (1.19)	80.03 (1.20)
95% CI of LS mean	(76.77, 81.44)	(77.66, 82.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-2.41, 4.25)
Absolute Change at Week 52 (MMRM)		
n	262	254
LS mean (SE)	-1.90 (0.99)	-2.09 (1.00)
95% CI of LS mean	(-3.83, 0.04)	(-4.05, -0.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-2.95, 2.55)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	-0.67 (0.79)	-1.63 (0.79)
95% CI of LS mean	(-2.23, 0.88)	(-3.19, -0.07)
P-value within Treatment	0.3943	0.0404
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.96 (-3.15, 1.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3939
Hedges' G (SE)		-0.07 (0.09)
Hedges' 95% CI		(-0.24, 0.10)
Hedges' P-value		0.3938

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	92.77 (14.46)	94.23 (11.95)
Week 8 (MMRM)		
n	277	274
LS mean (SE)	92.56 (0.82)	94.04 (0.83)
95% CI of LS mean	(90.94, 94.18)	(92.41, 95.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.48 (-0.82, 3.78)
Absolute Change at Week 8 (MMRM)		
n	270	271
LS mean (SE)	0.16 (0.66)	-0.15 (0.66)
95% CI of LS mean	(-1.14, 1.46)	(-1.45, 1.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-2.15, 1.53)
Week 16 (MMRM)		
n	273	268
LS mean (SE)	92.65 (0.87)	93.15 (0.88)
95% CI of LS mean	(90.93, 94.36)	(91.42, 94.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-1.94, 2.93)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	266	265
LS mean (SE)	0.26 (0.72)	-1.06 (0.73)
95% CI of LS mean	(-1.16, 1.68)	(-2.48, 0.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.32 (-3.33, 0.70)
Week 24 (MMRM)		
n	274	265
LS mean (SE)	92.50 (0.93)	92.55 (0.94)
95% CI of LS mean	(90.68, 94.32)	(90.71, 94.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-2.54, 2.64)
Absolute Change at Week 24 (MMRM)		
n	267	262
LS mean (SE)	0.03 (0.75)	-1.67 (0.75)
95% CI of LS mean	(-1.44, 1.50)	(-3.15, -0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.70 (-3.78, 0.39)
Week 52		
n	277	265
Mean (SD)	92.94 (14.93)	93.38 (13.50)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	261
Mean (SD)	0.47 (13.29)	-1.04 (11.45)
Week 52 (MMRM)		
n	269	259
LS mean (SE)	92.89 (0.86)	93.41 (0.87)
95% CI of LS mean	(91.20, 94.57)	(91.71, 95.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-1.87, 2.93)
Absolute Change at Week 52 (MMRM)		
n	262	255
LS mean (SE)	0.36 (0.76)	-0.80 (0.77)
95% CI of LS mean	(-1.14, 1.86)	(-2.31, 0.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.16 (-3.30, 0.98)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	0.22 (0.59)	-1.17 (0.59)
95% CI of LS mean	(-0.93, 1.37)	(-2.33, -0.02)
P-value within Treatment	0.7116	0.0462
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.39 (-3.02, 0.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0943
Hedges' G (SE)		-0.14 (0.09)
Hedges' 95% CI		(-0.31, 0.02)
Hedges' P-value		0.0946

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	81.81 (16.33)	81.75 (17.76)
Week 8 (MMRM)		
n	276	274
LS mean (SE)	82.27 (1.02)	82.90 (1.02)
95% CI of LS mean	(80.27, 84.27)	(80.89, 84.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-2.20, 3.46)
Absolute Change at Week 8 (MMRM)		
n	270	271
LS mean (SE)	0.64 (0.68)	1.09 (0.68)
95% CI of LS mean	(-0.70, 1.98)	(-0.25, 2.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-1.45, 2.34)
Week 16 (MMRM)		
n	273	268
LS mean (SE)	82.45 (1.03)	81.22 (1.03)
95% CI of LS mean	(80.43, 84.47)	(79.19, 83.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.23 (-4.09, 1.63)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	266	265
LS mean (SE)	1.01 (0.72)	-0.55 (0.72)
95% CI of LS mean	(-0.40, 2.42)	(-1.96, 0.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.56 (-3.55, 0.44)
Week 24 (MMRM)		
n	273	265
LS mean (SE)	81.68 (1.05)	81.19 (1.06)
95% CI of LS mean	(79.62, 83.73)	(79.12, 83.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-3.40, 2.44)
Absolute Change at Week 24 (MMRM)		
n	266	262
LS mean (SE)	0.07 (0.77)	-0.62 (0.77)
95% CI of LS mean	(-1.44, 1.58)	(-2.14, 0.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.69 (-2.83, 1.45)
Week 52		
n	277	265
Mean (SD)	81.69 (16.98)	81.90 (18.26)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	261
Mean (SD)	-0.36 (14.00)	0.34 (14.62)
Week 52 (MMRM)		
n	269	259
LS mean (SE)	81.38 (1.07)	81.81 (1.08)
95% CI of LS mean	(79.29, 83.47)	(79.69, 83.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-2.55, 3.41)
Absolute Change at Week 52 (MMRM)		
n	262	255
LS mean (SE)	-0.34 (0.88)	0.09 (0.89)
95% CI of LS mean	(-2.07, 1.39)	(-1.66, 1.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-2.03, 2.88)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	0.25 (0.66)	-0.36 (0.66)
95% CI of LS mean	(-1.06, 1.55)	(-1.67, 0.95)
P-value within Treatment	0.7106	0.5878
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.61 (-2.45, 1.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5186
Hedges' G (SE)		-0.06 (0.09)
Hedges' 95% CI		(-0.22, 0.11)
Hedges' P-value		0.5185

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	80.66 (20.30)	82.83 (18.60)
Week 8 (MMRM)		
n	276	274
LS mean (SE)	80.20 (1.20)	82.18 (1.20)
95% CI of LS mean	(77.85, 82.55)	(79.83, 84.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.98 (-1.35, 5.31)
Absolute Change at Week 8 (MMRM)		
n	270	271
LS mean (SE)	-0.60 (0.95)	-0.85 (0.95)
95% CI of LS mean	(-2.47, 1.27)	(-2.72, 1.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-2.90, 2.39)
Week 16 (MMRM)		
n	273	268
LS mean (SE)	81.34 (1.18)	82.60 (1.19)
95% CI of LS mean	(79.02, 83.67)	(80.26, 84.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.26 (-2.04, 4.56)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	266	265
LS mean (SE)	0.80 (0.92)	-0.33 (0.92)
95% CI of LS mean	(-1.00, 2.60)	(-2.13, 1.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.13 (-3.67, 1.42)
Week 24 (MMRM)		
n	273	265
LS mean (SE)	80.42 (1.21)	82.12 (1.22)
95% CI of LS mean	(78.05, 82.80)	(79.72, 84.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-1.69, 5.07)
Absolute Change at Week 24 (MMRM)		
n	266	262
LS mean (SE)	-0.35 (0.91)	-0.68 (0.91)
95% CI of LS mean	(-2.14, 1.44)	(-2.48, 1.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-2.87, 2.20)
Week 52		
n	277	265
Mean (SD)	81.43 (20.38)	84.37 (18.25)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	261
Mean (SD)	1.03 (16.44)	1.42 (12.43)
Week 52 (MMRM)		
n	269	259
LS mean (SE)	81.63 (1.12)	84.00 (1.13)
95% CI of LS mean	(79.43, 83.82)	(81.78, 86.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.37 (-0.75, 5.50)
Absolute Change at Week 52 (MMRM)		
n	262	255
LS mean (SE)	0.98 (0.90)	1.11 (0.91)
95% CI of LS mean	(-0.79, 2.75)	(-0.68, 2.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-2.38, 2.64)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	0.48 (0.73)	0.03 (0.73)
95% CI of LS mean	(-0.95, 1.90)	(-1.40, 1.46)
P-value within Treatment	0.5125	0.9659
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-2.47, 1.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6659
Hedges' G (SE)		-0.04 (0.09)
Hedges' 95% CI		(-0.21, 0.13)
Hedges' P-value		0.6658

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	72.51 (17.81)	75.03 (17.85)
Week 8 (MMRM)		
n	277	273
LS mean (SE)	73.78 (1.05)	75.71 (1.06)
95% CI of LS mean	(71.72, 75.84)	(73.64, 77.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.93 (-1.00, 4.85)
Absolute Change at Week 8 (MMRM)		
n	270	270
LS mean (SE)	0.87 (0.83)	0.48 (0.83)
95% CI of LS mean	(-0.76, 2.49)	(-1.15, 2.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-2.69, 1.91)
Week 16 (MMRM)		
n	273	267
LS mean (SE)	74.64 (1.05)	76.13 (1.06)
95% CI of LS mean	(72.58, 76.71)	(74.05, 78.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.49 (-1.45, 4.43)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	266	264
LS mean (SE)	1.97 (0.85)	0.98 (0.85)
95% CI of LS mean	(0.29, 3.64)	(-0.70, 2.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.99 (-3.36, 1.38)
Week 24 (MMRM)		
n	274	265
LS mean (SE)	73.47 (1.05)	77.23 (1.06)
95% CI of LS mean	(71.42, 75.53)	(75.15, 79.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.76 (0.83, 6.68)
Absolute Change at Week 24 (MMRM)		
n	267	262
LS mean (SE)	0.72 (0.86)	2.11 (0.86)
95% CI of LS mean	(-0.96, 2.41)	(0.41, 3.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-1.00, 3.78)
Week 52		
n	277	265
Mean (SD)	76.49 (18.05)	79.58 (17.54)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	261
Mean (SD)	4.08 (14.62)	4.29 (13.87)
Week 52 (MMRM)		
n	269	259
LS mean (SE)	76.41 (1.06)	79.35 (1.07)
95% CI of LS mean	(74.32, 78.49)	(77.24, 81.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.94 (-0.02, 5.91)
Absolute Change at Week 52 (MMRM)		
n	262	255
LS mean (SE)	3.64 (0.88)	4.19 (0.88)
95% CI of LS mean	(1.92, 5.36)	(2.45, 5.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-1.89, 2.99)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	2.11 (0.72)	2.42 (0.72)
95% CI of LS mean	(0.70, 3.52)	(1.01, 3.84)
P-value within Treatment	0.0035	0.0008
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-1.69, 2.32)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7569
Hedges' G (SE)		0.03 (0.09)
Hedges' 95% CI		(-0.14, 0.20)
Hedges' P-value		0.7567

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline		
n	282	280
Mean (SD)	70.33 (19.73)	71.67 (19.06)
Week 8 (MMRM)		
n	277	273
LS mean (SE)	70.72 (1.20)	73.47 (1.20)
95% CI of LS mean	(68.38, 73.07)	(71.11, 75.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.75 (-0.58, 6.08)
Absolute Change at Week 8 (MMRM)		
n	270	270
LS mean (SE)	0.82 (0.84)	1.77 (0.84)
95% CI of LS mean	(-0.83, 2.47)	(0.12, 3.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.95 (-1.38, 3.29)
Week 16 (MMRM)		
n	273	268
LS mean (SE)	71.79 (1.18)	73.38 (1.19)
95% CI of LS mean	(69.47, 74.11)	(71.04, 75.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.59 (-1.71, 4.88)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 16 (MMRM)		
n	266	265
LS mean (SE)	1.96 (0.88)	1.67 (0.88)
95% CI of LS mean	(0.24, 3.68)	(-0.05, 3.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-2.72, 2.15)
Week 24 (MMRM)		
n	274	265
LS mean (SE)	70.67 (1.21)	73.68 (1.22)
95% CI of LS mean	(68.29, 73.05)	(71.29, 76.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.01 (-0.36, 6.39)
Absolute Change at Week 24 (MMRM)		
n	267	262
LS mean (SE)	0.92 (0.89)	1.98 (0.90)
95% CI of LS mean	(-0.83, 2.67)	(0.22, 3.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.06 (-1.42, 3.55)
Week 52		
n	277	265
Mean (SD)	73.49 (19.93)	75.93 (19.33)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change at Week 52		
n	270	261
Mean (SD)	3.37 (16.58)	4.38 (15.26)
Week 52 (MMRM)		
n	269	259
LS mean (SE)	73.32 (1.18)	75.77 (1.19)
95% CI of LS mean	(71.00, 75.63)	(73.43, 78.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.45 (-0.84, 5.74)
Absolute Change at Week 52 (MMRM)		
n	262	255
LS mean (SE)	3.50 (0.99)	4.08 (0.99)
95% CI of LS mean	(1.56, 5.44)	(2.13, 6.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-2.17, 3.34)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Absolute Change through Week 52 (MMRM)		
n	270	268
LS mean (SE)	2.13 (0.78)	2.58 (0.78)
95% CI of LS mean	(0.60, 3.65)	(1.05, 4.11)
P-value within Treatment	0.0064	0.0010
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-1.71, 2.61)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6799
Hedges' G (SE)		0.04 (0.09)
Hedges' 95% CI		(-0.13, 0.20)
Hedges' P-value		0.6797

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Baseline		
n	269	266
Mean (SD)	71.46 (19.62)	72.79 (20.06)
Week 8 (MMRM)		
n	267	260
LS mean (SE)	71.38 (1.19)	71.87 (1.20)
95% CI of LS mean	(69.04, 73.72)	(69.50, 74.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-2.84, 3.83)
Absolute Change at Week 8 (MMRM)		
n	261	257
LS mean (SE)	0.00 (0.90)	-1.06 (0.91)
95% CI of LS mean	(-1.77, 1.77)	(-2.84, 0.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.06 (-3.58, 1.45)
Week 16 (MMRM)		
n	263	254
LS mean (SE)	71.13 (1.19)	71.94 (1.21)
95% CI of LS mean	(68.79, 73.47)	(69.57, 74.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-2.52, 4.14)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Absolute Change at Week 16 (MMRM)		
n	257	251
LS mean (SE)	0.03 (0.94)	-1.04 (0.95)
95% CI of LS mean	(-1.83, 1.88)	(-2.91, 0.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.07 (-3.70, 1.57)
Week 24 (MMRM)		
n	262	251
LS mean (SE)	69.67 (1.27)	72.07 (1.29)
95% CI of LS mean	(67.18, 72.17)	(69.53, 74.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.39 (-1.16, 5.95)
Absolute Change at Week 24 (MMRM)		
n	256	249
LS mean (SE)	-1.46 (1.01)	-0.90 (1.02)
95% CI of LS mean	(-3.45, 0.53)	(-2.91, 1.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.57 (-2.27, 3.40)
Week 52		
n	266	251
Mean (SD)	73.98 (19.45)	73.40 (19.65)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Absolute Change at Week 52		
n	260	248
Mean (SD)	2.39 (15.83)	0.47 (14.83)
Week 52 (MMRM)		
n	259	245
LS mean (SE)	73.64 (1.19)	73.10 (1.21)
95% CI of LS mean	(71.30, 75.97)	(70.72, 75.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-3.87, 2.81)
Absolute Change at Week 52 (MMRM)		
n	253	242
LS mean (SE)	2.31 (0.97)	0.20 (0.99)
95% CI of LS mean	(0.40, 4.21)	(-1.74, 2.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.11 (-4.83, 0.61)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Absolute Change through Week 52 (MMRM)		
n	259	254
LS mean (SE)	0.29 (0.79)	-0.58 (0.80)
95% CI of LS mean	(-1.26, 1.84)	(-2.14, 0.99)
P-value within Treatment	0.7128	0.4688
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.87 (-3.07, 1.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4393
Hedges' G (SE)		-0.07 (0.09)
Hedges' 95% CI		(-0.24, 0.11)
Hedges' P-value		0.4392

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Baseline		
n	269	266
Mean (SD)	86.65 (15.63)	86.75 (16.40)
Week 8 (MMRM)		
n	267	259
LS mean (SE)	86.39 (0.98)	87.43 (0.99)
95% CI of LS mean	(84.47, 88.31)	(85.49, 89.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-1.70, 3.78)
Absolute Change at Week 8 (MMRM)		
n	261	256
LS mean (SE)	-0.21 (0.83)	0.60 (0.83)
95% CI of LS mean	(-1.83, 1.42)	(-1.03, 2.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-1.50, 3.11)
Week 16 (MMRM)		
n	261	255
LS mean (SE)	86.56 (1.01)	86.74 (1.02)
95% CI of LS mean	(84.58, 88.54)	(84.74, 88.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-2.64, 3.00)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Absolute Change at Week 16 (MMRM)		
n	255	252
LS mean (SE)	0.02 (0.86)	0.04 (0.86)
95% CI of LS mean	(-1.67, 1.71)	(-1.66, 1.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-2.38, 2.41)
Week 24 (MMRM)		
n	262	250
LS mean (SE)	85.95 (1.06)	86.35 (1.08)
95% CI of LS mean	(83.87, 88.02)	(84.24, 88.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-2.56, 3.37)
Absolute Change at Week 24 (MMRM)		
n	256	248
LS mean (SE)	-0.57 (0.96)	-0.36 (0.97)
95% CI of LS mean	(-2.46, 1.31)	(-2.26, 1.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-2.46, 2.90)
Week 52		
n	266	250
Mean (SD)	87.14 (17.10)	88.97 (14.04)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Absolute Change at Week 52		
n	260	247
Mean (SD)	0.63 (15.08)	1.65 (13.31)
Week 52 (MMRM)		
n	259	244
LS mean (SE)	87.08 (0.97)	88.76 (1.00)
95% CI of LS mean	(85.17, 89.00)	(86.81, 90.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.68 (-1.06, 4.42)
Absolute Change at Week 52 (MMRM)		
n	253	241
LS mean (SE)	0.43 (0.89)	1.95 (0.91)
95% CI of LS mean	(-1.33, 2.18)	(0.16, 3.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-0.98, 4.04)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Absolute Change through Week 52 (MMRM)		
n	259	254
LS mean (SE)	-0.04 (0.73)	0.54 (0.74)
95% CI of LS mean	(-1.48, 1.39)	(-0.90, 1.99)
P-value within Treatment	0.9530	0.4610
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-1.45, 2.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5719
Hedges' G (SE)		0.05 (0.09)
Hedges' 95% CI		(-0.12, 0.22)
Hedges' P-value		0.5718

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Baseline		
n	269	266
Mean (SD)	66.76 (19.04)	66.82 (18.90)
Week 8 (MMRM)		
n	266	261
LS mean (SE)	63.99 (1.25)	66.46 (1.26)
95% CI of LS mean	(61.53, 66.45)	(63.98, 68.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.47 (-1.02, 5.96)
Absolute Change at Week 8 (MMRM)		
n	261	258
LS mean (SE)	-2.38 (1.00)	-0.46 (1.01)
95% CI of LS mean	(-4.34, -0.41)	(-2.44, 1.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.91 (-0.87, 4.70)
Week 16 (MMRM)		
n	263	255
LS mean (SE)	63.83 (1.24)	65.62 (1.26)
95% CI of LS mean	(61.40, 66.27)	(63.15, 68.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.78 (-1.68, 5.25)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Absolute Change at Week 16 (MMRM)		
n	257	252
LS mean (SE)	-2.35 (0.97)	-1.26 (0.97)
95% CI of LS mean	(-4.24, -0.45)	(-3.17, 0.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-1.61, 3.78)
Week 24 (MMRM)		
n	261	251
LS mean (SE)	62.81 (1.28)	64.72 (1.30)
95% CI of LS mean	(60.30, 65.32)	(62.17, 67.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.91 (-1.67, 5.49)
Absolute Change at Week 24 (MMRM)		
n	255	249
LS mean (SE)	-3.74 (1.06)	-2.16 (1.07)
95% CI of LS mean	(-5.81, -1.66)	(-4.26, -0.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.57 (-1.38, 4.53)
Week 52		
n	266	251
Mean (SD)	64.94 (19.94)	67.66 (18.44)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Absolute Change at Week 52		
n	260	248
Mean (SD)	-1.47 (16.26)	0.54 (15.12)
Week 52 (MMRM)		
n	259	245
LS mean (SE)	64.54 (1.17)	66.92 (1.20)
95% CI of LS mean	(62.23, 66.85)	(64.57, 69.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-0.91, 5.68)
Absolute Change at Week 52 (MMRM)		
n	253	242
LS mean (SE)	-1.79 (0.99)	0.07 (1.00)
95% CI of LS mean	(-3.73, 0.14)	(-1.90, 2.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.87 (-0.90, 4.63)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Absolute Change through Week 52 (MMRM)		
n	259	254
LS mean (SE)	-2.63 (0.81)	-1.12 (0.82)
95% CI of LS mean	(-4.21, -1.04)	(-2.72, 0.49)
P-value within Treatment	0.0012	0.1717
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-0.75, 3.77)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1897
Hedges' G (SE)		0.12 (0.09)
Hedges' 95% CI		(-0.06, 0.29)
Hedges' P-value		0.1898

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Baseline		
n	266	266
Mean (SD)	88.47 (24.07)	84.34 (27.03)
Week 8 (MMRM)		
n	262	260
LS mean (SE)	87.25 (1.63)	84.91 (1.64)
95% CI of LS mean	(84.04, 90.46)	(81.68, 88.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.34 (-6.89, 2.21)
Absolute Change at Week 8 (MMRM)		
n	258	257
LS mean (SE)	-1.63 (1.29)	0.40 (1.29)
95% CI of LS mean	(-4.17, 0.90)	(-2.13, 2.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.03 (-1.55, 5.62)
Week 16 (MMRM)		
n	257	255
LS mean (SE)	86.33 (1.69)	85.77 (1.70)
95% CI of LS mean	(83.01, 89.65)	(82.43, 89.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.56 (-5.27, 4.15)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Absolute Change at Week 16 (MMRM)		
n	253	252
LS mean (SE)	-2.56 (1.41)	1.27 (1.42)
95% CI of LS mean	(-5.34, 0.21)	(-1.51, 4.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.84 (-0.09, 7.77)
Week 24 (MMRM)		
n	257	251
LS mean (SE)	86.14 (1.71)	85.26 (1.73)
95% CI of LS mean	(82.79, 89.50)	(81.87, 88.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.88 (-5.65, 3.90)
Absolute Change at Week 24 (MMRM)		
n	253	249
LS mean (SE)	-2.61 (1.31)	0.91 (1.32)
95% CI of LS mean	(-5.19, -0.03)	(-1.69, 3.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.52 (-0.15, 7.18)
Week 52		
n	266	250
Mean (SD)	87.09 (26.31)	84.27 (28.05)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Absolute Change at Week 52		
n	257	247
Mean (SD)	-1.82 (22.56)	-0.13 (22.19)
Week 52 (MMRM)		
n	259	244
LS mean (SE)	86.64 (1.67)	84.25 (1.70)
95% CI of LS mean	(83.35, 89.92)	(80.90, 87.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.39 (-7.08, 2.30)
Absolute Change at Week 52 (MMRM)		
n	250	241
LS mean (SE)	-2.24 (1.42)	-0.11 (1.44)
95% CI of LS mean	(-5.03, 0.56)	(-2.94, 2.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.13 (-1.85, 6.11)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.3.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

	ELX/TEZ/IVA N = 275	VNZ/TEZ/D-IVA N = 269
Absolute Change through Week 52 (MMRM)		
n	256	254
LS mean (SE)	-2.47 (1.14)	0.69 (1.15)
95% CI of LS mean	(-4.72, -0.22)	(-1.56, 2.95)
P-value within Treatment	0.0313	0.5472
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.16 (-0.02, 6.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0517
Hedges' G (SE)		0.17 (0.09)
Hedges' 95% CI		(0.00, 0.35)
Hedges' P-value		0.0520

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	79.63 (23.61)	86.11 (17.81)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	74.53 (6.62)	91.67 (6.00)
95% CI of LS mean	(60.79, 88.27)	(79.20, 104.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	17.14 (-1.53, 35.81)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	-4.27 (6.01)	2.68 (5.06)
95% CI of LS mean	(-16.94, 8.40)	(-8.00, 13.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.95 (-9.82, 23.72)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	79.91 (3.99)	95.71 (3.56)
95% CI of LS mean	(71.59, 88.22)	(88.29, 103.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.81 (4.43, 27.18)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	2.78 (6.47)	11.92 (5.87)
95% CI of LS mean	(-10.81, 16.37)	(-0.41, 24.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.14 (-9.29, 27.57)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	77.95 (4.92)	91.32 (4.59)
95% CI of LS mean	(67.76, 88.13)	(81.84, 100.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	13.37 (-0.70, 27.45)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	0.07 (5.53)	8.47 (5.16)
95% CI of LS mean	(-11.53, 11.66)	(-2.32, 19.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.40 (-7.58, 24.39)
Week 52		
n	11	13
Mean (SD)	91.92 (15.78)	91.45 (11.25)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	6.17 (20.12)	4.44 (13.04)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	84.66 (4.89)	94.15 (4.34)
95% CI of LS mean	(74.46, 94.85)	(85.09, 103.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.49 (-4.31, 23.30)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	5.74 (6.57)	8.97 (5.88)
95% CI of LS mean	(-8.20, 19.68)	(-3.53, 21.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.23 (-15.67, 22.13)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	2.86 (5.60)	9.79 (5.11)
95% CI of LS mean	(-8.92, 14.65)	(-0.97, 20.54)
P-value within Treatment	0.6156	0.0719
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.92 (-9.19, 23.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3780
Hedges' G (SE)		0.38 (0.42)
Hedges' 95% CI		(-0.49, 1.24)
Hedges' P-value		0.3762

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	82.41 (17.38)	87.96 (10.00)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	79.61 (4.98)	86.27 (4.47)
95% CI of LS mean	(69.29, 89.93)	(77.02, 95.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.66 (-7.41, 20.73)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	1.11 (3.87)	-2.59 (3.35)
95% CI of LS mean	(-6.99, 9.21)	(-9.64, 4.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.70 (-14.58, 7.17)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	75.56 (4.96)	85.65 (4.44)
95% CI of LS mean	(65.26, 85.86)	(76.40, 94.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.09 (-3.98, 24.16)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	-4.91 (4.66)	-5.33 (3.82)
95% CI of LS mean	(-14.72, 4.90)	(-13.45, 2.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-13.31, 12.46)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	73.90 (5.51)	93.11 (5.10)
95% CI of LS mean	(62.51, 85.30)	(82.58, 103.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	19.21 (3.50, 34.91)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	-7.18 (4.58)	2.72 (4.34)
95% CI of LS mean	(-16.79, 2.43)	(-6.39, 11.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.90 (-3.44, 23.24)
Week 52		
n	11	13
Mean (SD)	82.83 (14.37)	84.62 (13.25)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	-4.94 (9.80)	-1.11 (8.20)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	72.58 (5.24)	85.33 (4.61)
95% CI of LS mean	(61.57, 83.59)	(75.60, 95.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.75 (-2.16, 27.65)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	-9.38 (4.40)	-2.82 (3.92)
95% CI of LS mean	(-19.18, 0.41)	(-11.64, 5.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.56 (-6.72, 19.84)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	-7.16 (3.34)	-1.81 (2.99)
95% CI of LS mean	(-14.20, -0.11)	(-8.15, 4.53)
P-value within Treatment	0.0468	0.5529
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.35 (-4.31, 15.00)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2585
Hedges' G (SE)		0.49 (0.42)
Hedges' 95% CI		(-0.38, 1.37)
Hedges' P-value		0.2531

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	94.44 (14.79)	91.67 (15.08)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	87.02 (4.90)	96.44 (4.55)
95% CI of LS mean	(76.92, 97.11)	(87.05, 105.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.42 (-4.43, 23.26)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	-6.50 (3.54)	5.57 (3.08)
95% CI of LS mean	(-13.96, 0.95)	(-0.95, 12.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.07 (2.12, 22.02)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	93.31 (4.13)	96.64 (3.87)
95% CI of LS mean	(84.76, 101.86)	(88.62, 104.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.33 (-8.46, 15.12)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	-2.50 (2.21)	4.24 (1.97)
95% CI of LS mean	(-7.12, 2.11)	(0.11, 8.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.74 (0.47, 13.02)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	91.77 (3.77)	96.46 (3.55)
95% CI of LS mean	(83.97, 99.57)	(89.12, 103.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.69 (-6.10, 15.48)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	-2.00 (2.94)	6.17 (2.72)
95% CI of LS mean	(-8.16, 4.15)	(0.49, 11.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.18 (-0.25, 16.61)
Week 52		
n	11	13
Mean (SD)	100.00 (0.00)	96.15 (9.99)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	0.00 (0.00)	-1.67 (14.59)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	99.48 (2.83)	95.36 (2.36)
95% CI of LS mean	(93.16, 105.81)	(90.03, 100.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.13 (-12.60, 4.35)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	-2.89 (5.13)	1.62 (4.64)
95% CI of LS mean	(-14.47, 8.68)	(-8.89, 12.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.51 (-11.14, 20.16)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	-2.47 (3.19)	4.01 (2.91)
95% CI of LS mean	(-9.35, 4.41)	(-2.26, 10.27)
P-value within Treatment	0.4533	0.1905
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.48 (-2.87, 15.82)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1590
Hedges' G (SE)		0.62 (0.42)
Hedges' 95% CI		(-0.26, 1.50)
Hedges' P-value		0.1590

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	82.22 (16.41)	79.44 (18.74)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	85.32 (3.63)	89.11 (3.27)
95% CI of LS mean	(77.75, 92.90)	(82.27, 95.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.78 (-6.56, 14.13)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	5.51 (4.90)	10.50 (4.35)
95% CI of LS mean	(-4.80, 15.81)	(1.32, 19.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.00 (-9.07, 19.06)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	82.87 (4.91)	84.69 (4.44)
95% CI of LS mean	(72.51, 93.23)	(75.32, 94.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.82 (-12.24, 15.88)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	4.41 (4.62)	5.76 (3.98)
95% CI of LS mean	(-5.27, 14.10)	(-2.65, 14.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-11.81, 14.51)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	81.63 (4.88)	86.71 (4.47)
95% CI of LS mean	(71.54, 91.72)	(77.49, 95.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.08 (-8.69, 18.85)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	1.75 (4.95)	8.50 (4.56)
95% CI of LS mean	(-8.64, 12.14)	(-1.06, 18.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.75 (-7.62, 21.12)
Week 52		
n	11	13
Mean (SD)	84.85 (12.33)	81.54 (12.22)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	0.00 (15.99)	-2.00 (12.98)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	82.81 (3.65)	81.82 (3.18)
95% CI of LS mean	(75.30, 90.32)	(75.26, 88.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.99 (-11.12, 9.14)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	0.83 (5.71)	2.64 (5.16)
95% CI of LS mean	(-11.93, 13.59)	(-8.96, 14.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.81 (-15.58, 19.19)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	2.33 (4.57)	5.63 (4.14)
95% CI of LS mean	(-7.42, 12.08)	(-3.21, 14.48)
P-value within Treatment	0.6175	0.1943
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.30 (-10.14, 16.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6082
Hedges' G (SE)		0.22 (0.41)
Hedges' 95% CI		(-0.64, 1.08)
Hedges' P-value		0.5993

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	79.63 (14.08)	75.93 (24.08)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	74.55 (5.74)	80.78 (5.19)
95% CI of LS mean	(62.57, 86.53)	(69.93, 91.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.22 (-10.07, 22.52)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	-5.19 (6.85)	7.73 (5.92)
95% CI of LS mean	(-19.47, 9.10)	(-4.69, 20.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.92 (-6.22, 32.06)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	75.12 (6.06)	74.79 (5.36)
95% CI of LS mean	(62.46, 87.78)	(63.54, 86.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-17.40, 16.74)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	-2.45 (6.33)	-2.59 (5.10)
95% CI of LS mean	(-15.80, 10.90)	(-13.45, 8.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-17.66, 17.39)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	79.60 (4.59)	82.77 (4.22)
95% CI of LS mean	(70.08, 89.12)	(74.03, 91.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.17 (-9.93, 16.27)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	1.02 (6.63)	7.77 (6.12)
95% CI of LS mean	(-12.87, 14.90)	(-5.03, 20.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.75 (-12.33, 25.83)
Week 52		
n	11	13
Mean (SD)	86.87 (10.91)	81.20 (17.20)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	2.47 (13.35)	-2.22 (20.82)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	84.94 (4.65)	81.41 (4.09)
95% CI of LS mean	(75.33, 94.56)	(72.93, 89.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.54 (-16.54, 9.47)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	6.16 (7.39)	5.05 (6.70)
95% CI of LS mean	(-9.61, 21.94)	(-9.28, 19.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.11 (-22.57, 20.35)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	1.58 (5.73)	3.41 (5.13)
95% CI of LS mean	(-10.44, 13.60)	(-7.38, 14.20)
P-value within Treatment	0.7863	0.5146
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.83 (-14.59, 18.25)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8173
Hedges' G (SE)		0.10 (0.41)
Hedges' 95% CI		(-0.76, 0.96)
Hedges' P-value		0.8137

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	86.11 (14.36)	85.42 (20.98)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	91.77 (3.30)	92.67 (2.99)
95% CI of LS mean	(84.94, 98.61)	(86.48, 98.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.90 (-8.51, 10.30)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	6.67 (4.19)	5.68 (3.79)
95% CI of LS mean	(-2.12, 15.47)	(-2.30, 13.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.00 (-13.08, 11.09)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	89.75 (3.57)	94.15 (3.27)
95% CI of LS mean	(82.34, 97.15)	(87.39, 100.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.41 (-5.79, 14.60)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	3.79 (4.66)	6.75 (4.21)
95% CI of LS mean	(-5.98, 13.56)	(-2.09, 15.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.96 (-10.40, 16.32)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	84.23 (4.07)	93.48 (3.76)
95% CI of LS mean	(75.81, 92.65)	(85.72, 101.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.25 (-2.35, 20.84)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	0.62 (5.94)	6.04 (5.47)
95% CI of LS mean	(-11.81, 13.05)	(-5.39, 17.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.42 (-11.61, 22.44)
Week 52		
n	11	13
Mean (SD)	93.94 (8.81)	93.27 (12.21)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	5.56 (12.50)	0.00 (7.08)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	93.53 (3.39)	92.52 (2.99)
95% CI of LS mean	(86.51, 100.55)	(86.30, 98.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.01 (-10.59, 8.56)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	10.14 (4.18)	3.84 (3.79)
95% CI of LS mean	(1.27, 19.02)	(-4.23, 11.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.31 (-18.51, 5.90)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	4.85 (4.58)	5.54 (4.17)
95% CI of LS mean	(-4.79, 14.50)	(-3.24, 14.32)
P-value within Treatment	0.3043	0.2010
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.69 (-12.54, 13.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9138
Hedges' G (SE)		0.05 (0.41)
Hedges' 95% CI		(-0.81, 0.91)
Hedges' P-value		0.9123

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	79.17 (23.44)	81.94 (15.01)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	75.62 (5.00)	84.21 (4.52)
95% CI of LS mean	(65.27, 85.97)	(74.83, 93.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.59 (-5.54, 22.72)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	-1.73 (5.67)	3.98 (4.86)
95% CI of LS mean	(-13.71, 10.25)	(-6.36, 14.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.71 (-10.30, 21.72)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	76.22 (5.79)	83.71 (5.26)
95% CI of LS mean	(64.06, 88.39)	(72.64, 94.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.49 (-9.09, 24.07)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	-5.30 (4.78)	1.63 (4.04)
95% CI of LS mean	(-15.36, 4.76)	(-6.94, 10.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.92 (-6.59, 20.43)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	77.15 (5.66)	85.72 (5.18)
95% CI of LS mean	(65.46, 88.83)	(75.06, 96.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.57 (-7.39, 24.54)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	-2.53 (5.09)	4.57 (4.75)
95% CI of LS mean	(-13.27, 8.21)	(-5.42, 14.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.10 (-7.78, 21.97)
Week 52		
n	11	13
Mean (SD)	77.78 (17.52)	79.49 (14.68)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	-8.64 (18.96)	-5.00 (11.25)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	74.29 (4.87)	80.58 (4.25)
95% CI of LS mean	(64.20, 84.39)	(71.74, 89.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.28 (-7.34, 19.90)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	-8.00 (6.48)	-2.52 (5.76)
95% CI of LS mean	(-22.21, 6.22)	(-15.26, 10.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.48 (-13.79, 24.75)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	-5.27 (4.52)	1.22 (4.04)
95% CI of LS mean	(-15.19, 4.64)	(-7.66, 10.11)
P-value within Treatment	0.2673	0.7676
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.50 (-7.10, 20.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3166
Hedges' G (SE)		0.44 (0.42)
Hedges' 95% CI		(-0.43, 1.31)
Hedges' P-value		0.3019

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	61.11 (30.89)	65.74 (19.80)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	69.55 (6.33)	71.37 (5.68)
95% CI of LS mean	(56.34, 82.76)	(59.49, 83.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.81 (-16.22, 19.85)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	13.30 (5.58)	4.69 (4.80)
95% CI of LS mean	(1.48, 25.11)	(-5.54, 14.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.61 (-24.40, 7.18)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	58.47 (6.73)	69.14 (6.07)
95% CI of LS mean	(44.40, 72.53)	(56.43, 81.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.68 (-8.54, 29.89)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	0.15 (6.55)	2.43 (5.77)
95% CI of LS mean	(-13.61, 13.90)	(-9.77, 14.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.29 (-16.19, 20.76)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	58.14 (7.31)	74.13 (6.75)
95% CI of LS mean	(43.01, 73.28)	(60.22, 88.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.99 (-4.80, 36.79)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	-2.30 (4.67)	8.95 (4.46)
95% CI of LS mean	(-12.23, 7.63)	(-0.51, 18.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.25 (-2.64, 25.15)
Week 52		
n	11	13
Mean (SD)	64.65 (22.67)	69.23 (15.15)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	-3.70 (23.57)	3.33 (15.76)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	62.27 (6.35)	69.20 (5.57)
95% CI of LS mean	(49.13, 75.41)	(57.66, 80.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.93 (-10.86, 24.73)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	-1.72 (6.78)	2.83 (6.09)
95% CI of LS mean	(-15.88, 12.43)	(-9.90, 15.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.55 (-14.59, 23.70)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	-1.29 (4.92)	4.74 (4.50)
95% CI of LS mean	(-11.68, 9.10)	(-4.77, 14.25)
P-value within Treatment	0.7958	0.3073
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.03 (-8.21, 20.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3840
Hedges' G (SE)		0.37 (0.42)
Hedges' 95% CI		(-0.49, 1.24)
Hedges' P-value		0.3807

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	72.92 (18.04)	70.00 (17.17)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	74.90 (5.08)	74.38 (4.56)
95% CI of LS mean	(64.34, 85.46)	(64.90, 83.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-14.93, 13.89)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	4.87 (5.87)	7.20 (5.26)
95% CI of LS mean	(-7.50, 17.23)	(-3.91, 18.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.33 (-14.55, 19.21)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	79.43 (5.43)	69.38 (4.90)
95% CI of LS mean	(68.19, 90.67)	(59.23, 79.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.05 (-25.41, 5.30)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	13.38 (6.05)	-0.36 (5.21)
95% CI of LS mean	(0.69, 26.07)	(-11.38, 10.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-13.74 (-30.82, 3.34)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	71.30 (5.83)	69.84 (5.40)
95% CI of LS mean	(59.22, 83.39)	(58.69, 80.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.47 (-18.08, 15.15)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	2.25 (6.03)	2.08 (5.59)
95% CI of LS mean	(-10.46, 14.95)	(-9.66, 13.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.16 (-17.71, 17.39)
Week 52		
n	11	13
Mean (SD)	81.21 (14.55)	74.87 (15.67)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	7.22 (17.00)	2.00 (11.78)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	80.47 (4.98)	74.73 (4.38)
95% CI of LS mean	(70.17, 90.77)	(65.63, 83.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.73 (-19.71, 8.24)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	8.40 (5.57)	4.05 (5.02)
95% CI of LS mean	(-3.39, 20.18)	(-6.59, 14.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.35 (-20.52, 11.82)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	8.01 (5.18)	1.92 (4.69)
95% CI of LS mean	(-2.90, 18.92)	(-7.97, 11.81)
P-value within Treatment	0.1401	0.6867
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.08 (-21.14, 8.97)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4059
Hedges' G (SE)		-0.36 (0.42)
Hedges' 95% CI		(-1.23, 0.51)
Hedges' P-value		0.3978

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Baseline		
n	12	12
Mean (SD)	86.11 (22.29)	80.56 (26.43)
Week 8 (MMRM)		
n	10	12
LS mean (SE)	75.67 (9.70)	75.82 (8.78)
95% CI of LS mean	(55.25, 96.09)	(57.37, 94.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-27.54, 27.85)
Absolute Change at Week 8 (MMRM)		
n	8	11
LS mean (SE)	-16.10 (10.43)	5.77 (9.29)
95% CI of LS mean	(-38.19, 5.98)	(-13.97, 25.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	21.88 (-7.98, 51.73)
Week 16 (MMRM)		
n	9	11
LS mean (SE)	79.56 (9.20)	80.38 (8.35)
95% CI of LS mean	(59.99, 99.14)	(62.64, 98.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.82 (-25.80, 27.44)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 16 (MMRM)		
n	7	10
LS mean (SE)	-14.49 (12.25)	9.08 (11.27)
95% CI of LS mean	(-40.72, 11.74)	(-15.01, 33.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	23.57 (-12.32, 59.46)
Week 24 (MMRM)		
n	12	13
LS mean (SE)	79.46 (6.99)	92.28 (6.57)
95% CI of LS mean	(64.60, 94.31)	(78.39, 106.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.82 (-7.76, 33.40)
Absolute Change at Week 24 (MMRM)		
n	10	11
LS mean (SE)	-11.11 (9.55)	12.34 (8.83)
95% CI of LS mean	(-31.28, 9.05)	(-6.26, 30.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	23.45 (-4.29, 51.19)
Week 52		
n	11	13
Mean (SD)	90.91 (21.56)	84.62 (32.25)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52		
n	9	10
Mean (SD)	-7.41 (27.78)	16.67 (23.57)
Week 52 (MMRM)		
n	10	13
LS mean (SE)	87.80 (8.39)	87.29 (7.36)
95% CI of LS mean	(70.50, 105.10)	(72.09, 102.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.51 (-23.80, 22.77)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	-8.62 (8.40)	12.64 (7.57)
95% CI of LS mean	(-26.22, 8.98)	(-3.24, 28.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	21.26 (-2.85, 45.37)

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.9.4
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

	ELX/TEZ/IVA N = 14	VNZ/TEZ/D-IVA N = 15
Absolute Change through Week 52 (MMRM)		
n	10	12
LS mean (SE)	-11.41 (8.95)	11.35 (8.19)
95% CI of LS mean	(-30.37, 7.55)	(-5.98, 28.68)
P-value within Treatment	0.2205	0.1843
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	22.76 (-3.29, 48.81)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0827
Hedges' G (SE)		0.77 (0.43)
Hedges' 95% CI		(-0.12, 1.67)
Hedges' P-value		0.0862

- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	35	38
Mean (SD)	81.27 (17.31)	79.24 (17.70)
Week 52		
n	35	39
Mean (SD)	87.46 (15.85)	82.34 (19.41)
Absolute Change at Week 52		
n	33	36
Mean (SD)	5.39 (21.22)	3.09 (19.76)
Absolute Change at Week 52 (MMRM)		
n	31	36
LS mean (SE)	5.08 (3.85)	3.19 (3.57)
95% CI of LS mean	(-2.63, 12.79)	(-3.96, 10.33)
P-value within Treatment	0.1924	0.3757
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.89 (-12.50, 8.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7223

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		-0.09 (0.24)
Hedges' 95% CI		(-0.57, 0.40)
Hedges' P-value		0.7198

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	35	38
Mean (SD)	100.00 (0.00)	95.23 (12.11)
Week 52		
n	35	39
Mean (SD)	94.29 (14.88)	96.47 (13.05)
Absolute Change at Week 52		
n	33	36
Mean (SD)	-6.06 (15.27)	0.35 (12.50)
Absolute Change at Week 52 (MMRM)		
n	31	36
LS mean (SE)	-6.07 (2.62)	0.02 (2.43)
95% CI of LS mean	(-11.31, -0.84)	(-4.83, 4.88)
P-value within Treatment	0.0238	0.9926
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.10 (-1.11, 13.31)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0959

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		0.41 (0.24)
Hedges' 95% CI		(-0.08, 0.90)
Hedges' P-value		0.0959

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	35	37
Mean (SD)	82.22 (15.41)	83.03 (16.19)
Week 52		
n	35	39
Mean (SD)	85.56 (14.52)	85.04 (13.01)
Absolute Change at Week 52		
n	33	35
Mean (SD)	2.53 (15.60)	-0.16 (16.36)
Absolute Change at Week 52 (MMRM)		
n	31	35
LS mean (SE)	2.10 (3.02)	0.04 (2.83)
95% CI of LS mean	(-3.93, 8.14)	(-5.63, 5.72)
P-value within Treatment	0.4886	0.9878
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.06 (-10.41, 6.30)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6240

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		-0.12 (0.24)
Hedges' 95% CI		(-0.61, 0.37)
Hedges' P-value		0.6211

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	35	38
Mean (SD)	86.33 (12.66)	86.02 (15.01)
Week 52		
n	35	39
Mean (SD)	89.80 (16.19)	88.64 (12.77)
Absolute Change at Week 52		
n	33	36
Mean (SD)	3.25 (18.99)	1.67 (16.56)
Absolute Change at Week 52 (MMRM)		
n	31	36
LS mean (SE)	2.83 (3.07)	2.20 (2.84)
95% CI of LS mean	(-3.31, 8.97)	(-3.48, 7.89)
P-value within Treatment	0.3597	0.4412
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-9.08, 7.82)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8823
Hedges' G (SE)		-0.04 (0.24)

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' 95% CI		(-0.52, 0.45)
Hedges' P-value		0.8812

- N is the number of subjects in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.1.12.1.1
Study VX21-121-103: Compliance Rate for TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Baseline	35 (92.11)	38 (92.68)
Week 52	35 (92.11)	39 (95.12)
Absolute Change at Week 52	33 (86.84)	36 (87.80)

- n (%): For "Change at Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and Week 52 are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.12.1.1
Study VX21-121-103: Compliance Rate for TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Baseline	35 (92.11)	38 (92.68)
Week 52	35 (92.11)	39 (95.12)
Absolute Change at Week 52	33 (86.84)	36 (87.80)

- n (%): For "Change at Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and Week 52 are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.12.1.1
Study VX21-121-103: Compliance Rate for TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Baseline	35 (92.11)	37 (90.24)
Week 52	35 (92.11)	39 (95.12)
Absolute Change at Week 52	33 (86.84)	35 (85.37)

- n (%): For "Change at Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and Week 52 are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.12.1.1
Study VX21-121-103: Compliance Rate for TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Baseline	35 (92.11)	38 (92.68)
Week 52	35 (92.11)	39 (95.12)
Absolute Change at Week 52	33 (86.84)	36 (87.80)

- n (%): For "Change at Week 52", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and Week 52 are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.5537
Age at screening (<18 years vs. ≥18 years) [2]	0.4366
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.4765
Sex (Male vs. Female) [1]	0.8589
Region (North America vs. Rest of the World) [1]	0.1906

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ through Week 52 for Additional Subgroups
Full Analysis Set

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.7124
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.3350

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype, baseline sweat chloride and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	167	154
mean (SD)	56.10 (9.26)	56.38 (8.74)
Week 52		
n	155	144
mean (SD)	56.26 (10.65)	56.66 (9.30)
Absolute Change at Week 52		
n	155	144
mean (SD)	0.25 (5.46)	0.41 (4.97)
Absolute Change through Week 52 (MMRM)		
n	159	149
LS mean (SE)	0.29 (0.34)	0.63 (0.35)
95% CI of LS mean	(-0.37, 0.96)	(-0.06, 1.31)
P-value within Treatment	0.3820	0.0714

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-0.62, 1.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4912
Hedges' G (SE)		0.08 (0.11)
Hedges' 95% CI		(-0.15, 0.30)
Hedges' P-value		0.4912

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	119	125
mean (SD)	80.90 (7.05)	80.60 (7.70)
Week 52		
n	114	110
mean (SD)	80.30 (8.11)	79.96 (8.27)
Absolute Change at Week 52		
n	114	110
mean (SD)	-0.53 (5.29)	-0.23 (4.75)
Absolute Change through Week 52 (MMRM)		
n	118	122
LS mean (SE)	-0.34 (0.34)	-0.15 (0.34)
95% CI of LS mean	(-1.01, 0.34)	(-0.82, 0.51)
P-value within Treatment	0.3269	0.6487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.77, 1.14)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7061
Hedges' G (SE)		0.05 (0.13)
Hedges' 95% CI		(-0.20, 0.30)
Hedges' P-value		0.7052

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	38	40
mean (SD)	80.82 (10.15)	79.42 (13.73)
Week 52		
n	35	33
mean (SD)	79.75 (10.70)	78.72 (13.50)
Absolute Change at Week 52		
n	35	33
mean (SD)	-1.18 (5.94)	0.47 (7.29)
Absolute Change through Week 52 (MMRM)		
n	34	39
LS mean (SE)	-0.36 (0.80)	0.94 (0.76)
95% CI of LS mean	(-1.96, 1.23)	(-0.58, 2.46)
P-value within Treatment	0.6499	0.2204

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.30 (-0.91, 3.52)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2434
Hedges' G (SE)		0.27 (0.23)
Hedges' 95% CI		(-0.19, 0.74)
Hedges' P-value		0.2434

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	248	239
mean (SD)	64.21 (14.22)	65.20 (13.79)
Week 52		
n	236	224
mean (SD)	64.40 (14.87)	65.06 (14.25)
Absolute Change at Week 52		
n	234	221
mean (SD)	0.08 (5.30)	0.09 (4.42)
Absolute Change through Week 52 (MMRM)		
n	243	232
LS mean (SE)	0.08 (0.25)	0.21 (0.25)
95% CI of LS mean	(-0.41, 0.56)	(-0.29, 0.71)
P-value within Treatment	0.7591	0.4156

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.57, 0.83)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7138
Hedges' G (SE)		0.03 (0.09)
Hedges' 95% CI		(-0.15, 0.21)
Hedges' P-value		0.7136

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	79	69
mean (SD)	64.72 (14.87)	65.27 (13.99)
Week 52		
n	74	65
mean (SD)	64.55 (14.63)	65.31 (14.12)
Absolute Change at Week 52		
n	73	63
mean (SD)	-0.30 (5.34)	0.71 (5.14)
Absolute Change through Week 52 (MMRM)		
n	79	66
LS mean (SE)	-0.19 (0.44)	0.60 (0.48)
95% CI of LS mean	(-1.06, 0.67)	(-0.34, 1.55)
P-value within Treatment	0.6594	0.2096

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.80 (-0.49, 2.08)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2226
Hedges' G (SE)		0.20 (0.17)
Hedges' 95% CI		(-0.13, 0.53)
Hedges' P-value		0.2232

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	200	208
mean (SD)	67.30 (14.89)	67.91 (14.76)
Week 52		
n	191	190
mean (SD)	67.31 (15.61)	67.34 (15.07)
Absolute Change at Week 52		
n	190	189
mean (SD)	0.05 (5.47)	-0.07 (4.79)
Absolute Change through Week 52 (MMRM)		
n	198	205
LS mean (SE)	0.09 (0.29)	0.19 (0.28)
95% CI of LS mean	(-0.47, 0.66)	(-0.37, 0.74)
P-value within Treatment	0.7453	0.5048

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.69, 0.88)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8132
Hedges' G (SE)		0.02 (0.10)
Hedges' 95% CI		(-0.17, 0.22)
Hedges' P-value		0.8131

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	141	146
mean (SD)	67.75 (14.73)	66.55 (14.84)
Week 52		
n	135	137
mean (SD)	67.57 (15.29)	66.55 (15.09)
Absolute Change at Week 52		
n	133	134
mean (SD)	-0.35 (5.38)	0.11 (4.42)
Absolute Change through Week 52 (MMRM)		
n	134	141
LS mean (SE)	-0.15 (0.32)	0.34 (0.32)
95% CI of LS mean	(-0.79, 0.49)	(-0.29, 0.96)
P-value within Treatment	0.6527	0.2910

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-0.42, 1.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2919
Hedges' G (SE)		0.13 (0.12)
Hedges' 95% CI		(-0.11, 0.36)
Hedges' P-value		0.2900

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	145	133
mean (SD)	65.12 (14.91)	67.99 (14.42)
Week 52		
n	136	120
mean (SD)	65.20 (15.24)	67.12 (14.63)
Absolute Change at Week 52		
n	136	120
mean (SD)	0.17 (5.41)	0.17 (5.35)
Absolute Change through Week 52 (MMRM)		
n	143	130
LS mean (SE)	0.10 (0.36)	0.28 (0.37)
95% CI of LS mean	(-0.60, 0.80)	(-0.46, 1.01)
P-value within Treatment	0.7758	0.4618

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-0.85, 1.20)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7382
Hedges' G (SE)		0.04 (0.12)
Hedges' 95% CI		(-0.20, 0.28)
Hedges' P-value		0.7369

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	101	113
mean (SD)	68.03 (15.01)	67.07 (13.31)
Week 52		
n	97	100
mean (SD)	68.20 (15.32)	66.42 (12.29)
Absolute Change at Week 52		
n	96	100
mean (SD)	-0.28 (6.01)	0.02 (4.32)
Absolute Change through Week 52 (MMRM)		
n	99	110
LS mean (SE)	-0.40 (0.39)	0.36 (0.37)
95% CI of LS mean	(-1.17, 0.38)	(-0.38, 1.10)
P-value within Treatment	0.3169	0.3360

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.76 (-0.32, 1.83)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1660
Hedges' G (SE)		0.19 (0.14)
Hedges' 95% CI		(-0.08, 0.46)
Hedges' P-value		0.1664

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	185	166
mean (SD)	65.54 (14.73)	67.35 (15.50)
Week 52		
n	174	157
mean (SD)	65.36 (15.21)	67.07 (16.30)
Absolute Change at Week 52		
n	173	154
mean (SD)	0.02 (5.03)	0.21 (5.21)
Absolute Change through Week 52 (MMRM)		
n	178	161
LS mean (SE)	0.21 (0.30)	0.26 (0.32)
95% CI of LS mean	(-0.38, 0.81)	(-0.37, 0.88)
P-value within Treatment	0.4847	0.4159

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups
Full Analysis Set
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-0.82, 0.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9139
Hedges' G (SE)		0.01 (0.11)
Hedges' 95% CI		(-0.20, 0.23)
Hedges' P-value		0.9138

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Baseline		
n	247	237
mean (SD)	66.22 (14.85)	66.56 (14.39)
Week 52		
n	235	218
mean (SD)	66.26 (15.06)	65.51 (14.07)
Absolute Change at Week 52		
n	233	216
mean (SD)	-0.03 (5.29)	-0.07 (4.40)
Absolute Change through Week 52 (MMRM)		
n	240	232
LS mean (SE)	-0.13 (0.24)	0.23 (0.25)
95% CI of LS mean	(-0.60, 0.35)	(-0.26, 0.72)
P-value within Treatment	0.6006	0.3525

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-0.32, 1.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3031
Hedges' G (SE)		0.09 (0.09)
Hedges' 95% CI		(-0.09, 0.28)
Hedges' P-value		0.3032

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Baseline		
n	39	42
mean (SD)	67.70 (14.98)	71.03 (15.59)
Week 52		
n	36	39
mean (SD)	67.17 (16.87)	74.15 (17.04)
Absolute Change at Week 52		
n	36	38
mean (SD)	-0.45 (6.06)	1.28 (6.95)
Absolute Change through Week 52 (MMRM)		
n	37	39
LS mean (SE)	0.79 (0.86)	0.74 (0.83)
95% CI of LS mean	(-0.93, 2.51)	(-0.92, 2.40)
P-value within Treatment	0.3645	0.3748

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-2.47, 2.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9714
Hedges' G (SE)		-0.01 (0.23)
Hedges' 95% CI		(-0.46, 0.44)
Hedges' P-value		0.9710

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set
Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Baseline		
n	222	219
mean (SD)	66.55 (14.68)	66.92 (14.73)
Week 52		
n	207	202
mean (SD)	67.24 (15.52)	66.49 (14.53)
Absolute Change at Week 52		
n	206	201
mean (SD)	0.43 (5.34)	0.11 (4.88)
Absolute Change through Week 52 (MMRM)		
n	215	215
LS mean (SE)	0.41 (0.27)	0.42 (0.27)
95% CI of LS mean	(-0.12, 0.95)	(-0.12, 0.95)
P-value within Treatment	0.1305	0.1271

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in ppFEV$_1$ (percentage points) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set
Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.75, 0.76)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9906
Hedges' G (SE)		0.00 (0.10)
Hedges' 95% CI		(-0.19, 0.19)
Hedges' P-value		0.9906

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set
Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	19	18
mean (SD)	64.86 (15.27)	67.81 (12.91)
Week 52		
n	20	16
mean (SD)	64.63 (13.82)	66.44 (12.46)
Absolute Change at Week 52		
n	19	15
mean (SD)	-0.12 (5.16)	2.11 (4.60)
Absolute Change through Week 52 (MMRM)		
n	19	16
LS mean (SE)	-0.01 (0.74)	1.97 (0.79)
95% CI of LS mean	(-1.51, 1.49)	(0.36, 3.58)
P-value within Treatment	0.9883	0.0181

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set
Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.98 (-0.23, 4.19)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0772
Hedges' G (SE)		0.61 (0.34)
Hedges' 95% CI		(-0.08, 1.30)
Hedges' P-value		0.0830

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set
Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Baseline		
n	23	23
mean (SD)	68.85 (15.96)	70.98 (15.30)
Week 52		
n	22	23
mean (SD)	66.26 (15.38)	70.87 (16.06)
Absolute Change at Week 52		
n	22	23
mean (SD)	-0.97 (4.42)	-0.11 (3.15)
Absolute Change through Week 52 (MMRM)		
n	23	23
LS mean (SE)	-1.13 (0.65)	-0.93 (0.65)
95% CI of LS mean	(-2.44, 0.18)	(-2.24, 0.37)
P-value within Treatment	0.0896	0.1574

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set
Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-1.66, 2.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8314
Hedges' G (SE)		0.06 (0.29)
Hedges' 95% CI		(-0.52, 0.65)
Hedges' P-value		0.8312

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	19
mean (SD)	63.94 (15.59)	65.80 (14.64)
Week 52		
n	22	16
mean (SD)	59.95 (13.33)	65.53 (19.29)
Absolute Change at Week 52		
n	22	15
mean (SD)	-3.99 (5.53)	-1.07 (6.82)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	-3.49 (1.20)	-0.97 (1.29)
95% CI of LS mean	(-5.92, -1.07)	(-3.58, 1.63)
P-value within Treatment	0.0060	0.4542

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.52 (-1.08, 6.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1643
Hedges' G (SE)		0.46 (0.33)
Hedges' 95% CI		(-0.20, 1.13)
Hedges' P-value		0.1658

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6314
Age at screening (<18 years vs. ≥18 years) [2]	0.1467
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1661
Sex (Male vs. Female) [1]	0.1494
Region (North America vs. Rest of the World) [1]	0.3866

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 for Additional Subgroups
Full Analysis Set

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.5115
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.3217

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype , baseline sweat chloride and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	167	151
mean (SD)	23.13 (2.96)	23.69 (3.89)
Week 52		
n	157	138
mean (SD)	23.46 (3.20)	24.04 (4.27)
Absolute Change at Week 52		
n	157	135
mean (SD)	0.21 (1.13)	0.28 (1.27)
Absolute Change at Week 52 (MMRM)		
n	152	134
LS mean (SE)	0.14 (0.10)	0.27 (0.10)
95% CI of LS mean	(-0.05, 0.33)	(0.08, 0.47)
P-value within Treatment	0.1452	0.0070

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-0.14, 0.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3360
Hedges' G (SE)		0.11 (0.12)
Hedges' 95% CI		(-0.12, 0.35)
Hedges' P-value		0.3367

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	119	124
mean (SD)	22.64 (3.68)	22.80 (4.15)
Week 52		
n	115	116
mean (SD)	23.03 (3.79)	23.37 (4.02)
Absolute Change at Week 52		
n	115	115
mean (SD)	0.36 (1.28)	0.49 (1.29)
Absolute Change at Week 52 (MMRM)		
n	114	114
LS mean (SE)	0.32 (0.12)	0.50 (0.12)
95% CI of LS mean	(0.09, 0.55)	(0.27, 0.73)
P-value within Treatment	0.0073	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-0.15, 0.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2764
Hedges' G (SE)		0.14 (0.13)
Hedges' 95% CI		(-0.12, 0.40)
Hedges' P-value		0.2768

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	38	41
mean (SD)	19.68 (2.49)	20.37 (3.80)
Week 52		
n	36	36
mean (SD)	20.05 (2.25)	21.58 (4.14)
Absolute Change at Week 52		
n	36	36
mean (SD)	0.35 (1.43)	1.07 (1.10)
Absolute Change at Week 52 (MMRM)		
n	34	36
LS mean (SE)	0.24 (0.21)	1.06 (0.20)
95% CI of LS mean	(-0.18, 0.66)	(0.66, 1.47)
P-value within Treatment	0.2639	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.83 (0.25, 1.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0059
Hedges' G (SE)		0.67 (0.24)
Hedges' 95% CI		(0.19, 1.16)
Hedges' P-value		0.0074

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	251	239
mean (SD)	23.42 (3.09)	23.76 (3.86)
Week 52		
n	239	222
mean (SD)	23.75 (3.34)	24.07 (4.06)
Absolute Change at Week 52		
n	239	218
mean (SD)	0.25 (1.16)	0.26 (1.27)
Absolute Change at Week 52 (MMRM)		
n	232	212
LS mean (SE)	0.22 (0.08)	0.26 (0.08)
95% CI of LS mean	(0.06, 0.37)	(0.10, 0.42)
P-value within Treatment	0.0058	0.0017

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-0.18, 0.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7321
Hedges' G (SE)		0.03 (0.09)
Hedges' 95% CI		(-0.15, 0.22)
Hedges' P-value		0.7322

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	80	72
mean (SD)	23.45 (3.64)	23.38 (4.55)
Week 52		
n	78	67
mean (SD)	23.71 (3.91)	23.90 (4.77)
Absolute Change at Week 52		
n	78	67
mean (SD)	0.25 (1.22)	0.37 (1.05)
Absolute Change at Week 52 (MMRM)		
n	77	64
LS mean (SE)	0.24 (0.13)	0.41 (0.14)
95% CI of LS mean	(-0.02, 0.50)	(0.13, 0.69)
P-value within Treatment	0.0656	0.0044

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-0.21, 0.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3791
Hedges' G (SE)		0.15 (0.17)
Hedges' 95% CI		(-0.18, 0.48)
Hedges' P-value		0.3798

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	202	206
mean (SD)	22.76 (3.09)	23.21 (3.84)
Week 52		
n	191	189
mean (SD)	23.07 (3.22)	23.64 (3.93)
Absolute Change at Week 52		
n	191	185
mean (SD)	0.23 (1.15)	0.37 (1.34)
Absolute Change at Week 52 (MMRM)		
n	189	184
LS mean (SE)	0.21 (0.09)	0.36 (0.09)
95% CI of LS mean	(0.03, 0.38)	(0.18, 0.54)
P-value within Treatment	0.0214	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.10, 0.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2331
Hedges' G (SE)		0.12 (0.10)
Hedges' 95% CI		(-0.08, 0.33)
Hedges' P-value		0.2336

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	144	147
mean (SD)	23.41 (3.29)	23.53 (3.72)
Week 52		
n	139	138
mean (SD)	23.67 (3.45)	23.74 (3.79)
Absolute Change at Week 52		
n	139	136
mean (SD)	0.19 (1.16)	0.23 (1.08)
Absolute Change at Week 52 (MMRM)		
n	131	132
LS mean (SE)	0.11 (0.10)	0.23 (0.09)
95% CI of LS mean	(-0.08, 0.29)	(0.04, 0.41)
P-value within Treatment	0.2651	0.0155

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-0.14, 0.39)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3607
Hedges' G (SE)		0.11 (0.12)
Hedges' 95% CI		(-0.13, 0.36)
Hedges' P-value		0.3607

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	145	133
mean (SD)	22.44 (3.18)	22.97 (4.33)
Week 52		
n	136	120
mean (SD)	22.86 (3.40)	23.70 (4.54)
Absolute Change at Week 52		
n	136	118
mean (SD)	0.35 (1.22)	0.55 (1.46)
Absolute Change at Week 52 (MMRM)		
n	135	116
LS mean (SE)	0.33 (0.11)	0.53 (0.12)
95% CI of LS mean	(0.11, 0.55)	(0.30, 0.77)
P-value within Treatment	0.0040	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-0.12, 0.53)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2206
Hedges' G (SE)		0.15 (0.13)
Hedges' 95% CI		(-0.09, 0.40)
Hedges' P-value		0.2214

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	103	113
mean (SD)	24.05 (3.69)	24.16 (4.71)
Week 52		
n	100	104
mean (SD)	24.41 (3.96)	24.57 (4.86)
Absolute Change at Week 52		
n	100	103
mean (SD)	0.21 (1.32)	0.21 (1.27)
Absolute Change at Week 52 (MMRM)		
n	96	103
LS mean (SE)	0.18 (0.13)	0.19 (0.13)
95% CI of LS mean	(-0.08, 0.44)	(-0.06, 0.44)
P-value within Treatment	0.1726	0.1294

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-0.35, 0.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9487
Hedges' G (SE)		0.01 (0.14)
Hedges' 95% CI		(-0.27, 0.29)
Hedges' P-value		0.9487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	186	167
mean (SD)	22.30 (2.83)	22.66 (3.36)
Week 52		
n	175	154
mean (SD)	22.61 (2.93)	23.15 (3.50)
Absolute Change at Week 52		
n	175	151
mean (SD)	0.30 (1.12)	0.49 (1.27)
Absolute Change at Week 52 (MMRM)		
n	170	145
LS mean (SE)	0.24 (0.09)	0.49 (0.09)
95% CI of LS mean	(0.06, 0.41)	(0.31, 0.68)
P-value within Treatment	0.0073	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (0.00, 0.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0488
Hedges' G (SE)		0.22 (0.11)
Hedges' 95% CI		(0.00, 0.45)
Hedges' P-value		0.0497

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Baseline		
n	250	239
mean (SD)	22.91 (3.32)	23.32 (4.04)
Week 52		
n	239	217
mean (SD)	23.16 (3.50)	23.66 (4.17)
Absolute Change at Week 52		
n	239	215
mean (SD)	0.19 (1.18)	0.26 (1.22)
Absolute Change at Week 52 (MMRM)		
n	232	212
LS mean (SE)	0.17 (0.08)	0.27 (0.08)
95% CI of LS mean	(0.02, 0.33)	(0.11, 0.43)
P-value within Treatment	0.0296	0.0009

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.12, 0.32)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3748
Hedges' G (SE)		0.08 (0.09)
Hedges' 95% CI		(-0.10, 0.27)
Hedges' P-value		0.3753

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Baseline		
n	39	41
mean (SD)	23.03 (2.89)	22.97 (3.96)
Week 52		
n	36	41
mean (SD)	23.95 (3.03)	24.08 (4.07)
Absolute Change at Week 52		
n	36	39
mean (SD)	0.78 (1.15)	1.01 (1.37)
Absolute Change at Week 52 (MMRM)		
n	34	36
LS mean (SE)	0.49 (0.21)	1.00 (0.21)
95% CI of LS mean	(0.08, 0.91)	(0.58, 1.41)
P-value within Treatment	0.0216	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-0.09, 1.09)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0941
Hedges' G (SE)		0.40 (0.24)
Hedges' 95% CI		(-0.07, 0.88)
Hedges' P-value		0.0967

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Baseline		
n	224	218
mean (SD)	22.70 (3.05)	22.89 (3.69)
Week 52		
n	210	202
mean (SD)	23.04 (3.21)	23.33 (3.79)
Absolute Change at Week 52		
n	210	198
mean (SD)	0.25 (1.14)	0.38 (1.26)
Absolute Change at Week 52 (MMRM)		
n	204	195
LS mean (SE)	0.21 (0.08)	0.36 (0.08)
95% CI of LS mean	(0.05, 0.37)	(0.19, 0.52)
P-value within Treatment	0.0108	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.08, 0.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2119
Hedges' G (SE)		0.12 (0.10)
Hedges' 95% CI		(-0.07, 0.32)
Hedges' P-value		0.2124

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	20	19
mean (SD)	23.84 (3.45)	23.45 (3.77)
Week 52		
n	20	16
mean (SD)	23.88 (3.52)	24.02 (4.00)
Absolute Change at Week 52		
n	20	16
mean (SD)	0.03 (1.51)	0.11 (0.81)
Absolute Change at Week 52 (MMRM)		
n	19	15
LS mean (SE)	0.05 (0.29)	0.14 (0.32)
95% CI of LS mean	(-0.53, 0.64)	(-0.51, 0.79)
P-value within Treatment	0.8513	0.6617

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.09 (-0.79, 0.96)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8419
Hedges' G (SE)		0.07 (0.34)
Hedges' 95% CI		(-0.62, 0.75)
Hedges' P-value		0.8422

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Baseline		
n	23	23
mean (SD)	24.19 (4.28)	24.98 (4.18)
Week 52		
n	23	23
mean (SD)	24.44 (4.69)	25.24 (4.48)
Absolute Change at Week 52		
n	23	23
mean (SD)	0.26 (1.31)	0.25 (1.40)
Absolute Change at Week 52 (MMRM)		
n	23	23
LS mean (SE)	0.26 (0.28)	0.25 (0.28)
95% CI of LS mean	(-0.32, 0.83)	(-0.32, 0.82)
P-value within Treatment	0.3722	0.3768

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-0.81, 0.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9951
Hedges' G (SE)		0.00 (0.29)
Hedges' 95% CI		(-0.59, 0.58)
Hedges' P-value		0.9951

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	20
mean (SD)	23.02 (3.80)	25.20 (6.26)
Week 52		
n	22	17
mean (SD)	23.69 (3.96)	26.11 (6.49)
Absolute Change at Week 52		
n	22	17
mean (SD)	0.66 (1.27)	0.77 (1.64)
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	0.40 (0.31)	1.03 (0.34)
95% CI of LS mean	(-0.23, 1.02)	(0.34, 1.73)
P-value within Treatment	0.2023	0.0047

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-0.30, 1.57)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1765
Hedges' G (SE)		0.46 (0.34)
Hedges' 95% CI		(-0.23, 1.15)
Hedges' P-value		0.1833

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.2.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52
for Subjects ≤20 Years at Baseline
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6533
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.3241
Sex (Male vs. Female) [1]	0.9032
Region (North America vs. Rest of the World) [1]	0.2317

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 for Subjects ≤20 Years at Baseline for Additional Subgroups
Full Analysis Set

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.3579
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype , and baseline sweat chloride as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Baseline		
n	8	11
mean (SD)	-0.34 (0.68)	-0.25 (1.26)
Week 52		
n	5	8
mean (SD)	-0.43 (0.94)	-0.09 (1.30)
Absolute Change at Week 52		
n	5	8
mean (SD)	0.00 (0.54)	0.03 (0.41)
Absolute Change at Week 52 (MMRM)		
n	4	8
LS mean (SE)	-0.12 (0.22)	0.01 (0.14)
95% CI of LS mean	(-0.60, 0.36)	(-0.29, 0.32)
P-value within Treatment	0.5980	0.9190

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-0.44, 0.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6189
Hedges' G (SE)		0.30 (0.57)
Hedges' 95% CI		(-0.96, 1.57)
Hedges' P-value		0.6045

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 34	VNZ/TEZ/D-IVA N = 41
Baseline		
n	34	41
mean (SD)	-0.29 (1.04)	-0.14 (0.88)
Week 52		
n	32	34
mean (SD)	-0.34 (1.03)	0.04 (0.88)
Absolute Change at Week 52		
n	32	34
mean (SD)	-0.10 (0.48)	0.17 (0.36)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	-0.14 (0.07)	0.16 (0.07)
95% CI of LS mean	(-0.28, 0.01)	(0.02, 0.30)
P-value within Treatment	0.0645	0.0230

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 34	VNZ/TEZ/D-IVA N = 41
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.30 (0.10, 0.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0043
Hedges' G (SE)		0.73 (0.25)
Hedges' 95% CI		(0.22, 1.23)
Hedges' P-value		0.0056

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 14
Baseline		
n	8	14
mean (SD)	0.02 (0.91)	-0.56 (0.97)
Week 52		
n	8	10
mean (SD)	-0.13 (0.71)	-0.33 (1.06)
Absolute Change at Week 52		
n	8	10
mean (SD)	-0.16 (0.60)	0.13 (0.55)
Absolute Change at Week 52 (MMRM)		
n	8	10
LS mean (SE)	-0.16 (0.19)	0.16 (0.16)
95% CI of LS mean	(-0.56, 0.24)	(-0.18, 0.51)
P-value within Treatment	0.4004	0.3352

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 14
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-0.20, 0.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2121
Hedges' G (SE)		0.59 (0.46)
Hedges' 95% CI		(-0.39, 1.57)
Hedges' P-value		0.2208

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 32	VNZ/TEZ/D-IVA N = 39
Baseline		
n	32	39
mean (SD)	-0.42 (1.01)	-0.03 (0.92)
Week 52		
n	27	32
mean (SD)	-0.50 (1.06)	0.13 (0.92)
Absolute Change at Week 52		
n	27	32
mean (SD)	-0.10 (0.44)	0.15 (0.31)
Absolute Change at Week 52 (MMRM)		
n	27	32
LS mean (SE)	-0.13 (0.07)	0.12 (0.06)
95% CI of LS mean	(-0.26, 0.01)	(-0.01, 0.25)
P-value within Treatment	0.0776	0.0621

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 32	VNZ/TEZ/D-IVA N = 39
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (0.06, 0.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0116
Hedges' G (SE)		0.67 (0.27)
Hedges' 95% CI		(0.14, 1.20)
Hedges' P-value		0.0140

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 21
Baseline		
n	25	21
mean (SD)	-0.22 (1.14)	-0.23 (1.07)
Week 52		
n	21	18
mean (SD)	-0.36 (1.12)	-0.12 (1.06)
Absolute Change at Week 52		
n	21	18
mean (SD)	-0.20 (0.52)	0.10 (0.39)
Absolute Change at Week 52 (MMRM)		
n	19	18
LS mean (SE)	-0.30 (0.10)	0.05 (0.10)
95% CI of LS mean	(-0.49, -0.10)	(-0.15, 0.26)
P-value within Treatment	0.0041	0.5839

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 25	VNZ/TEZ/D-IVA N = 21
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.35 (0.07, 0.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0158
Hedges' G (SE)		0.82 (0.34)
Hedges' 95% CI		(0.13, 1.50)
Hedges' P-value		0.0204

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 17	VNZ/TEZ/D-IVA N = 32
Baseline		
n	17	32
mean (SD)	-0.43 (0.68)	-0.13 (0.88)
Week 52		
n	16	24
mean (SD)	-0.35 (0.87)	0.12 (0.88)
Absolute Change at Week 52		
n	16	24
mean (SD)	0.07 (0.38)	0.18 (0.36)
Absolute Change at Week 52 (MMRM)		
n	16	24
LS mean (SE)	0.05 (0.09)	0.16 (0.07)
95% CI of LS mean	(-0.13, 0.24)	(0.01, 0.30)
P-value within Treatment	0.5461	0.0337

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 17	VNZ/TEZ/D-IVA N = 32
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.10 (-0.13, 0.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3840
Hedges' G (SE)		0.28 (0.32)
Hedges' 95% CI		(-0.36, 0.92)
Hedges' P-value		0.3823

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 20
Baseline		
n	12	20
mean (SD)	-0.19 (1.24)	0.01 (1.06)
Week 52		
n	11	13
mean (SD)	-0.46 (1.03)	0.21 (1.33)
Absolute Change at Week 52		
n	11	13
mean (SD)	-0.31 (0.54)	-0.06 (0.35)
Absolute Change at Week 52 (MMRM)		
n	11	13
LS mean (SE)	-0.30 (0.14)	-0.09 (0.12)
95% CI of LS mean	(-0.58, -0.01)	(-0.34, 0.15)
P-value within Treatment	0.0404	0.4354

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 20
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.20 (-0.17, 0.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2801
Hedges' G (SE)		0.44 (0.40)
Hedges' 95% CI		(-0.39, 1.27)
Hedges' P-value		0.2812

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 30	VNZ/TEZ/D-IVA N = 33
Baseline		
n	30	33
mean (SD)	-0.35 (0.87)	-0.28 (0.88)
Week 52		
n	26	29
mean (SD)	-0.31 (1.01)	-0.07 (0.75)
Absolute Change at Week 52		
n	26	29
mean (SD)	0.01 (0.42)	0.24 (0.35)
Absolute Change at Week 52 (MMRM)		
n	24	29
LS mean (SE)	-0.02 (0.07)	0.23 (0.07)
95% CI of LS mean	(-0.17, 0.13)	(0.09, 0.36)
P-value within Treatment	0.7585	0.0014

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 30	VNZ/TEZ/D-IVA N = 33
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (0.05, 0.45)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0161
Hedges' G (SE)		0.68 (0.28)
Hedges' 95% CI		(0.12, 1.24)
Hedges' P-value		0.0191

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups
for Subjects ≤20 Years at Baseline for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 40	VNZ/TEZ/D-IVA N = 45
Baseline		
n	40	45
mean (SD)	-0.28 (0.97)	-0.13 (0.96)
Week 52		
n	36	35
mean (SD)	-0.39 (1.00)	0.08 (1.00)
Absolute Change at Week 52		
n	36	35
mean (SD)	-0.10 (0.47)	0.12 (0.35)
Absolute Change at Week 52 (MMRM)		
n	35	35
LS mean (SE)	-0.14 (0.07)	0.08 (0.07)
95% CI of LS mean	(-0.28, 0.00)	(-0.06, 0.21)
P-value within Treatment	0.0503	0.2664

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 40	VNZ/TEZ/D-IVA N = 45
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.21 (0.02, 0.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0305
Hedges' G (SE)		0.52 (0.24)
Hedges' 95% CI		(0.04, 1.00)
Hedges' P-value		0.0334

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups
for Subjects ≤20 Years at Baseline for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 2	VNZ/TEZ/D-IVA N = 8
Baseline		
n	2	8
mean (SD)	-0.71 (1.32)	-0.40 (0.93)
Week 52		
n	1	7
mean (SD)	0.88 (-)	-0.27 (0.71)
Absolute Change at Week 52		
n	1	7
mean (SD)	0.66 (-)	0.31 (0.46)
Absolute Change at Week 52 (MMRM)		
n	0	7
LS mean (SE)	-	-
95% CI of LS mean	-	-
P-value within Treatment	-	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 2	VNZ/TEZ/D-IVA N = 8
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	-
Hedges' G (SE)		-
Hedges' 95% CI		-
Hedges' P-value		-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline for Additional Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 37	VNZ/TEZ/D-IVA N = 42

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline for Additional Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 2	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline for Additional Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in BMI-for-age Z-score at Week 52 by Subgroups for Subjects ≤20 Years at Baseline for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 2	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≤20 years of age at baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.2.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0895
Age at screening (<18 years vs. ≥18 years) [2]	0.6470
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0227
Sex (Male vs. Female) [1]	0.0117
Region (North America vs. Rest of the World) [1]	0.9448

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride,genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$,genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.4.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 for Additional Subgroups
Full Analysis Set

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.6738
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.0076

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype , baseline sweat chloride and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years) as covariates.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	161	153
mean (SD)	42.26 (18.50)	42.16 (19.18)
Week 52		
n	155	138
mean (SD)	38.10 (18.34)	36.34 (20.93)
Absolute Change at Week 52		
n	153	137
mean (SD)	-3.90 (12.17)	-6.14 (14.06)
Absolute Change through Week 52 (MMRM)		
n	159	149
LS mean (SE)	-2.78 (0.81)	-4.65 (0.84)
95% CI of LS mean	(-4.38, -1.18)	(-6.31, -2.99)
P-value within Treatment	0.0007	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.87 (-4.18, 0.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1121
Hedges' G (SE)		-0.18 (0.11)
Hedges' 95% CI		(-0.41, 0.04)
Hedges' P-value		0.1125

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	118	124
mean (SD)	41.74 (16.77)	45.21 (17.17)
Week 52		
n	111	112
mean (SD)	42.77 (22.65)	40.99 (19.91)
Absolute Change at Week 52		
n	110	112
mean (SD)	-0.22 (17.86)	-3.85 (14.19)
Absolute Change through Week 52 (MMRM)		
n	118	122
LS mean (SE)	-1.45 (1.02)	-5.30 (1.01)
95% CI of LS mean	(-3.46, 0.57)	(-7.29, -3.32)
P-value within Treatment	0.1578	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.85 (-6.69, -1.02)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0079
Hedges' G (SE)		-0.35 (0.13)
Hedges' 95% CI		(-0.60, -0.09)
Hedges' P-value		0.0082

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	36	41
mean (SD)	45.85 (18.39)	43.68 (17.58)
Week 52		
n	35	36
mean (SD)	47.30 (26.94)	40.75 (19.79)
Absolute Change at Week 52		
n	34	36
mean (SD)	0.43 (21.14)	-1.62 (12.31)
Absolute Change through Week 52 (MMRM)		
n	34	39
LS mean (SE)	0.40 (2.15)	-2.54 (2.04)
95% CI of LS mean	(-3.91, 4.70)	(-6.63, 1.55)
P-value within Treatment	0.8541	0.2190

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.94 (-8.91, 3.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3289
Hedges' G (SE)		-0.23 (0.23)
Hedges' 95% CI		(-0.69, 0.23)
Hedges' P-value		0.3275

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	246	241
mean (SD)	41.52 (17.78)	43.39 (18.73)
Week 52		
n	234	218
mean (SD)	38.98 (19.08)	37.73 (20.72)
Absolute Change at Week 52		
n	232	217
mean (SD)	-2.79 (13.66)	-5.68 (14.24)
Absolute Change through Week 52 (MMRM)		
n	243	232
LS mean (SE)	-2.54 (0.66)	-5.24 (0.68)
95% CI of LS mean	(-3.83, -1.24)	(-6.57, -3.91)
P-value within Treatment	0.0001	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.70 (-4.56, -0.84)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0045
Hedges' G (SE)		-0.26 (0.09)
Hedges' 95% CI		(-0.44, -0.08)
Hedges' P-value		0.0046

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	80	72
mean (SD)	21.39 (5.38)	21.20 (5.86)
Week 52		
n	74	63
mean (SD)	22.41 (8.73)	19.29 (9.06)
Absolute Change at Week 52		
n	74	63
mean (SD)	0.96 (7.77)	-1.61 (7.77)
Absolute Change through Week 52 (MMRM)		
n	79	67
LS mean (SE)	1.04 (0.86)	0.00 (0.93)
95% CI of LS mean	(-0.66, 2.74)	(-1.85, 1.86)
P-value within Treatment	0.2269	0.9970

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.04 (-3.56, 1.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4154
Hedges' G (SE)		-0.14 (0.17)
Hedges' 95% CI		(-0.46, 0.19)
Hedges' P-value		0.4141

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	202	210
mean (SD)	50.27 (14.07)	51.05 (14.89)
Week 52		
n	192	190
mean (SD)	46.57 (19.33)	44.57 (19.39)
Absolute Change at Week 52		
n	192	190
mean (SD)	-3.67 (16.60)	-6.26 (15.40)
Absolute Change through Week 52 (MMRM)		
n	198	204
LS mean (SE)	-3.39 (0.82)	-6.68 (0.81)
95% CI of LS mean	(-5.00, -1.77)	(-8.28, -5.09)
P-value within Treatment	<0.0001	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.29 (-5.56, -1.03)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0046
Hedges' G (SE)		-0.28 (0.10)
Hedges' 95% CI		(-0.48, -0.09)
Hedges' P-value		0.0047

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	139	148
mean (SD)	43.95 (17.37)	45.90 (17.62)
Week 52		
n	135	136
mean (SD)	43.28 (22.51)	39.73 (19.01)
Absolute Change at Week 52		
n	133	135
mean (SD)	-1.01 (17.72)	-6.57 (13.02)
Absolute Change through Week 52 (MMRM)		
n	134	142
LS mean (SE)	-1.35 (0.90)	-6.54 (0.87)
95% CI of LS mean	(-3.11, 0.42)	(-8.27, -4.82)
P-value within Treatment	0.1347	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.20 (-7.68, -2.72)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-0.50 (0.12)
Hedges' 95% CI		(-0.74, -0.26)
Hedges' P-value		<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	143	134
mean (SD)	40.25 (18.24)	40.70 (19.20)
Week 52		
n	134	118
mean (SD)	36.82 (17.53)	36.36 (22.20)
Absolute Change at Week 52		
n	133	118
mean (SD)	-3.75 (11.08)	-3.42 (14.98)
Absolute Change through Week 52 (MMRM)		
n	143	129
LS mean (SE)	-3.01 (0.91)	-3.27 (0.96)
95% CI of LS mean	(-4.80, -1.23)	(-5.17, -1.38)
P-value within Treatment	0.0010	0.0008

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-2.87, 2.35)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8448
Hedges' G (SE)		-0.02 (0.12)
Hedges' 95% CI		(-0.26, 0.21)
Hedges' P-value		0.8442

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	101	114
mean (SD)	43.35 (17.11)	44.25 (17.10)
Week 52		
n	97	100
mean (SD)	43.32 (22.54)	40.35 (18.80)
Absolute Change at Week 52		
n	96	100
mean (SD)	0.09 (16.96)	-3.93 (13.60)
Absolute Change through Week 52 (MMRM)		
n	99	110
LS mean (SE)	0.18 (1.08)	-3.03 (1.03)
95% CI of LS mean	(-1.95, 2.32)	(-5.05, -1.00)
P-value within Treatment	0.8665	0.0037

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.21 (-6.16, -0.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0332
Hedges' G (SE)		-0.30 (0.14)
Hedges' 95% CI		(-0.57, -0.02)
Hedges' P-value		0.0338

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	181	168
mean (SD)	41.36 (18.31)	42.88 (19.49)
Week 52		
n	172	154
mean (SD)	38.22 (18.92)	36.74 (21.61)
Absolute Change at Week 52		
n	170	153
mean (SD)	-3.77 (13.30)	-5.87 (14.29)
Absolute Change through Week 52 (MMRM)		
n	178	161
LS mean (SE)	-3.65 (0.75)	-6.15 (0.79)
95% CI of LS mean	(-5.12, -2.18)	(-7.71, -4.60)
P-value within Treatment	<0.0001	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.50 (-4.64, -0.36)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0223
Hedges' G (SE)		-0.25 (0.11)
Hedges' 95% CI		(-0.46, -0.04)
Hedges' P-value		0.0226

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Baseline		
n	245	241
mean (SD)	41.44 (16.99)	42.54 (18.12)
Week 52		
n	235	216
mean (SD)	39.53 (19.61)	37.73 (20.31)
Absolute Change at Week 52		
n	233	216
mean (SD)	-2.27 (14.58)	-4.60 (13.85)
Absolute Change through Week 52 (MMRM)		
n	240	232
LS mean (SE)	-1.86 (0.67)	-4.39 (0.68)
95% CI of LS mean	(-3.17, -0.55)	(-5.73, -3.04)
P-value within Treatment	0.0056	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.53 (-4.40, -0.65)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0084
Hedges' G (SE)		-0.24 (0.09)
Hedges' 95% CI		(-0.42, -0.06)
Hedges' P-value		0.0086

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Baseline		
n	37	41
mean (SD)	46.26 (22.79)	48.67 (20.30)
Week 52		
n	34	38
mean (SD)	43.72 (25.27)	40.61 (22.23)
Absolute Change at Week 52		
n	33	37
mean (SD)	-3.18 (16.58)	-8.07 (14.88)
Absolute Change through Week 52 (MMRM)		
n	37	39
LS mean (SE)	-5.00 (2.05)	-7.85 (1.98)
95% CI of LS mean	(-9.12, -0.88)	(-11.82, -3.88)
P-value within Treatment	0.0183	0.0002

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.85 (-8.67, 2.97)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3298
Hedges' G (SE)		-0.23 (0.23)
Hedges' 95% CI		(-0.68, 0.23)
Hedges' P-value		0.3216

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Baseline		
n	219	221
mean (SD)	43.76 (16.27)	45.63 (17.35)
Week 52		
n	207	200
mean (SD)	41.23 (19.05)	40.21 (20.34)
Absolute Change at Week 52		
n	205	200
mean (SD)	-2.58 (15.68)	-5.39 (14.96)
Absolute Change through Week 52 (MMRM)		
n	215	214
LS mean (SE)	-2.52 (0.72)	-5.54 (0.72)
95% CI of LS mean	(-3.93, -1.10)	(-6.96, -4.12)
P-value within Treatment	0.0005	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.03 (-5.03, -1.02)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0032
Hedges' G (SE)		-0.29 (0.10)
Hedges' 95% CI		(-0.48, -0.10)
Hedges' P-value		0.0033

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	20	19
mean (SD)	28.20 (13.09)	27.68 (15.73)
Week 52		
n	19	16
mean (SD)	24.71 (10.06)	22.25 (12.92)
Absolute Change at Week 52		
n	19	16
mean (SD)	-4.42 (9.73)	-3.64 (7.95)
Absolute Change through Week 52 (MMRM)		
n	19	17
LS mean (SE)	-2.29 (2.30)	2.26 (2.44)
95% CI of LS mean	(-7.01, 2.42)	(-2.75, 7.26)
P-value within Treatment	0.3275	0.3634

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.55 (-2.34, 11.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1871
Hedges' G (SE)		0.44 (0.33)
Hedges' 95% CI		(-0.23, 1.11)
Hedges' P-value		0.1892

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Baseline		
n	23	23
mean (SD)	35.93 (18.36)	38.12 (17.17)
Week 52		
n	22	22
mean (SD)	34.89 (20.37)	38.59 (18.05)
Absolute Change at Week 52		
n	22	22
mean (SD)	-1.69 (9.64)	-0.51 (8.14)
Absolute Change through Week 52 (MMRM)		
n	23	23
LS mean (SE)	-1.29 (1.62)	-3.03 (1.61)
95% CI of LS mean	(-4.55, 1.98)	(-6.29, 0.23)
P-value within Treatment	0.4313	0.0679

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.74 (-6.36, 2.88)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4509
Hedges' G (SE)		-0.22 (0.29)
Hedges' 95% CI		(-0.81, 0.37)
Hedges' P-value		0.4514

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	20	19
mean (SD)	44.51 (29.08)	40.03 (26.65)
Week 52		
n	21	16
mean (SD)	47.86 (31.38)	27.84 (24.33)
Absolute Change at Week 52		
n	20	15
mean (SD)	0.81 (14.55)	-9.60 (11.61)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	-0.59 (3.84)	-4.70 (4.18)
95% CI of LS mean	(-8.63, 7.45)	(-13.41, 4.01)
P-value within Treatment	0.8800	0.2740

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.4.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.11 (-16.07, 7.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4816
Hedges' G (SE)		-0.23 (0.32)
Hedges' 95% CI		(-0.89, 0.42)
Hedges' P-value		0.4749

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, 36, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.2.4.2.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1076*
Age at screening (<18 years vs. ≥18 years) [2]	0.4326*
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.6086*
Sex (Male vs. Female) [1]	0.1505*
Region (North America vs. Rest of the World) [1]	0.4406*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.2.2.4.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 for Additional Subgroups
Full Analysis Set

Subgroup	P-value for Interaction based on Relative Risk
Prior CFTR modulator use (yes vs. no) [1]	0.6986*
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.6370*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values for relative risk are obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
- [2] P-values for relative risk are obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline <70%

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Non-missing value at Week 52, N1	155	138
Number of subjects with missing value at Week 52	12	16
SwCl <60 mmol/L at Week 52, n (%)	139 (83.23)	121 (78.57)
Relative Risk (RR) (95% CI)		0.9180 (0.8316, 1.0135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0902*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline $ppFEV_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline ≥70%

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Non-missing value at Week 52, N1	111	112
Number of subjects with missing value at Week 52	8	13
SwCl <60 mmol/L at Week 52, n (%)	93 (78.15)	98 (78.40)
Relative Risk (RR) (95% CI)		1.0548 (0.9461, 1.1760)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3364

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years),and baseline $ppFEV_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening < 18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Non-missing value at Week 52, N1	35	36
Number of subjects with missing value at Week 52	3	5
SwCl <60 mmol/L at Week 52, n (%)	27 (71.05)	32 (78.05)
Relative Risk (RR) (95% CI)		1.0466 (0.8449, 1.2964)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6768*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening ≥ 18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Non-missing value at Week 52, N1	234	218
Number of subjects with missing value at Week 52	17	25
SwCl <60 mmol/L at Week 52, n (%)	207 (82.47)	191 (78.60)
Relative Risk (RR) (95% CI)		0.9556 (0.8796, 1.0382)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2831*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Non-missing value at Week 52, N1	74	63
Number of subjects with missing value at Week 52	6	9
SwCl <60 mmol/L at Week 52, n (%)	74 (92.50)	63 (87.50)
Relative Risk (RR) (95% CI)		0.9399 (0.8419, 1.0494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2704*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Non-missing value at Week 52, N1	192	190
Number of subjects with missing value at Week 52	10	20
SwCl <60 mmol/L at Week 52, n (%)	158 (78.22)	159 (75.71)
Relative Risk (RR) (95% CI)		0.9776 (0.8864, 1.0782)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6502*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Non-missing value at Week 52, N1	135	136
Number of subjects with missing value at Week 52	9	13
SwCl <60 mmol/L at Week 52, n (%)	111 (77.08)	120 (80.54)
Relative Risk (RR) (95% CI)		1.0156 (0.9020, 1.1436)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7980

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years),and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Non-missing value at Week 52, N1	134	118
Number of subjects with missing value at Week 52	11	17
SwCl <60 mmol/L at Week 52, n (%)	123 (84.83)	103 (76.30)
Relative Risk (RR) (95% CI)		0.9176 (0.8239, 1.0220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1177*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Non-missing value at Week 52, N1	97	100
Number of subjects with missing value at Week 52	6	14
SwCl <60 mmol/L at Week 52, n (%)	80 (77.67)	89 (78.07)
Relative Risk (RR) (95% CI)		1.0132 (0.8866, 1.1578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8475*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Non-missing value at Week 52, N1	172	154
Number of subjects with missing value at Week 52	14	16
SwCl <60 mmol/L at Week 52, n (%)	154 (82.80)	134 (78.82)
Relative Risk (RR) (95% CI)		0.9460 (0.8601, 1.0404)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2528*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.2.2.1
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Non-missing value at Week 52, N1	235	216
Number of subjects with missing value at Week 52	15	25
SwCl <60 mmol/L at Week 52, n (%)	207 (82.80)	192 (79.67)
Relative Risk (RR) (95% CI)		0.9618 (0.8874, 1.0423)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3419*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.2.2.4.2.2.1
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Non-missing value at Week 52, N1	34	38
Number of subjects with missing value at Week 52	5	5
SwCl <60 mmol/L at Week 52, n (%)	27 (69.23)	31 (72.09)
Relative Risk (RR) (95% CI)		1.0045 (0.7562, 1.3344)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9752*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.2.2.4.2.2.1
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Non-missing value at Week 52, N1	207	200
Number of subjects with missing value at Week 52	17	22
SwCl <60 mmol/L at Week 52, n (%)	180 (80.36)	173 (77.93)
Relative Risk (RR) (95% CI)		0.9798 (0.8955, 1.0720)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6563*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.2.2.4.2.2.1
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Non-missing value at Week 52, N1	19	16
Number of subjects with missing value at Week 52	1	3
SwCl <60 mmol/L at Week 52, n (%)	19 (95.00)	16 (84.21)
Relative Risk (RR) (95% CI)		0.8949 (0.7201, 1.1122)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3168*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.2.2.4.2.2.1
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Non-missing value at Week 52, N1	22	22
Number of subjects with missing value at Week 52	1	1
SwCl <60 mmol/L at Week 52, n (%)	20 (86.96)	20 (86.96)
Relative Risk (RR) (95% CI)		1.0233 (0.8236, 1.2713)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8353*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.2.2.4.2.2.1
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Non-missing value at Week 52, N1	21	16
Number of subjects with missing value at Week 52	1	4
SwCl <60 mmol/L at Week 52, n (%)	15 (68.18)	14 (70.00)
Relative Risk (RR) (95% CI)		0.8904 (0.6315, 1.2554)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5078*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.2.4.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9805*
Age at screening (<18 years vs. ≥18 years) [2]	0.2502*
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.2430*
Sex (Male vs. Female) [1]	0.4742*
Region (North America vs. Rest of the World) [1]	0.8645*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.2.2.4.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 for Additional Subgroups
Full Analysis Set

Subgroup	P-value for Interaction based on Relative Risk
Prior CFTR modulator use (yes vs. no) [1]	0.2585*
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.1509*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values for relative risk are obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
- [2] P-values for relative risk are obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline <70%

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Non-missing value at Week 52, N1	155	138
Number of subjects with missing value at Week 52	12	16
SwCl <30 mmol/L at Week 52, n (%)	55 (32.93)	62 (40.26)
Relative Risk (RR) (95% CI)		1.1089 (0.8756, 1.4044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3911*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline $ppFEV_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline ≥70%

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Non-missing value at Week 52, N1	111	112
Number of subjects with missing value at Week 52	8	13
SwCl <30 mmol/L at Week 52, n (%)	37 (31.09)	35 (28.00)
Relative Risk (RR) (95% CI)		1.1134 (0.8133, 1.5244)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5026*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline $ppFEV_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening < 18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Non-missing value at Week 52, N1	35	36
Number of subjects with missing value at Week 52	3	5
SwCl <30 mmol/L at Week 52, n (%)	11 (28.95)	11 (26.83)
Relative Risk (RR) (95% CI)		0.7228 (0.3696, 1.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3428*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Age at Screening ≥ 18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Non-missing value at Week 52, N1	234	218
Number of subjects with missing value at Week 52	17	25
SwCl <30 mmol/L at Week 52, n (%)	82 (32.67)	89 (36.63)
Relative Risk (RR) (95% CI)		1.1520 (0.9428, 1.4077)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1664*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Non-missing value at Week 52, N1	74	63
Number of subjects with missing value at Week 52	6	9
SwCl <30 mmol/L at Week 52, n (%)	61 (76.25)	57 (79.17)
Relative Risk (RR) (95% CI)		1.0236 (0.8633, 1.2136)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7887*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Non-missing value at Week 52, N1	192	190
Number of subjects with missing value at Week 52	10	20
SwCl <30 mmol/L at Week 52, n (%)	32 (15.84)	42 (20.00)
Relative Risk (RR) (95% CI)		1.3275 (0.9116, 1.9332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1396*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Non-missing value at Week 52, N1	135	136
Number of subjects with missing value at Week 52	9	13
SwCl <30 mmol/L at Week 52, n (%)	39 (27.08)	47 (31.54)
Relative Risk (RR) (95% CI)		1.1734 (0.8563, 1.6080)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3199*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Non-missing value at Week 52, N1	134	118
Number of subjects with missing value at Week 52	11	17
SwCl <30 mmol/L at Week 52, n (%)	54 (37.24)	53 (39.26)
Relative Risk (RR) (95% CI)		1.0219 (0.8078, 1.2926)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8569*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Non-missing value at Week 52, N1	97	100
Number of subjects with missing value at Week 52	6	14
SwCl <30 mmol/L at Week 52, n (%)	28 (27.18)	33 (28.95)
Relative Risk (RR) (95% CI)		1.1699 (0.8123, 1.6849)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3993*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Non-missing value at Week 52, N1	172	154
Number of subjects with missing value at Week 52	14	16
SwCl <30 mmol/L at Week 52, n (%)	65 (34.95)	67 (39.41)
Relative Risk (RR) (95% CI)		1.1250 (0.8998, 1.4064)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3013*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.
- N/C: model does not converge.

Table 2.2.2.4.3.2.1
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Non-missing value at Week 52, N1	235	216
Number of subjects with missing value at Week 52	15	25
SwCl <30 mmol/L at Week 52, n (%)	82 (32.80)	86 (35.68)
Relative Risk (RR) (95% CI)		1.0699 (0.8748, 1.3085)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5105*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.2.2.4.3.2.1
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Non-missing value at Week 52, N1	34	38
Number of subjects with missing value at Week 52	5	5
SwCl <30 mmol/L at Week 52, n (%)	11 (28.21)	14 (32.56)
Relative Risk (RR) (95% CI)		1.4184 (0.7533, 2.6709)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2790*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.2.2.4.3.2.1
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Non-missing value at Week 52, N1	207	200
Number of subjects with missing value at Week 52	17	22
SwCl <30 mmol/L at Week 52, n (%)	60 (26.79)	69 (31.08)
Relative Risk (RR) (95% CI)		1.2220 (0.9630, 1.5507)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0990*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.2.2.4.3.2.1
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Non-missing value at Week 52, N1	19	16
Number of subjects with missing value at Week 52	1	3
SwCl <30 mmol/L at Week 52, n (%)	15 (75.00)	12 (63.16)
Relative Risk (RR) (95% CI)		0.8036 (0.5355, 1.2059)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2911*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.2.2.4.3.2.1
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Non-missing value at Week 52, N1	22	22
Number of subjects with missing value at Week 52	1	1
SwCl <30 mmol/L at Week 52, n (%)	12 (52.17)	8 (34.78)
Relative Risk (RR) (95% CI)		0.7609 (0.4624, 1.2522)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2823*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.2.2.4.3.2.1
Study VX20-121-103: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Non-missing value at Week 52, N1	21	16
Number of subjects with missing value at Week 52	1	4
SwCl <30 mmol/L at Week 52, n (%)	6 (27.27)	11 (55.00)
Relative Risk (RR) (95% CI)		1.8311 (0.9657, 3.4721)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0639*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1 is the number of subjects with non-missing SwCl at Week 52.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline ppFEV$_1$, and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.2.2.5.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52
Full Analysis Set

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.5752
Age at screening (<18 years vs. ≥18 years) [2]	0.2218
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1729
Sex (Male vs. Female) [1]	0.2002
Region (North America vs. Rest of the World) [1]	0.2801

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.2.5.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 for Additional Subgroups
Full Analysis Set

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.3079
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.2171

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	167	151
mean (SD)	65.49 (12.13)	68.06 (12.76)
Week 52		
n	157	138
mean (SD)	66.64 (12.30)	68.94 (13.35)
Absolute Change at Week 52		
n	157	135
mean (SD)	0.60 (3.20)	0.75 (3.38)
Absolute Change at Week 52 (MMRM)		
n	152	134
LS mean (SE)	0.38 (0.26)	0.75 (0.27)
95% CI of LS mean	(-0.13, 0.89)	(0.21, 1.28)
P-value within Treatment	0.1401	0.0064

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-0.37, 1.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3310
Hedges' G (SE)		0.12 (0.12)
Hedges' 95% CI		(-0.12, 0.35)
Hedges' P-value		0.3317

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	119	124
mean (SD)	64.33 (14.89)	64.90 (15.05)
Week 52		
n	115	116
mean (SD)	66.04 (14.44)	67.14 (14.74)
Absolute Change at Week 52		
n	115	115
mean (SD)	1.53 (3.88)	2.02 (4.41)
Absolute Change at Week 52 (MMRM)		
n	114	114
LS mean (SE)	1.38 (0.38)	2.02 (0.37)
95% CI of LS mean	(0.64, 2.13)	(1.28, 2.75)
P-value within Treatment	0.0003	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-0.41, 1.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2343
Hedges' G (SE)		0.16 (0.13)
Hedges' 95% CI		(-0.10, 0.42)
Hedges' P-value		0.2349

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	38	41
mean (SD)	52.50 (9.78)	54.20 (11.96)
Week 52		
n	36	36
mean (SD)	55.32 (8.73)	59.35 (13.26)
Absolute Change at Week 52		
n	36	36
mean (SD)	2.93 (4.39)	4.94 (4.03)
Absolute Change at Week 52 (MMRM)		
n	34	36
LS mean (SE)	2.54 (0.70)	4.87 (0.67)
95% CI of LS mean	(1.14, 3.93)	(3.53, 6.22)
P-value within Treatment	0.0005	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.33 (0.40, 4.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0188
Hedges' G (SE)		0.57 (0.24)
Hedges' 95% CI		(0.09, 1.05)
Hedges' P-value		0.0212

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	251	239
mean (SD)	66.95 (12.79)	68.70 (13.20)
Week 52		
n	239	222
mean (SD)	68.07 (12.98)	69.58 (13.63)
Absolute Change at Week 52		
n	239	218
mean (SD)	0.68 (3.28)	0.73 (3.57)
Absolute Change at Week 52 (MMRM)		
n	232	212
LS mean (SE)	0.57 (0.22)	0.72 (0.23)
95% CI of LS mean	(0.14, 1.00)	(0.27, 1.17)
P-value within Treatment	0.0099	0.0017

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-0.47, 0.77)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6389
Hedges' G (SE)		0.04 (0.09)
Hedges' 95% CI		(-0.14, 0.23)
Hedges' P-value		0.6390

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	80	72
mean (SD)	66.01 (13.23)	66.56 (15.17)
Week 52		
n	78	67
mean (SD)	67.12 (13.76)	68.03 (15.47)
Absolute Change at Week 52		
n	78	67
mean (SD)	0.80 (3.41)	1.12 (3.09)
Absolute Change at Week 52 (MMRM)		
n	77	64
LS mean (SE)	0.79 (0.37)	1.23 (0.40)
95% CI of LS mean	(0.06, 1.52)	(0.43, 2.02)
P-value within Treatment	0.0337	0.0029

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-0.65, 1.52)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4304
Hedges' G (SE)		0.13 (0.17)
Hedges' 95% CI		(-0.20, 0.47)
Hedges' P-value		0.4309

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	202	206
mean (SD)	64.79 (13.40)	66.51 (13.57)
Week 52		
n	191	189
mean (SD)	65.99 (12.97)	68.08 (13.51)
Absolute Change at Week 52		
n	191	185
mean (SD)	0.87 (3.40)	1.38 (4.17)
Absolute Change at Week 52 (MMRM)		
n	189	184
LS mean (SE)	0.82 (0.27)	1.34 (0.27)
95% CI of LS mean	(0.29, 1.35)	(0.80, 1.87)
P-value within Treatment	0.0027	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-0.24, 1.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1785
Hedges' G (SE)		0.14 (0.10)
Hedges' 95% CI		(-0.06, 0.34)
Hedges' P-value		0.1791

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	144	147
mean (SD)	71.57 (13.16)	71.42 (13.53)
Week 52		
n	139	138
mean (SD)	72.79 (12.86)	72.52 (13.65)
Absolute Change at Week 52		
n	139	136
mean (SD)	0.91 (3.71)	1.15 (3.88)
Absolute Change at Week 52 (MMRM)		
n	131	132
LS mean (SE)	0.63 (0.32)	1.16 (0.32)
95% CI of LS mean	(0.00, 1.26)	(0.54, 1.79)
P-value within Treatment	0.0511	0.0003

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-0.35, 1.42)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2375
Hedges' G (SE)		0.15 (0.12)
Hedges' 95% CI		(-0.10, 0.39)
Hedges' P-value		0.2378

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	145	133
mean (SD)	58.57 (9.96)	61.23 (12.47)
Week 52		
n	136	120
mean (SD)	59.88 (10.03)	63.13 (12.72)
Absolute Change at Week 52		
n	136	118
mean (SD)	1.03 (3.32)	1.53 (3.95)
Absolute Change at Week 52 (MMRM)		
n	135	116
LS mean (SE)	0.99 (0.31)	1.49 (0.33)
95% CI of LS mean	(0.39, 1.60)	(0.85, 2.13)
P-value within Treatment	0.0014	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-0.39, 1.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2679
Hedges' G (SE)		0.14 (0.13)
Hedges' 95% CI		(-0.11, 0.39)
Hedges' P-value		0.2687

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	103	113
mean (SD)	67.86 (14.29)	68.77 (15.46)
Week 52		
n	100	104
mean (SD)	69.25 (14.85)	70.47 (15.30)
Absolute Change at Week 52		
n	100	103
mean (SD)	0.91 (3.86)	0.75 (3.80)
Absolute Change at Week 52 (MMRM)		
n	96	103
LS mean (SE)	0.83 (0.39)	0.70 (0.37)
95% CI of LS mean	(0.06, 1.59)	(-0.04, 1.43)
P-value within Treatment	0.0338	0.0627

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-1.19, 0.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8034
Hedges' G (SE)		-0.04 (0.14)
Hedges' 95% CI		(-0.31, 0.24)
Hedges' P-value		0.8034

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	186	167
mean (SD)	63.49 (12.56)	65.10 (12.72)
Week 52		
n	175	154
mean (SD)	64.78 (11.93)	66.58 (12.89)
Absolute Change at Week 52		
n	175	151
mean (SD)	1.01 (3.32)	1.72 (3.95)
Absolute Change at Week 52 (MMRM)		
n	170	145
LS mean (SE)	0.80 (0.27)	1.73 (0.28)
95% CI of LS mean	(0.28, 1.33)	(1.18, 2.29)
P-value within Treatment	0.0026	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups
Full Analysis Set

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (0.17, 1.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0173
Hedges' G (SE)		0.27 (0.11)
Hedges' 95% CI		(0.05, 0.49)
Hedges' P-value		0.0179

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Baseline		
n	250	239
mean (SD)	65.04 (13.64)	66.55 (14.24)
Week 52		
n	239	217
mean (SD)	66.21 (13.43)	67.79 (14.26)
Absolute Change at Week 52		
n	239	215
mean (SD)	0.78 (3.50)	0.98 (3.75)
Absolute Change at Week 52 (MMRM)		
n	232	212
LS mean (SE)	0.72 (0.23)	1.00 (0.24)
95% CI of LS mean	(0.26, 1.18)	(0.53, 1.48)
P-value within Treatment	0.0021	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.28 (-0.38, 0.94)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4049
Hedges' G (SE)		0.08 (0.09)
Hedges' 95% CI		(-0.11, 0.27)
Hedges' P-value		0.4054

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Baseline		
n	39	41
mean (SD)	65.08 (11.47)	66.77 (12.48)
Week 52		
n	36	41
mean (SD)	67.69 (11.77)	70.09 (12.60)
Absolute Change at Week 52		
n	36	39
mean (SD)	2.25 (3.43)	3.26 (4.27)
Absolute Change at Week 52 (MMRM)		
n	34	36
LS mean (SE)	1.30 (0.64)	3.24 (0.63)
95% CI of LS mean	(0.03, 2.57)	(1.99, 4.49)
P-value within Treatment	0.0448	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.94 (0.15, 3.72)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0338
Hedges' G (SE)		0.51 (0.24)
Hedges' 95% CI		(0.03, 0.99)
Hedges' P-value		0.0364

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Baseline		
n	224	218
mean (SD)	64.08 (12.83)	65.44 (13.52)
Week 52		
n	210	202
mean (SD)	65.46 (12.54)	67.00 (13.41)
Absolute Change at Week 52		
n	210	198
mean (SD)	0.95 (3.35)	1.42 (3.98)
Absolute Change at Week 52 (MMRM)		
n	204	195
LS mean (SE)	0.83 (0.25)	1.35 (0.25)
95% CI of LS mean	(0.33, 1.32)	(0.85, 1.85)
P-value within Treatment	0.0010	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-0.17, 1.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1397
Hedges' G (SE)		0.15 (0.10)
Hedges' 95% CI		(-0.05, 0.34)
Hedges' P-value		0.1403

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	20	19
mean (SD)	72.48 (12.65)	66.19 (13.33)
Week 52		
n	20	16
mean (SD)	72.68 (12.57)	67.19 (13.81)
Absolute Change at Week 52		
n	20	16
mean (SD)	0.20 (4.27)	0.15 (2.10)
Absolute Change at Week 52 (MMRM)		
n	19	15
LS mean (SE)	0.29 (0.81)	0.18 (0.90)
95% CI of LS mean	(-1.36, 1.93)	(-1.64, 2.00)
P-value within Treatment	0.7259	0.8391

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-2.56, 2.35)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9330
Hedges' G (SE)		-0.03 (0.34)
Hedges' 95% CI		(-0.72, 0.66)
Hedges' P-value		0.9331

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Baseline		
n	23	23
mean (SD)	68.13 (15.80)	73.49 (12.55)
Week 52		
n	23	23
mean (SD)	68.91 (16.46)	74.23 (12.98)
Absolute Change at Week 52		
n	23	23
mean (SD)	0.78 (3.99)	0.74 (3.78)
Absolute Change at Week 52 (MMRM)		
n	23	23
LS mean (SE)	0.78 (0.81)	0.74 (0.81)
95% CI of LS mean	(-0.86, 2.41)	(-0.89, 2.38)
P-value within Treatment	0.3427	0.3646

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-2.35, 2.28)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9759
Hedges' G (SE)		-0.01 (0.29)
Hedges' 95% CI		(-0.59, 0.58)
Hedges' P-value		0.9759

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	20
mean (SD)	64.95 (14.71)	71.42 (18.29)
Week 52		
n	22	17
mean (SD)	67.05 (15.27)	74.49 (19.24)
Absolute Change at Week 52		
n	22	17
mean (SD)	2.09 (3.83)	2.22 (4.56)
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	1.20 (0.83)	2.83 (0.93)
95% CI of LS mean	(-0.49, 2.89)	(0.95, 4.72)
P-value within Treatment	0.1587	0.0044

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.5.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-0.90, 4.17)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1992
Hedges' G (SE)		0.44 (0.34)
Hedges' 95% CI		(-0.25, 1.12)
Hedges' P-value		0.2056

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.6.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3664
Age at screening (<18 years vs. ≥18 years) [2]	0.5177
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.4264
Sex (Male vs. Female) [1]	0.7052
Region (North America vs. Rest of the World) [1]	0.9381

-Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$,(F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride.

Table 2.2.2.6.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation through Week 52 for Additional Subgroups
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
Prior CFTR modulator use (yes vs. no) [1]	0.0610
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.2840

-Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
-P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline ppFEV$_1$ and baseline sweat chloride, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline ppFEV$_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	41 (24.55)	36 (23.38)
Subjects Censored	126 (75.45)	118 (76.62)
Event-free time (weeks)		
75 percent subjects	51.4286	52.5714
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9940 (0.9583, 0.9992)	1.0000 (-, -)
4 Weeks	0.9760 (0.9374, 0.9909)	0.9935 (0.9548, 0.9991)
8 Weeks	0.9519 (0.9062, 0.9757)	0.9803 (0.9403, 0.9936)
12 Weeks	0.9218 (0.8692, 0.9538)	0.9407 (0.8891, 0.9687)
16 Weeks	0.8915 (0.8333, 0.9302)	0.9007 (0.8406, 0.9389)
24 Weeks	0.8485 (0.7841, 0.8950)	0.8398 (0.7705, 0.8896)
36 Weeks	0.8051 (0.7358, 0.8580)	0.7991 (0.7254, 0.8550)
52 Weeks	0.7486 (0.6744, 0.8082)	0.7650 (0.6883, 0.8253)
Hazard Ratio (95% CI)*	-	0.9453 (0.6010, 1.4867)
Two-sided P-value, superiority*	-	0.8076

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	18 (15.13)	24 (19.20)
Subjects Censored	101 (84.87)	101 (80.80)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9664 (0.9129, 0.9872)	0.9760 (0.9274, 0.9922)
4 Weeks	0.9580 (0.9020, 0.9823)	0.9600 (0.9066, 0.9832)
8 Weeks	0.9412 (0.8806, 0.9715)	0.9440 (0.8861, 0.9729)
12 Weeks	0.9328 (0.8701, 0.9658)	0.9038 (0.8368, 0.9442)
16 Weeks	0.9328 (0.8701, 0.9658)	0.8956 (0.8271, 0.9380)
24 Weeks	0.9244 (0.8597, 0.9599)	0.8793 (0.8078, 0.9254)
36 Weeks	0.8908 (0.8193, 0.9351)	0.8374 (0.7593, 0.8919)
52 Weeks	0.8451 (0.7649, 0.8997)	0.8035 (0.7211, 0.8638)
Hazard Ratio (95% CI)*	-	1.2934 (0.6985, 2.3952)
Two-sided P-value, superiority*	-	0.4131

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	4 (10.53)	8 (19.51)
Subjects Censored	34 (89.47)	33 (80.49)
Event-free time (weeks)		
75 percent subjects	-	52.5714
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9512 (0.8187, 0.9876)
4 Weeks	1.0000 (-, -)	0.9512 (0.8187, 0.9876)
8 Weeks	1.0000 (-, -)	0.9512 (0.8187, 0.9876)
12 Weeks	1.0000 (-, -)	0.9512 (0.8187, 0.9876)
16 Weeks	0.9730 (0.8232, 0.9961)	0.9018 (0.7591, 0.9620)
24 Weeks	0.9452 (0.7980, 0.9860)	0.9018 (0.7591, 0.9620)
36 Weeks	0.9174 (0.7652, 0.9726)	0.8745 (0.7238, 0.9458)
52 Weeks	0.8868 (0.7253, 0.9560)	0.8198 (0.6580, 0.9100)
Hazard Ratio (95% CI)*	-	1.6933 (0.4743, 6.0448)
Two-sided P-value, superiority*	-	0.4173

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	55 (21.91)	53 (21.81)
Subjects Censored	196 (78.09)	190 (78.19)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9801 (0.9528, 0.9917)	0.9959 (0.9711, 0.9994)
4 Weeks	0.9641 (0.9322, 0.9812)	0.9835 (0.9567, 0.9938)
8 Weeks	0.9402 (0.9028, 0.9635)	0.9669 (0.9350, 0.9833)
12 Weeks	0.9163 (0.8746, 0.9446)	0.9210 (0.8790, 0.9489)
16 Weeks	0.9003 (0.8561, 0.9315)	0.8958 (0.8497, 0.9284)
24 Weeks	0.8722 (0.8242, 0.9079)	0.8491 (0.7971, 0.8888)
36 Weeks	0.8318 (0.7793, 0.8728)	0.8067 (0.7505, 0.8515)
52 Weeks	0.7775 (0.7201, 0.8245)	0.7766 (0.7180, 0.8245)
Hazard Ratio (95% CI)*	-	1.0374 (0.7089, 1.5183)
Two-sided P-value, superiority*	-	0.8500

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	21 (26.25)	15 (20.83)
Subjects Censored	59 (73.75)	57 (79.17)
Event-free time (weeks)		
75 percent subjects	51.4286	52.5714
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
8 Weeks	0.9625 (0.8882, 0.9877)	1.0000 (-, -)
12 Weeks	0.9375 (0.8563, 0.9735)	0.9859 (0.9042, 0.9980)
16 Weeks	0.9125 (0.8252, 0.9573)	0.9432 (0.8558, 0.9783)
24 Weeks	0.8875 (0.7950, 0.9398)	0.8990 (0.7997, 0.9506)
36 Weeks	0.8246 (0.7219, 0.8922)	0.8543 (0.7460, 0.9189)
52 Weeks	0.7320 (0.6185, 0.8166)	0.7944 (0.6774, 0.8728)
Hazard Ratio (95% CI)*	-	0.8727 (0.4469, 1.7043)
Two-sided P-value, superiority*	-	0.6901

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	37 (18.32)	46 (21.90)
Subjects Censored	165 (81.68)	164 (78.10)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9752 (0.9416, 0.9896)	0.9857 (0.9564, 0.9954)
4 Weeks	0.9604 (0.9224, 0.9800)	0.9714 (0.9375, 0.9871)
8 Weeks	0.9405 (0.8976, 0.9658)	0.9523 (0.9131, 0.9740)
12 Weeks	0.9206 (0.8736, 0.9506)	0.9041 (0.8554, 0.9371)
16 Weeks	0.9056 (0.8560, 0.9387)	0.8799 (0.8274, 0.9172)
24 Weeks	0.8754 (0.8211, 0.9140)	0.8408 (0.7834, 0.8841)
36 Weeks	0.8501 (0.7926, 0.8927)	0.8015 (0.7403, 0.8498)
52 Weeks	0.8142 (0.7529, 0.8618)	0.7766 (0.7133, 0.8277)
Hazard Ratio (95% CI)*	-	1.1967 (0.7732, 1.8523)
Two-sided P-value, superiority*	-	0.4204

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	23 (15.97)	25 (16.78)
Subjects Censored	121 (84.03)	124 (83.22)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9861 (0.9456, 0.9965)	0.9866 (0.9474, 0.9966)
4 Weeks	0.9792 (0.9368, 0.9932)	0.9732 (0.9301, 0.9898)
8 Weeks	0.9512 (0.9003, 0.9764)	0.9664 (0.9212, 0.9859)
12 Weeks	0.9232 (0.8656, 0.9567)	0.9459 (0.8948, 0.9726)
16 Weeks	0.9232 (0.8656, 0.9567)	0.9321 (0.8775, 0.9629)
24 Weeks	0.9162 (0.8571, 0.9515)	0.9113 (0.8520, 0.9475)
36 Weeks	0.8878 (0.8233, 0.9297)	0.8765 (0.8111, 0.9203)
52 Weeks	0.8375 (0.7655, 0.8889)	0.8347 (0.7636, 0.8861)
Hazard Ratio (95% CI)*	-	1.0445 (0.5832, 1.8707)
Two-sided P-value, superiority*	-	0.8836

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	36 (24.83)	36 (26.67)
Subjects Censored	109 (75.17)	99 (73.33)
Event-free time (weeks)		
75 percent subjects	52.0000	37.5714
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9793 (0.9372, 0.9933)	0.9926 (0.9486, 0.9990)
4 Weeks	0.9586 (0.9102, 0.9812)	0.9852 (0.9421, 0.9963)
8 Weeks	0.9448 (0.8927, 0.9720)	0.9628 (0.9129, 0.9843)
12 Weeks	0.9310 (0.8756, 0.9623)	0.9031 (0.8390, 0.9425)
16 Weeks	0.8963 (0.8339, 0.9361)	0.8581 (0.7866, 0.9071)
24 Weeks	0.8475 (0.7777, 0.8968)	0.7969 (0.7179, 0.8560)
36 Weeks	0.7984 (0.7230, 0.8553)	0.7503 (0.6671, 0.8155)
52 Weeks	0.7457 (0.6648, 0.8098)	0.7263 (0.6412, 0.7944)
Hazard Ratio (95% CI)*	-	1.1903 (0.7420, 1.9092)
Two-sided P-value, superiority*	-	0.4700

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	21 (20.39)	26 (22.81)
Subjects Censored	82 (79.61)	88 (77.19)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9612 (0.8998, 0.9852)	1.0000 (-, -)
4 Weeks	0.9417 (0.8749, 0.9734)	0.9912 (0.9394, 0.9988)
8 Weeks	0.9223 (0.8507, 0.9604)	0.9735 (0.9202, 0.9914)
12 Weeks	0.9126 (0.8388, 0.9535)	0.9558 (0.8971, 0.9814)
16 Weeks	0.9028 (0.8269, 0.9465)	0.9200 (0.8519, 0.9576)
24 Weeks	0.9028 (0.8269, 0.9465)	0.8654 (0.7866, 0.9166)
36 Weeks	0.8537 (0.7692, 0.9091)	0.8196 (0.7344, 0.8797)
52 Weeks	0.7949 (0.7029, 0.8611)	0.7639 (0.6729, 0.8327)
Hazard Ratio (95% CI)*	-	1.0432 (0.5812, 1.8723)
Two-sided P-value, superiority*	-	0.8874

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	38 (20.43)	35 (20.59)
Subjects Censored	148 (79.57)	135 (79.41)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9946 (0.9625, 0.9992)	0.9824 (0.9463, 0.9943)
4 Weeks	0.9839 (0.9508, 0.9948)	0.9706 (0.9308, 0.9877)
8 Weeks	0.9622 (0.9224, 0.9818)	0.9588 (0.9154, 0.9801)
12 Weeks	0.9352 (0.8887, 0.9627)	0.9052 (0.8500, 0.9408)
16 Weeks	0.9136 (0.8628, 0.9462)	0.8812 (0.8220, 0.9217)
24 Weeks	0.8699 (0.8122, 0.9109)	0.8509 (0.7874, 0.8967)
36 Weeks	0.8368 (0.7750, 0.8830)	0.8143 (0.7464, 0.8656)
52 Weeks	0.7900 (0.7228, 0.8428)	0.7957 (0.7260, 0.8495)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Hazard Ratio (95% CI)*	-	1.0859 (0.6831, 1.7260)
Two-sided P-value, superiority*	-	0.7275

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.6.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	54 (21.60)	49 (20.33)
Subjects Censored	196 (78.40)	192 (79.67)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9800 (0.9526, 0.9916)	0.9876 (0.9619, 0.9960)
4 Weeks	0.9680 (0.9370, 0.9839)	0.9793 (0.9509, 0.9913)
8 Weeks	0.9439 (0.9071, 0.9664)	0.9626 (0.9293, 0.9804)
12 Weeks	0.9198 (0.8784, 0.9475)	0.9291 (0.8884, 0.9553)
16 Weeks	0.9037 (0.8598, 0.9344)	0.9037 (0.8586, 0.9349)
24 Weeks	0.8754 (0.8276, 0.9107)	0.8693 (0.8193, 0.9062)
36 Weeks	0.8306 (0.7777, 0.8719)	0.8303 (0.7759, 0.8726)
52 Weeks	0.7795 (0.7219, 0.8266)	0.7953 (0.7377, 0.8416)
Hazard Ratio (95% CI)*	-	0.9295 (0.6286, 1.3744)
Two-sided P-value, superiority*	-	0.7142

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.6.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	5 (12.82)	12 (27.91)
Subjects Censored	34 (87.18)	31 (72.09)
Event-free time (weeks)		
75 percent subjects	-	36.1429
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9744 (0.8316, 0.9963)	0.9767 (0.8462, 0.9967)
8 Weeks	0.9744 (0.8316, 0.9963)	0.9767 (0.8462, 0.9967)
12 Weeks	0.9744 (0.8316, 0.9963)	0.9053 (0.7670, 0.9634)
16 Weeks	0.9480 (0.8077, 0.9867)	0.8576 (0.7102, 0.9334)
24 Weeks	0.9217 (0.7765, 0.9741)	0.7862 (0.6293, 0.8825)
36 Weeks	0.9217 (0.7765, 0.9741)	0.7385 (0.5777, 0.8458)
52 Weeks	0.8675 (0.7103, 0.9426)	0.7147 (0.5526, 0.8268)
Hazard Ratio (95% CI)*	-	2.8661 (0.9466, 8.6782)
Two-sided P-value, superiority*	-	0.0625

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.6.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	50 (22.32)	46 (20.72)
Subjects Censored	174 (77.68)	176 (79.28)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9821 (0.9531, 0.9933)	0.9865 (0.9587, 0.9956)
4 Weeks	0.9643 (0.9299, 0.9820)	0.9730 (0.9408, 0.9878)
8 Weeks	0.9374 (0.8965, 0.9624)	0.9549 (0.9177, 0.9755)
12 Weeks	0.9239 (0.8805, 0.9520)	0.9184 (0.8737, 0.9478)
16 Weeks	0.9104 (0.8646, 0.9412)	0.8909 (0.8417, 0.9255)
24 Weeks	0.8740 (0.8228, 0.9113)	0.8677 (0.8152, 0.9061)
36 Weeks	0.8282 (0.7717, 0.8719)	0.8260 (0.7688, 0.8702)
52 Weeks	0.7708 (0.7088, 0.8213)	0.7932 (0.7331, 0.8413)
Hazard Ratio (95% CI)*	-	0.9277 (0.6184, 1.3918)
Two-sided P-value, superiority*	-	0.7170

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.6.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	2 (10.00)	4 (21.05)
Subjects Censored	18 (90.00)	15 (78.95)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	0.9500 (0.6947, 0.9928)	0.9474 (0.6812, 0.9924)
16 Weeks	0.9500 (0.6947, 0.9928)	0.9474 (0.6812, 0.9924)
24 Weeks	0.9500 (0.6947, 0.9928)	0.8882 (0.6207, 0.9709)
36 Weeks	0.9000 (0.6560, 0.9740)	0.8247 (0.5471, 0.9403)
52 Weeks	0.9000 (0.6560, 0.9740)	0.7613 (0.4798, 0.9037)
Hazard Ratio (95% CI)*	-	2.8134 (0.4852, 16.3119)
Two-sided P-value, superiority*	-	0.2487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.6.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	5 (21.74)	6 (26.09)
Subjects Censored	18 (78.26)	17 (73.91)
Event-free time (weeks)		
75 percent subjects	-	42.7143
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	0.9565 (0.7293, 0.9938)	1.0000 (-, -)
4 Weeks	0.9565 (0.7293, 0.9938)	1.0000 (-, -)
8 Weeks	0.9565 (0.7293, 0.9938)	1.0000 (-, -)
12 Weeks	0.9130 (0.6949, 0.9775)	1.0000 (-, -)
16 Weeks	0.8696 (0.6481, 0.9560)	0.9565 (0.7293, 0.9938)
24 Weeks	0.8696 (0.6481, 0.9560)	0.8261 (0.6006, 0.9309)
36 Weeks	0.8696 (0.6481, 0.9560)	0.7826 (0.5542, 0.9032)
52 Weeks	0.7802 (0.5497, 0.9022)	0.7391 (0.5092, 0.8734)
Hazard Ratio (95% CI)*	-	1.2620 (0.3740, 4.2588)
Two-sided P-value, superiority*	-	0.7077

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.6.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Any Pulmonary Exacerbation		
Overall		
Subjects with Events	2 (9.09)	5 (25.00)
Subjects Censored	20 (90.91)	15 (75.00)
Event-free time (weeks)		
75 percent subjects	-	19.7143
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	0.9545 (0.7187, 0.9935)	0.8947 (0.6408, 0.9726)
16 Weeks	0.9091 (0.6830, 0.9765)	0.8421 (0.5865, 0.9462)
24 Weeks	0.9091 (0.6830, 0.9765)	0.7368 (0.4789, 0.8810)
36 Weeks	0.9091 (0.6830, 0.9765)	0.7368 (0.4789, 0.8810)
52 Weeks	0.9091 (0.6830, 0.9765)	0.7368 (0.4789, 0.8810)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.6.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Hazard Ratio (95% CI)*	-	3.3603 (0.6178, 18.2778)
Two-sided P-value, superiority*	-	0.1607

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.2.7.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation Requiring Hospitalizatio through Week 52
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3882
Age at screening (<18 years vs. ≥18 years) [2]	0.2962
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1969
Sex (Male vs. Female) [1]	0.5194
Region (North America vs. Rest of the World) [1]	0.4918

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$,(F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride.

Table 2.2.2.7.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Additional Subgroups
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
Prior CFTR modulator use (yes vs. no) [1]	0.9988
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	>0.9999

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline ppFEV$_1$ and baseline sweat chloride, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline ppFEV$_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

$ppFEV_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	6 (3.59)	6 (3.90)
Subjects Censored	161 (96.41)	148 (96.10)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	0.9935 (0.9548, 0.9991)
8 Weeks	1.0000 (-, -)	0.9935 (0.9548, 0.9991)
12 Weeks	0.9940 (0.9580, 0.9991)	0.9935 (0.9548, 0.9991)
16 Weeks	0.9940 (0.9580, 0.9991)	0.9935 (0.9548, 0.9991)
24 Weeks	0.9755 (0.9361, 0.9907)	0.9800 (0.9392, 0.9935)
36 Weeks	0.9755 (0.9361, 0.9907)	0.9597 (0.9125, 0.9817)
52 Weeks	0.9629 (0.9194, 0.9832)	0.9597 (0.9125, 0.9817)
Hazard Ratio (95% CI)*	-	1.0039 (0.3213, 3.1364)
Two-sided P-value, superiority*	-	0.9946

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

$ppFEV_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	3 (2.52)	7 (5.60)
Subjects Censored	116 (97.48)	118 (94.40)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9920 (0.9446, 0.9989)
4 Weeks	0.9916 (0.9419, 0.9988)	0.9920 (0.9446, 0.9989)
8 Weeks	0.9916 (0.9419, 0.9988)	0.9920 (0.9446, 0.9989)
12 Weeks	0.9916 (0.9419, 0.9988)	0.9920 (0.9446, 0.9989)
16 Weeks	0.9916 (0.9419, 0.9988)	0.9839 (0.9370, 0.9959)
24 Weeks	0.9916 (0.9419, 0.9988)	0.9757 (0.9265, 0.9921)
36 Weeks	0.9748 (0.9239, 0.9918)	0.9507 (0.8934, 0.9775)
52 Weeks	0.9748 (0.9239, 0.9918)	0.9421 (0.8823, 0.9720)
Hazard Ratio (95% CI)*	-	2.1496 (0.5502, 8.3978)
Two-sided P-value, superiority*	-	0.2710

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	1 (2.63)	5 (12.20)
Subjects Censored	37 (97.37)	36 (87.80)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
4 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
8 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
12 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
16 Weeks	1.0000 (-, -)	0.9262 (0.7883, 0.9756)
24 Weeks	0.9722 (0.8187, 0.9960)	0.9262 (0.7883, 0.9756)
36 Weeks	0.9722 (0.8187, 0.9960)	0.8989 (0.7523, 0.9609)
52 Weeks	0.9722 (0.8187, 0.9960)	0.8717 (0.7182, 0.9446)
Hazard Ratio (95% CI)*	-	13.4580 (0.7881, 229.8245)
Two-sided P-value, superiority*	-	0.0726

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	8 (3.19)	9 (3.70)
Subjects Censored	243 (96.81)	234 (96.30)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9960 (0.9721, 0.9994)	0.9959 (0.9711, 0.9994)
8 Weeks	0.9960 (0.9721, 0.9994)	0.9959 (0.9711, 0.9994)
12 Weeks	0.9920 (0.9685, 0.9980)	0.9959 (0.9711, 0.9994)
16 Weeks	0.9920 (0.9685, 0.9980)	0.9959 (0.9711, 0.9994)
24 Weeks	0.9840 (0.9578, 0.9940)	0.9832 (0.9558, 0.9937)
36 Weeks	0.9759 (0.9471, 0.9891)	0.9620 (0.9282, 0.9800)
52 Weeks	0.9677 (0.9364, 0.9837)	0.9620 (0.9282, 0.9800)
Hazard Ratio (95% CI)*	-	1.1516 (0.4431, 2.9925)
Two-sided P-value, superiority*	-	0.7721

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	4 (5.00)	2 (2.78)
Subjects Censored	76 (95.00)	70 (97.22)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
8 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
12 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
16 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
24 Weeks	0.9625 (0.8882, 0.9877)	1.0000 (-, -)
36 Weeks	0.9625 (0.8882, 0.9877)	0.9704 (0.8867, 0.9925)
52 Weeks	0.9497 (0.8714, 0.9808)	0.9704 (0.8867, 0.9925)
Hazard Ratio (95% CI)*	-	0.5144 (0.0900, 2.9397)
Two-sided P-value, superiority*	-	0.4548

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	5 (2.48)	12 (5.71)
Subjects Censored	197 (97.52)	198 (94.29)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9952 (0.9667, 0.9993)
4 Weeks	1.0000 (-, -)	0.9905 (0.9625, 0.9976)
8 Weeks	1.0000 (-, -)	0.9905 (0.9625, 0.9976)
12 Weeks	0.9950 (0.9652, 0.9993)	0.9905 (0.9625, 0.9976)
16 Weeks	0.9950 (0.9652, 0.9993)	0.9808 (0.9496, 0.9927)
24 Weeks	0.9900 (0.9606, 0.9975)	0.9662 (0.9303, 0.9837)
36 Weeks	0.9799 (0.9473, 0.9924)	0.9465 (0.9055, 0.9700)
52 Weeks	0.9748 (0.9406, 0.9894)	0.9415 (0.8993, 0.9664)
Hazard Ratio (95% CI)*	-	2.1398 (0.7423, 6.1685)
Two-sided P-value, superiority*	-	0.1590

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	2 (1.39)	5 (3.36)
Subjects Censored	142 (98.61)	144 (96.64)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9933 (0.9533, 0.9991)
4 Weeks	1.0000 (-, -)	0.9866 (0.9474, 0.9966)
8 Weeks	1.0000 (-, -)	0.9866 (0.9474, 0.9966)
12 Weeks	0.9930 (0.9514, 0.9990)	0.9866 (0.9474, 0.9966)
16 Weeks	0.9930 (0.9514, 0.9990)	0.9866 (0.9474, 0.9966)
24 Weeks	0.9930 (0.9514, 0.9990)	0.9866 (0.9474, 0.9966)
36 Weeks	0.9930 (0.9514, 0.9990)	0.9727 (0.9288, 0.9897)
52 Weeks	0.9858 (0.9442, 0.9964)	0.9657 (0.9196, 0.9856)
Hazard Ratio (95% CI)*	-	2.3632 (0.4520, 12.3556)
Two-sided P-value, superiority*	-	0.3082

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	7 (4.83)	9 (6.67)
Subjects Censored	138 (95.17)	126 (93.33)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9931 (0.9521, 0.9990)	1.0000 (-, -)
8 Weeks	0.9931 (0.9521, 0.9990)	1.0000 (-, -)
12 Weeks	0.9931 (0.9521, 0.9990)	1.0000 (-, -)
16 Weeks	0.9931 (0.9521, 0.9990)	0.9850 (0.9414, 0.9962)
24 Weeks	0.9722 (0.9276, 0.9895)	0.9621 (0.9114, 0.9841)
36 Weeks	0.9582 (0.9093, 0.9810)	0.9312 (0.8719, 0.9636)
52 Weeks	0.9511 (0.9002, 0.9764)	0.9312 (0.8719, 0.9636)
Hazard Ratio (95% CI)*	-	1.2198 (0.4374, 3.4020)
Two-sided P-value, superiority*	-	0.7041

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	3 (2.91)	8 (7.02)
Subjects Censored	100 (97.09)	106 (92.98)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	1.0000 (-, -)
16 Weeks	1.0000 (-, -)	0.9821 (0.9302, 0.9955)
24 Weeks	1.0000 (-, -)	0.9548 (0.8948, 0.9809)
36 Weeks	0.9804 (0.9239, 0.9951)	0.9364 (0.8712, 0.9692)
52 Weeks	0.9705 (0.9113, 0.9904)	0.9271 (0.8596, 0.9629)
Hazard Ratio (95% CI)*	-	2.1660 (0.5519, 8.5007)
Two-sided P-value, superiority*	-	0.2679

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	6 (3.23)	6 (3.53)
Subjects Censored	180 (96.77)	164 (96.47)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9941 (0.9590, 0.9992)
4 Weeks	0.9946 (0.9625, 0.9992)	0.9882 (0.9538, 0.9970)
8 Weeks	0.9946 (0.9625, 0.9992)	0.9882 (0.9538, 0.9970)
12 Weeks	0.9892 (0.9576, 0.9973)	0.9882 (0.9538, 0.9970)
16 Weeks	0.9892 (0.9576, 0.9973)	0.9882 (0.9538, 0.9970)
24 Weeks	0.9728 (0.9359, 0.9886)	0.9882 (0.9538, 0.9970)
36 Weeks	0.9728 (0.9359, 0.9886)	0.9639 (0.9213, 0.9836)
52 Weeks	0.9672 (0.9285, 0.9851)	0.9639 (0.9213, 0.9836)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Hazard Ratio (95% CI)*	-	1.1096 (0.3577, 3.4427)
Two-sided P-value, superiority*	-	0.8571

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.7.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	8 (3.20)	12 (4.98)
Subjects Censored	242 (96.80)	229 (95.02)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9959 (0.9709, 0.9994)
4 Weeks	1.0000 (-, -)	0.9917 (0.9672, 0.9979)
8 Weeks	1.0000 (-, -)	0.9917 (0.9672, 0.9979)
12 Weeks	0.9960 (0.9718, 0.9994)	0.9917 (0.9672, 0.9979)
16 Weeks	0.9960 (0.9718, 0.9994)	0.9833 (0.9560, 0.9937)
24 Weeks	0.9838 (0.9575, 0.9939)	0.9704 (0.9389, 0.9858)
36 Weeks	0.9757 (0.9467, 0.9890)	0.9531 (0.9169, 0.9737)
52 Weeks	0.9674 (0.9359, 0.9836)	0.9487 (0.9114, 0.9705)
Hazard Ratio (95% CI)*	-	1.4202 (0.5699, 3.5389)
Two-sided P-value, superiority*	-	0.4515

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.7.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	1 (2.56)	2 (4.65)
Subjects Censored	38 (97.44)	41 (95.35)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9744 (0.8316, 0.9963)	1.0000 (-, -)
8 Weeks	0.9744 (0.8316, 0.9963)	1.0000 (-, -)
12 Weeks	0.9744 (0.8316, 0.9963)	1.0000 (-, -)
16 Weeks	0.9744 (0.8316, 0.9963)	1.0000 (-, -)
24 Weeks	0.9744 (0.8316, 0.9963)	1.0000 (-, -)
36 Weeks	0.9744 (0.8316, 0.9963)	0.9524 (0.8227, 0.9879)
52 Weeks	0.9744 (0.8316, 0.9963)	0.9524 (0.8227, 0.9879)
Hazard Ratio (95% CI)*	-	1.3088 (0.0677, 25.3193)
Two-sided P-value, superiority*	-	0.8587

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.7.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Additional Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	5 (2.23)	14 (6.31)
Subjects Censored	219 (97.77)	208 (93.69)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9955 (0.9685, 0.9994)
4 Weeks	0.9955 (0.9687, 0.9994)	0.9910 (0.9645, 0.9977)
8 Weeks	0.9955 (0.9687, 0.9994)	0.9910 (0.9645, 0.9977)
12 Weeks	0.9911 (0.9647, 0.9978)	0.9910 (0.9645, 0.9977)
16 Weeks	0.9911 (0.9647, 0.9978)	0.9818 (0.9523, 0.9931)
24 Weeks	0.9911 (0.9647, 0.9978)	0.9679 (0.9339, 0.9846)
36 Weeks	0.9865 (0.9587, 0.9956)	0.9402 (0.8992, 0.9648)
52 Weeks	0.9772 (0.9460, 0.9904)	0.9355 (0.8934, 0.9613)
Hazard Ratio (95% CI)*	-	2.6357 (0.9384, 7.4028)
Two-sided P-value, superiority*	-	0.0659

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.7.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Additional Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	1 (5.00)	0
Subjects Censored	19 (95.00)	19 (100.00)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	1.0000 (-, -)
16 Weeks	1.0000 (-, -)	1.0000 (-, -)
24 Weeks	0.9500 (0.6947, 0.9928)	1.0000 (-, -)
36 Weeks	0.9500 (0.6947, 0.9928)	1.0000 (-, -)
52 Weeks	0.9500 (0.6947, 0.9928)	1.0000 (-, -)
Hazard Ratio (95% CI)*	-	N/C
Two-sided P-value, superiority*	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.7.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Additional Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	2 (8.70)	0
Subjects Censored	21 (91.30)	23 (100.00)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	1.0000 (-, -)
16 Weeks	1.0000 (-, -)	1.0000 (-, -)
24 Weeks	0.9565 (0.7293, 0.9938)	1.0000 (-, -)
36 Weeks	0.9130 (0.6949, 0.9775)	1.0000 (-, -)
52 Weeks	0.9130 (0.6949, 0.9775)	1.0000 (-, -)
Hazard Ratio (95% CI)*	-	N/C
Two-sided P-value, superiority*	-	0.9977

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.7.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization		
Overall		
Subjects with Events	1 (4.55)	0
Subjects Censored	21 (95.45)	20 (100.00)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	1.0000 (-, -)
16 Weeks	1.0000 (-, -)	1.0000 (-, -)
24 Weeks	0.9545 (0.7187, 0.9935)	1.0000 (-, -)
36 Weeks	0.9545 (0.7187, 0.9935)	1.0000 (-, -)
52 Weeks	0.9545 (0.7187, 0.9935)	1.0000 (-, -)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.7.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Hazard Ratio (95% CI)*	-	N/C
Two-sided P-value, superiority*	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.8.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1668
Age at screening (<18 years vs. ≥18 years) [2]	0.2029
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.7654
Sex (Male vs. Female) [1]	0.8345
Region (North America vs. Rest of the World) [1]	0.2591

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$ and baseline sweat chloride,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline $ppFEV_1$,(F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride.

Table 2.2.2.8.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Additional Subgroups
Full Analysis Set

Subgroup	P-value for Interaction based on Hazard Ratio
Prior CFTR modulator use (yes vs. no) [1]	0.7751
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	>0.9999

- Subgroup Criteria (SC): subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when SC are fulfilled. If not, display '-'.
- [1] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline ppFEV$_1$ and baseline sweat chloride, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- [2] P-values are for the Hazard ratio from the Cox proportional hazards regression model for time to first event or censoring, with treatment, subgroup, treatment*subgroup, and adjustment for baseline ppFEV$_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

$ppFEV_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	13 (7.78)	9 (5.84)
Subjects Censored	154 (92.22)	145 (94.16)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9940 (0.9583, 0.9992)	0.9935 (0.9548, 0.9991)
8 Weeks	0.9880 (0.9528, 0.9970)	0.9869 (0.9487, 0.9967)
12 Weeks	0.9759 (0.9372, 0.9909)	0.9869 (0.9487, 0.9967)
16 Weeks	0.9759 (0.9372, 0.9909)	0.9869 (0.9487, 0.9967)
24 Weeks	0.9452 (0.8973, 0.9711)	0.9600 (0.9131, 0.9818)
36 Weeks	0.9329 (0.8820, 0.9622)	0.9397 (0.8873, 0.9682)
52 Weeks	0.9202 (0.8666, 0.9529)	0.9397 (0.8873, 0.9682)
Hazard Ratio (95% CI)*	-	0.7584 (0.3187, 1.8044)
Two-sided P-value, superiority*	-	0.5317

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

$ppFEV_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	4 (3.36)	9 (7.20)
Subjects Censored	115 (96.64)	116 (92.80)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9920 (0.9446, 0.9989)
4 Weeks	0.9916 (0.9419, 0.9988)	0.9920 (0.9446, 0.9989)
8 Weeks	0.9916 (0.9419, 0.9988)	0.9920 (0.9446, 0.9989)
12 Weeks	0.9832 (0.9345, 0.9958)	0.9839 (0.9373, 0.9960)
16 Weeks	0.9832 (0.9345, 0.9958)	0.9758 (0.9269, 0.9921)
24 Weeks	0.9832 (0.9345, 0.9958)	0.9676 (0.9160, 0.9877)
36 Weeks	0.9748 (0.9239, 0.9918)	0.9426 (0.8833, 0.9722)
52 Weeks	0.9664 (0.9129, 0.9872)	0.9256 (0.8618, 0.9606)
Hazard Ratio (95% CI)*	-	2.0885 (0.6364, 6.8540)
Two-sided P-value, superiority*	-	0.2245

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	1 (2.63)	5 (12.20)
Subjects Censored	37 (97.37)	36 (87.80)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
4 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
8 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
12 Weeks	1.0000 (-, -)	0.9756 (0.8392, 0.9965)
16 Weeks	1.0000 (-, -)	0.9262 (0.7883, 0.9756)
24 Weeks	0.9722 (0.8187, 0.9960)	0.9262 (0.7883, 0.9756)
36 Weeks	0.9722 (0.8187, 0.9960)	0.8989 (0.7523, 0.9609)
52 Weeks	0.9722 (0.8187, 0.9960)	0.8717 (0.7182, 0.9446)
Hazard Ratio (95% CI)*	-	13.4580 (0.7881, 229.8245)
Two-sided P-value, superiority*	-	0.0726

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	16 (6.37)	14 (5.76)
Subjects Censored	235 (93.63)	229 (94.24)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9920 (0.9685, 0.9980)	0.9959 (0.9711, 0.9994)
8 Weeks	0.9880 (0.9634, 0.9961)	0.9917 (0.9674, 0.9979)
12 Weeks	0.9761 (0.9476, 0.9892)	0.9876 (0.9619, 0.9960)
16 Weeks	0.9761 (0.9476, 0.9892)	0.9876 (0.9619, 0.9960)
24 Weeks	0.9600 (0.9269, 0.9783)	0.9664 (0.9339, 0.9831)
36 Weeks	0.9479 (0.9119, 0.9694)	0.9452 (0.9075, 0.9678)
52 Weeks	0.9356 (0.8971, 0.9601)	0.9409 (0.9023, 0.9646)
Hazard Ratio (95% CI)*	-	0.9219 (0.4433, 1.9169)
Two-sided P-value, superiority*	-	0.8276

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	4 (5.00)	3 (4.17)
Subjects Censored	76 (95.00)	69 (95.83)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
8 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
12 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
16 Weeks	0.9875 (0.9146, 0.9982)	1.0000 (-, -)
24 Weeks	0.9625 (0.8882, 0.9877)	0.9855 (0.9016, 0.9979)
36 Weeks	0.9625 (0.8882, 0.9877)	0.9559 (0.8693, 0.9856)
52 Weeks	0.9497 (0.8714, 0.9808)	0.9559 (0.8693, 0.9856)
Hazard Ratio (95% CI)*	-	0.8429 (0.1775, 4.0019)
Two-sided P-value, superiority*	-	0.8297

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	12 (5.94)	16 (7.62)
Subjects Censored	190 (94.06)	194 (92.38)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9952 (0.9667, 0.9993)
4 Weeks	0.9950 (0.9654, 0.9993)	0.9905 (0.9625, 0.9976)
8 Weeks	0.9901 (0.9609, 0.9975)	0.9857 (0.9563, 0.9954)
12 Weeks	0.9751 (0.9413, 0.9896)	0.9809 (0.9498, 0.9928)
16 Weeks	0.9751 (0.9413, 0.9896)	0.9712 (0.9370, 0.9869)
24 Weeks	0.9600 (0.9217, 0.9798)	0.9517 (0.9120, 0.9737)
36 Weeks	0.9499 (0.9089, 0.9727)	0.9320 (0.8879, 0.9592)
52 Weeks	0.9398 (0.8964, 0.9654)	0.9221 (0.8759, 0.9515)
Hazard Ratio (95% CI)*	-	1.1670 (0.5450, 2.4990)
Two-sided P-value, superiority*	-	0.6909

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	5 (3.47)	5 (3.36)
Subjects Censored	139 (96.53)	144 (96.64)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9933 (0.9533, 0.9991)
4 Weeks	1.0000 (-, -)	0.9866 (0.9474, 0.9966)
8 Weeks	0.9930 (0.9514, 0.9990)	0.9866 (0.9474, 0.9966)
12 Weeks	0.9860 (0.9452, 0.9965)	0.9866 (0.9474, 0.9966)
16 Weeks	0.9860 (0.9452, 0.9965)	0.9866 (0.9474, 0.9966)
24 Weeks	0.9860 (0.9452, 0.9965)	0.9866 (0.9474, 0.9966)
36 Weeks	0.9789 (0.9361, 0.9932)	0.9727 (0.9288, 0.9897)
52 Weeks	0.9646 (0.9170, 0.9851)	0.9657 (0.9196, 0.9856)
Hazard Ratio (95% CI)*	-	1.0971 (0.2900, 4.1506)
Two-sided P-value, superiority*	-	0.8914

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	12 (8.28)	14 (10.37)
Subjects Censored	133 (91.72)	121 (89.63)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9862 (0.9460, 0.9965)	1.0000 (-, -)
8 Weeks	0.9862 (0.9460, 0.9965)	0.9925 (0.9482, 0.9989)
12 Weeks	0.9724 (0.9282, 0.9896)	0.9851 (0.9416, 0.9962)
16 Weeks	0.9724 (0.9282, 0.9896)	0.9701 (0.9223, 0.9887)
24 Weeks	0.9375 (0.8834, 0.9670)	0.9320 (0.8733, 0.9640)
36 Weeks	0.9235 (0.8662, 0.9569)	0.9010 (0.8356, 0.9413)
52 Weeks	0.9165 (0.8576, 0.9517)	0.8932 (0.8263, 0.9353)
Hazard Ratio (95% CI)*	-	1.2211 (0.5520, 2.7015)
Two-sided P-value, superiority*	-	0.6219

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	4 (3.88)	10 (8.77)
Subjects Censored	99 (96.12)	104 (91.23)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9903 (0.9331, 0.9986)	1.0000 (-, -)
8 Weeks	0.9903 (0.9331, 0.9986)	1.0000 (-, -)
12 Weeks	0.9806 (0.9246, 0.9951)	1.0000 (-, -)
16 Weeks	0.9806 (0.9246, 0.9951)	0.9821 (0.9302, 0.9955)
24 Weeks	0.9806 (0.9246, 0.9951)	0.9457 (0.8831, 0.9752)
36 Weeks	0.9708 (0.9121, 0.9905)	0.9273 (0.8599, 0.9630)
52 Weeks	0.9609 (0.8991, 0.9851)	0.9089 (0.8372, 0.9499)
Hazard Ratio (95% CI)*	-	1.9655 (0.5995, 6.4444)
Two-sided P-value, superiority*	-	0.2647

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	13 (6.99)	9 (5.29)
Subjects Censored	173 (93.01)	161 (94.71)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9941 (0.9590, 0.9992)
4 Weeks	0.9946 (0.9625, 0.9992)	0.9882 (0.9538, 0.9970)
8 Weeks	0.9892 (0.9576, 0.9973)	0.9823 (0.9462, 0.9943)
12 Weeks	0.9784 (0.9435, 0.9918)	0.9764 (0.9383, 0.9911)
16 Weeks	0.9784 (0.9435, 0.9918)	0.9764 (0.9383, 0.9911)
24 Weeks	0.9510 (0.9080, 0.9742)	0.9704 (0.9303, 0.9876)
36 Weeks	0.9400 (0.8944, 0.9663)	0.9460 (0.8988, 0.9715)
52 Weeks	0.9290 (0.8808, 0.9581)	0.9460 (0.8988, 0.9715)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Hazard Ratio (95% CI)*	-	0.8210 (0.3448, 1.9545)
Two-sided P-value, superiority*	-	0.6558

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl,(F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Table 2.2.2.8.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	16 (6.40)	17 (7.05)
Subjects Censored	234 (93.60)	224 (92.95)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9959 (0.9709, 0.9994)
4 Weeks	0.9960 (0.9719, 0.9994)	0.9917 (0.9672, 0.9979)
8 Weeks	0.9920 (0.9683, 0.9980)	0.9875 (0.9619, 0.9960)
12 Weeks	0.9799 (0.9525, 0.9916)	0.9833 (0.9562, 0.9937)
16 Weeks	0.9799 (0.9525, 0.9916)	0.9749 (0.9450, 0.9886)
24 Weeks	0.9597 (0.9263, 0.9781)	0.9535 (0.9175, 0.9740)
36 Weeks	0.9475 (0.9113, 0.9692)	0.9362 (0.8963, 0.9610)
52 Weeks	0.9351 (0.8962, 0.9597)	0.9274 (0.8859, 0.9543)
Hazard Ratio (95% CI)*	-	1.0612 (0.5236, 2.1510)
Two-sided P-value, superiority*	-	0.8691

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.8.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Additional Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	1 (2.56)	2 (4.65)
Subjects Censored	38 (97.44)	41 (95.35)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	0.9744 (0.8316, 0.9963)	1.0000 (-, -)
8 Weeks	0.9744 (0.8316, 0.9963)	1.0000 (-, -)
12 Weeks	0.9744 (0.8316, 0.9963)	1.0000 (-, -)
16 Weeks	0.9744 (0.8316, 0.9963)	1.0000 (-, -)
24 Weeks	0.9744 (0.8316, 0.9963)	1.0000 (-, -)
36 Weeks	0.9744 (0.8316, 0.9963)	0.9524 (0.8227, 0.9879)
52 Weeks	0.9744 (0.8316, 0.9963)	0.9524 (0.8227, 0.9879)
Hazard Ratio (95% CI)*	-	1.3088 (0.0677, 25.3193)
Two-sided P-value, superiority*	-	0.8587

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.8.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Additional Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	12 (5.36)	19 (8.56)
Subjects Censored	212 (94.64)	203 (91.44)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	0.9955 (0.9685, 0.9994)
4 Weeks	0.9911 (0.9648, 0.9978)	0.9910 (0.9645, 0.9977)
8 Weeks	0.9866 (0.9590, 0.9957)	0.9865 (0.9586, 0.9956)
12 Weeks	0.9821 (0.9530, 0.9932)	0.9819 (0.9525, 0.9932)
16 Weeks	0.9821 (0.9530, 0.9932)	0.9727 (0.9403, 0.9877)
24 Weeks	0.9730 (0.9409, 0.9878)	0.9496 (0.9108, 0.9718)
36 Weeks	0.9593 (0.9232, 0.9786)	0.9218 (0.8772, 0.9507)
52 Weeks	0.9454 (0.9058, 0.9686)	0.9125 (0.8662, 0.9433)
Hazard Ratio (95% CI)*	-	1.6238 (0.7653, 3.4453)
Two-sided P-value, superiority*	-	0.2066

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.8.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Additional Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	1 (5.00)	0
Subjects Censored	19 (95.00)	19 (100.00)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	1.0000 (-, -)
16 Weeks	1.0000 (-, -)	1.0000 (-, -)
24 Weeks	0.9500 (0.6947, 0.9928)	1.0000 (-, -)
36 Weeks	0.9500 (0.6947, 0.9928)	1.0000 (-, -)
52 Weeks	0.9500 (0.6947, 0.9928)	1.0000 (-, -)
Hazard Ratio (95% CI)*	-	N/C
Two-sided P-value, superiority*	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.8.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Additional Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	3 (13.04)	0
Subjects Censored	20 (86.96)	23 (100.00)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	0.9130 (0.6949, 0.9775)	1.0000 (-, -)
16 Weeks	0.9130 (0.6949, 0.9775)	1.0000 (-, -)
24 Weeks	0.8696 (0.6481, 0.9560)	1.0000 (-, -)
36 Weeks	0.8696 (0.6481, 0.9560)	1.0000 (-, -)
52 Weeks	0.8696 (0.6481, 0.9560)	1.0000 (-, -)
Hazard Ratio (95% CI)*	-	N/C
Two-sided P-value, superiority*	-	0.9971

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.8.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics		
Overall		
Subjects with Events	1 (4.55)	0
Subjects Censored	21 (95.45)	20 (100.00)
Event-free time (weeks)		
75 percent subjects	-	-
50 percent subjects (Median)	-	-
25 percent subjects	-	-
Event-free Probability, Kaplan-Meier Estimation (95% CI)		
2 Weeks	1.0000 (-, -)	1.0000 (-, -)
4 Weeks	1.0000 (-, -)	1.0000 (-, -)
8 Weeks	1.0000 (-, -)	1.0000 (-, -)
12 Weeks	1.0000 (-, -)	1.0000 (-, -)
16 Weeks	1.0000 (-, -)	1.0000 (-, -)
24 Weeks	0.9545 (0.7187, 0.9935)	1.0000 (-, -)
36 Weeks	0.9545 (0.7187, 0.9935)	1.0000 (-, -)
52 Weeks	0.9545 (0.7187, 0.9935)	1.0000 (-, -)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.8.1.2.1
Study VX20-121-103: Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 for Additional Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Hazard Ratio (95% CI)*	-	N/C
Two-sided P-value, superiority*	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- CI: Confidence interval.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.
- *Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$ and baseline SwCl, and age at screening (<18 vs ≥18 years).
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Table 2.2.2.9.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0580
Age at screening (<18 years vs. ≥18 years) [2]	0.1215
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.9161
Sex (Male vs. Female) [1]	0.7890
Region (North America vs. Rest of the World) [1]	0.2167

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.2.9.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.6563
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.2491

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	83.63 (12.75)	84.21 (14.14)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	81.61 (1.36)	82.80 (1.39)
95% CI of LS mean	(78.94, 84.27)	(80.06, 85.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.19 (-2.63, 5.01)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	-1.96 (1.33)	-1.36 (1.36)
95% CI of LS mean	(-4.59, 0.67)	(-4.04, 1.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (-3.15, 4.36)
Week 16 (MMRM)		
n	157	149
LS mean (SE)	81.54 (1.40)	83.96 (1.43)
95% CI of LS mean	(78.79, 84.29)	(81.14, 86.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.42 (-1.52, 6.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 16 (MMRM)		
n	154	147
LS mean (SE)	-1.92 (1.35)	-0.12 (1.38)
95% CI of LS mean	(-4.57, 0.72)	(-2.83, 2.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.80 (-1.99, 5.59)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	79.65 (1.30)	82.67 (1.34)
95% CI of LS mean	(77.09, 82.21)	(80.03, 85.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.02 (-0.66, 6.70)
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	-3.87 (1.18)	-1.23 (1.21)
95% CI of LS mean	(-6.18, -1.55)	(-3.61, 1.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-0.69, 5.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52		
n	159	144
Mean (SD)	81.80 (17.88)	85.22 (13.79)
Absolute Change at Week 52		
n	156	142
Mean (SD)	-1.45 (17.14)	1.36 (13.82)
Week 52 (MMRM)		
n	155	143
LS mean (SE)	81.82 (1.26)	84.96 (1.31)
95% CI of LS mean	(79.34, 84.31)	(82.38, 87.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.13 (-0.45, 6.72)
Absolute Change at Week 52 (MMRM)		
n	152	141
LS mean (SE)	-1.65 (1.28)	1.05 (1.32)
95% CI of LS mean	(-4.16, 0.86)	(-1.55, 3.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.70 (-0.92, 6.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	-2.48 (0.95)	-0.10 (0.98)
95% CI of LS mean	(-4.36, -0.60)	(-2.03, 1.83)
P-value within Treatment	0.0098	0.9179
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-0.32, 5.07)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0833
Hedges' G (SE)		0.20 (0.11)
Hedges' 95% CI		(-0.03, 0.42)
Hedges' P-value		0.0837

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	88.33 (13.47)	87.89 (11.66)
Week 8 (MMRM)		
n	116	121
LS mean (SE)	89.95 (1.25)	87.00 (1.22)
95% CI of LS mean	(87.49, 92.41)	(84.59, 89.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.95 (-6.40, 0.49)
Absolute Change at Week 8 (MMRM)		
n	112	120
LS mean (SE)	1.33 (1.46)	-0.97 (1.41)
95% CI of LS mean	(-1.53, 4.20)	(-3.75, 1.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.31 (-6.31, 1.69)
Week 16 (MMRM)		
n	115	119
LS mean (SE)	90.29 (1.26)	86.70 (1.24)
95% CI of LS mean	(87.80, 92.77)	(84.26, 89.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.59 (-7.08, -0.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	1.66 (1.35)	-1.24 (1.31)
95% CI of LS mean	(-1.00, 4.33)	(-3.82, 1.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.91 (-6.63, 0.81)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	89.11 (1.30)	85.06 (1.29)
95% CI of LS mean	(86.55, 91.66)	(82.52, 87.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.04 (-7.65, -0.44)
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	0.57 (1.43)	-2.61 (1.40)
95% CI of LS mean	(-2.24, 3.39)	(-5.37, 0.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.18 (-7.14, 0.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52		
n	115	116
Mean (SD)	89.13 (14.70)	89.70 (11.91)
Absolute Change at Week 52		
n	111	114
Mean (SD)	0.28 (17.65)	1.60 (12.86)
Week 52 (MMRM)		
n	114	115
LS mean (SE)	89.28 (1.24)	89.61 (1.23)
95% CI of LS mean	(86.84, 91.71)	(87.19, 92.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (-3.10, 3.78)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	0.52 (1.47)	1.61 (1.44)
95% CI of LS mean	(-2.38, 3.42)	(-1.23, 4.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-2.97, 5.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	0.92 (1.17)	-0.75 (1.14)
95% CI of LS mean	(-1.38, 3.22)	(-2.99, 1.50)
P-value within Treatment	0.4313	0.5127
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.67 (-4.89, 1.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3093
Hedges' G (SE)		-0.13 (0.13)
Hedges' 95% CI		(-0.39, 0.12)
Hedges' P-value		0.3083

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	87.76 (16.41)	89.97 (11.92)
Week 8 (MMRM)		
n	34	37
LS mean (SE)	92.73 (1.83)	91.92 (1.75)
95% CI of LS mean	(89.09, 96.38)	(88.42, 95.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-5.90, 4.27)
Absolute Change at Week 8 (MMRM)		
n	33	37
LS mean (SE)	5.30 (2.73)	1.45 (2.58)
95% CI of LS mean	(-0.14, 10.75)	(-3.70, 6.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.86 (-11.40, 3.68)
Week 16 (MMRM)		
n	32	36
LS mean (SE)	91.75 (2.12)	87.78 (2.02)
95% CI of LS mean	(87.51, 96.00)	(83.75, 91.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.97 (-9.85, 1.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	3.83 (2.48)	-2.58 (2.33)
95% CI of LS mean	(-1.12, 8.78)	(-7.24, 2.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.41 (-13.27, 0.45)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	87.79 (2.29)	88.51 (2.22)
95% CI of LS mean	(83.21, 92.37)	(84.08, 92.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.72 (-5.67, 7.11)
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	-0.58 (3.02)	-1.51 (2.90)
95% CI of LS mean	(-6.61, 5.45)	(-7.29, 4.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-9.31, 7.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52		
n	33	34
Mean (SD)	93.27 (9.45)	93.06 (8.98)
Absolute Change at Week 52		
n	32	33
Mean (SD)	4.60 (17.61)	0.25 (11.23)
Week 52 (MMRM)		
n	32	34
LS mean (SE)	93.76 (1.69)	92.64 (1.65)
95% CI of LS mean	(90.37, 97.15)	(89.34, 95.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.12 (-5.87, 3.63)
Absolute Change at Week 52 (MMRM)		
n	31	33
LS mean (SE)	4.84 (2.70)	1.62 (2.60)
95% CI of LS mean	(-0.58, 10.25)	(-3.57, 6.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.21 (-10.75, 4.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	2.69 (2.31)	-0.82 (2.20)
95% CI of LS mean	(-1.92, 7.31)	(-5.21, 3.57)
P-value within Treatment	0.2477	0.7101
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.52 (-9.94, 2.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2784
Hedges' G (SE)		-0.26 (0.24)
Hedges' 95% CI		(-0.73, 0.21)
Hedges' P-value		0.2770

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	85.30 (12.66)	85.00 (13.27)
Week 8 (MMRM)		
n	243	237
LS mean (SE)	84.00 (1.04)	83.52 (1.06)
95% CI of LS mean	(81.95, 86.05)	(81.44, 85.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-3.40, 2.44)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	-1.44 (1.05)	-1.60 (1.06)
95% CI of LS mean	(-3.51, 0.62)	(-3.68, 0.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-3.09, 2.78)
Week 16 (MMRM)		
n	240	232
LS mean (SE)	84.21 (1.06)	84.74 (1.08)
95% CI of LS mean	(82.13, 86.29)	(82.63, 86.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-2.43, 3.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 16 (MMRM)		
n	234	229
LS mean (SE)	-1.10 (1.03)	-0.28 (1.04)
95% CI of LS mean	(-3.12, 0.92)	(-2.32, 1.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.82 (-2.05, 3.69)
Week 24 (MMRM)		
n	240	229
LS mean (SE)	83.02 (1.01)	82.95 (1.03)
95% CI of LS mean	(81.03, 85.01)	(80.92, 84.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-2.92, 2.77)
Absolute Change at Week 24 (MMRM)		
n	234	227
LS mean (SE)	-2.28 (0.95)	-1.92 (0.96)
95% CI of LS mean	(-4.14, -0.41)	(-3.82, -0.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.35 (-2.31, 3.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52		
n	244	230
Mean (SD)	83.74 (17.40)	86.38 (13.47)
Absolute Change at Week 52		
n	238	227
Mean (SD)	-1.51 (17.16)	1.74 (13.71)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	83.72 (0.99)	86.12 (1.02)
95% CI of LS mean	(81.77, 85.67)	(84.12, 88.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.40 (-0.40, 5.19)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	-1.60 (1.03)	1.34 (1.05)
95% CI of LS mean	(-3.62, 0.42)	(-0.72, 3.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.94 (0.05, 5.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	-1.66 (0.77)	-0.29 (0.78)
95% CI of LS mean	(-3.17, -0.14)	(-1.83, 1.25)
P-value within Treatment	0.0324	0.7152
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.37 (-0.79, 3.54)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2140
Hedges' G (SE)		0.12 (0.09)
Hedges' 95% CI		(-0.07, 0.30)
Hedges' P-value		0.2137

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	84.15 (14.64)	87.03 (12.24)
Week 8 (MMRM)		
n	79	69
LS mean (SE)	85.58 (1.79)	85.03 (1.91)
95% CI of LS mean	(82.05, 89.11)	(81.25, 88.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.55 (-5.74, 4.63)
Absolute Change at Week 8 (MMRM)		
n	77	68
LS mean (SE)	1.31 (2.04)	-2.04 (2.17)
95% CI of LS mean	(-2.72, 5.34)	(-6.33, 2.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.35 (-9.25, 2.55)
Week 16 (MMRM)		
n	76	67
LS mean (SE)	81.99 (2.04)	84.79 (2.18)
95% CI of LS mean	(77.95, 86.03)	(80.48, 89.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.80 (-3.11, 8.72)

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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 16 (MMRM)		
n	74	66
LS mean (SE)	-2.07 (2.02)	-2.14 (2.15)
95% CI of LS mean	(-6.08, 1.93)	(-6.39, 2.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-5.92, 5.78)
Week 24 (MMRM)		
n	79	63
LS mean (SE)	79.71 (1.91)	83.65 (2.13)
95% CI of LS mean	(75.92, 83.49)	(79.44, 87.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.94 (-1.72, 9.61)
Absolute Change at Week 24 (MMRM)		
n	77	63
LS mean (SE)	-4.43 (1.88)	-2.90 (2.06)
95% CI of LS mean	(-8.14, -0.71)	(-6.98, 1.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.52 (-4.01, 7.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52		
n	78	66
Mean (SD)	82.30 (17.74)	87.96 (13.49)
Absolute Change at Week 52		
n	76	65
Mean (SD)	-1.90 (18.85)	1.84 (13.59)
Week 52 (MMRM)		
n	77	63
LS mean (SE)	82.74 (1.76)	88.09 (1.94)
95% CI of LS mean	(79.27, 86.22)	(84.25, 91.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.35 (0.17, 10.54)
Absolute Change at Week 52 (MMRM)		
n	75	62
LS mean (SE)	-1.51 (1.93)	1.77 (2.12)
95% CI of LS mean	(-5.33, 2.31)	(-2.42, 5.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.28 (-2.41, 8.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	-2.67 (1.46)	-1.09 (1.58)
95% CI of LS mean	(-5.56, 0.22)	(-4.22, 2.03)
P-value within Treatment	0.0704	0.4912
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.58 (-2.70, 5.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4672
Hedges' G (SE)		0.12 (0.17)
Hedges' 95% CI		(-0.21, 0.45)
Hedges' P-value		0.4658

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	86.25 (12.52)	85.28 (13.51)
Week 8 (MMRM)		
n	198	205
LS mean (SE)	84.98 (1.11)	84.54 (1.09)
95% CI of LS mean	(82.79, 87.17)	(82.39, 86.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-3.51, 2.63)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	-1.32 (1.13)	-0.91 (1.10)
95% CI of LS mean	(-3.54, 0.90)	(-3.07, 1.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-2.69, 3.50)
Week 16 (MMRM)		
n	196	201
LS mean (SE)	86.53 (1.09)	85.29 (1.08)
95% CI of LS mean	(84.39, 88.68)	(83.17, 87.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.25 (-4.26, 1.77)

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- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 16 (MMRM)		
n	191	199
LS mean (SE)	0.24 (1.09)	-0.16 (1.07)
95% CI of LS mean	(-1.90, 2.38)	(-2.25, 1.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.40 (-3.39, 2.60)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	85.25 (1.04)	83.80 (1.03)
95% CI of LS mean	(83.20, 87.31)	(81.78, 85.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.46 (-4.33, 1.42)
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	-1.01 (1.03)	-1.54 (1.01)
95% CI of LS mean	(-3.04, 1.03)	(-3.53, 0.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.54 (-3.38, 2.31)

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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52		
n	194	196
Mean (SD)	85.81 (16.61)	87.04 (13.02)
Absolute Change at Week 52		
n	189	193
Mean (SD)	-0.44 (16.81)	1.47 (13.44)
Week 52 (MMRM)		
n	192	195
LS mean (SE)	85.81 (1.03)	86.73 (1.02)
95% CI of LS mean	(83.78, 87.83)	(84.72, 88.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-1.93, 3.77)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	-0.45 (1.11)	1.18 (1.09)
95% CI of LS mean	(-2.63, 1.73)	(-0.96, 3.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-1.43, 4.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	-0.41 (0.86)	-0.18 (0.84)
95% CI of LS mean	(-2.09, 1.28)	(-1.82, 1.47)
P-value within Treatment	0.6347	0.8339
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-2.13, 2.59)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8471
Hedges' G (SE)		0.02 (0.10)
Hedges' 95% CI		(-0.18, 0.22)
Hedges' P-value		0.8470

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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	86.85 (12.51)	86.70 (13.45)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	86.83 (1.27)	86.21 (1.23)
95% CI of LS mean	(84.34, 89.32)	(83.80, 88.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.62 (-4.10, 2.86)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	-0.08 (1.28)	-0.57 (1.23)
95% CI of LS mean	(-2.60, 2.45)	(-3.00, 1.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-4.01, 3.01)
Week 16 (MMRM)		
n	129	139
LS mean (SE)	88.01 (1.19)	85.98 (1.15)
95% CI of LS mean	(85.67, 90.36)	(83.72, 88.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.03 (-5.30, 1.24)

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- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 16 (MMRM)		
n	125	137
LS mean (SE)	0.99 (1.13)	-0.59 (1.08)
95% CI of LS mean	(-1.23, 3.22)	(-2.72, 1.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-4.67, 1.51)
Week 24 (MMRM)		
n	133	140
LS mean (SE)	86.25 (1.17)	84.83 (1.14)
95% CI of LS mean	(83.94, 88.55)	(82.59, 87.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.42 (-4.65, 1.82)
Absolute Change at Week 24 (MMRM)		
n	129	137
LS mean (SE)	-0.64 (1.23)	-1.62 (1.19)
95% CI of LS mean	(-3.06, 1.78)	(-3.96, 0.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.98 (-4.36, 2.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52		
n	139	143
Mean (SD)	85.95 (15.97)	88.90 (11.70)
Absolute Change at Week 52		
n	135	140
Mean (SD)	-1.03 (15.78)	2.45 (12.12)
Week 52 (MMRM)		
n	132	139
LS mean (SE)	85.74 (1.19)	88.86 (1.15)
95% CI of LS mean	(83.40, 88.07)	(86.58, 91.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.12 (-0.15, 6.39)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	-1.35 (1.23)	2.33 (1.19)
95% CI of LS mean	(-3.76, 1.07)	(-0.02, 4.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.67 (0.29, 7.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	-0.33 (0.93)	0.04 (0.90)
95% CI of LS mean	(-2.16, 1.50)	(-1.73, 1.81)
P-value within Treatment	0.7223	0.9633
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.37 (-2.18, 2.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7750
Hedges' G (SE)		0.04 (0.12)
Hedges' 95% CI		(-0.20, 0.27)
Hedges' P-value		0.7738

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	84.42 (13.80)	84.63 (12.85)
Week 8 (MMRM)		
n	143	131
LS mean (SE)	83.71 (1.39)	82.83 (1.45)
95% CI of LS mean	(80.97, 86.46)	(79.96, 85.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-4.87, 3.09)
Absolute Change at Week 8 (MMRM)		
n	140	130
LS mean (SE)	-1.14 (1.50)	-1.75 (1.56)
95% CI of LS mean	(-4.10, 1.82)	(-4.82, 1.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.61 (-4.89, 3.67)
Week 16 (MMRM)		
n	143	129
LS mean (SE)	82.86 (1.51)	84.14 (1.59)
95% CI of LS mean	(79.88, 85.84)	(81.02, 87.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.28 (-3.04, 5.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	-1.85 (1.55)	-0.43 (1.61)
95% CI of LS mean	(-4.91, 1.20)	(-3.61, 2.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-3.00, 5.84)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	81.40 (1.44)	82.41 (1.53)
95% CI of LS mean	(78.56, 84.25)	(79.41, 85.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-3.14, 5.16)
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	-3.35 (1.36)	-2.03 (1.42)
95% CI of LS mean	(-6.02, -0.68)	(-4.82, 0.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.32 (-2.56, 5.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52		
n	138	121
Mean (SD)	83.80 (17.82)	85.28 (14.49)
Absolute Change at Week 52		
n	135	120
Mean (SD)	-0.55 (18.75)	0.51 (14.76)
Week 52 (MMRM)		
n	137	119
LS mean (SE)	84.39 (1.34)	84.88 (1.43)
95% CI of LS mean	(81.75, 87.03)	(82.07, 87.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-3.38, 4.36)
Absolute Change at Week 52 (MMRM)		
n	134	118
LS mean (SE)	-0.29 (1.48)	0.38 (1.56)
95% CI of LS mean	(-3.20, 2.62)	(-2.70, 3.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.66 (-3.58, 4.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	-1.83 (1.15)	-0.70 (1.20)
95% CI of LS mean	(-4.10, 0.44)	(-3.06, 1.67)
P-value within Treatment	0.1136	0.5634
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.13 (-2.17, 4.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4991
Hedges' G (SE)		0.08 (0.12)
Hedges' 95% CI		(-0.16, 0.32)
Hedges' P-value		0.4966

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	85.36 (12.71)	87.51 (12.23)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	83.92 (1.50)	85.94 (1.40)
95% CI of LS mean	(80.96, 86.88)	(83.17, 88.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.03 (-2.03, 6.08)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	-1.46 (1.57)	-1.84 (1.48)
95% CI of LS mean	(-4.57, 1.64)	(-4.77, 1.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-4.65, 3.89)
Week 16 (MMRM)		
n	96	108
LS mean (SE)	85.84 (1.51)	86.36 (1.43)
95% CI of LS mean	(82.86, 88.82)	(83.55, 89.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-3.58, 4.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	0.18 (1.36)	-1.28 (1.30)
95% CI of LS mean	(-2.51, 2.87)	(-3.84, 1.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.47 (-5.18, 2.25)
Week 24 (MMRM)		
n	98	108
LS mean (SE)	84.46 (1.50)	84.68 (1.43)
95% CI of LS mean	(81.50, 87.42)	(81.86, 87.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.22 (-3.87, 4.31)
Absolute Change at Week 24 (MMRM)		
n	97	106
LS mean (SE)	-0.86 (1.43)	-2.81 (1.37)
95% CI of LS mean	(-3.68, 1.96)	(-5.51, -0.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.95 (-5.86, 1.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52		
n	101	104
Mean (SD)	84.93 (15.91)	87.04 (13.88)
Absolute Change at Week 52		
n	100	101
Mean (SD)	-0.24 (15.48)	-0.51 (13.28)
Week 52 (MMRM)		
n	97	104
LS mean (SE)	84.59 (1.48)	86.65 (1.42)
95% CI of LS mean	(81.67, 87.51)	(83.84, 89.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.06 (-2.00, 6.12)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	-0.72 (1.49)	-0.64 (1.44)
95% CI of LS mean	(-3.65, 2.21)	(-3.49, 2.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-4.01, 4.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	-0.47 (1.09)	-1.58 (1.05)
95% CI of LS mean	(-2.62, 1.69)	(-3.64, 0.48)
P-value within Treatment	0.6701	0.1321
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.11 (-4.10, 1.87)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4626
Hedges' G (SE)		-0.10 (0.14)
Hedges' 95% CI		(-0.38, 0.17)
Hedges' P-value		0.4620

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	85.77 (13.52)	84.53 (13.68)
Week 8 (MMRM)		
n	179	162
LS mean (SE)	85.80 (1.22)	83.81 (1.28)
95% CI of LS mean	(83.41, 88.19)	(81.30, 86.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.99 (-5.46, 1.48)
Absolute Change at Week 8 (MMRM)		
n	173	162
LS mean (SE)	-0.13 (1.27)	-0.70 (1.31)
95% CI of LS mean	(-2.62, 2.37)	(-3.28, 1.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.57 (-4.17, 3.02)
Week 16 (MMRM)		
n	176	160
LS mean (SE)	84.89 (1.27)	84.36 (1.33)
95% CI of LS mean	(82.40, 87.38)	(81.75, 86.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-4.14, 3.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 16 (MMRM)		
n	170	160
LS mean (SE)	-0.85 (1.30)	-0.12 (1.34)
95% CI of LS mean	(-3.40, 1.70)	(-2.75, 2.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.73 (-2.93, 4.40)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	83.20 (1.19)	83.13 (1.26)
95% CI of LS mean	(80.86, 85.54)	(80.66, 85.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-3.47, 3.34)
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	-2.68 (1.18)	-1.16 (1.23)
95% CI of LS mean	(-5.01, -0.36)	(-3.59, 1.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.52 (-1.84, 4.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52		
n	176	160
Mean (SD)	84.85 (17.52)	87.38 (12.70)
Absolute Change at Week 52		
n	170	159
Mean (SD)	-1.11 (18.32)	2.86 (13.37)
Week 52 (MMRM)		
n	172	154
LS mean (SE)	85.10 (1.13)	87.34 (1.19)
95% CI of LS mean	(82.88, 87.31)	(85.00, 89.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.24 (-0.99, 5.46)
Absolute Change at Week 52 (MMRM)		
n	166	153
LS mean (SE)	-0.83 (1.25)	2.79 (1.30)
95% CI of LS mean	(-3.29, 1.62)	(0.24, 5.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.63 (0.08, 7.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	-1.46 (0.98)	0.50 (1.01)
95% CI of LS mean	(-3.38, 0.47)	(-1.49, 2.50)
P-value within Treatment	0.1375	0.6195
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.96 (-0.82, 4.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1657
Hedges' G (SE)		0.15 (0.11)
Hedges' 95% CI		(-0.06, 0.37)
Hedges' P-value		0.1656

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Baseline		
n	243	237
Mean (SD)	85.71 (13.28)	86.22 (12.69)
Week 8 (MMRM)		
n	240	235
LS mean (SE)	85.07 (0.99)	85.37 (1.00)
95% CI of LS mean	(83.13, 87.02)	(83.40, 87.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.30 (-2.47, 3.07)
Absolute Change at Week 8 (MMRM)		
n	233	232
LS mean (SE)	-0.66 (1.05)	-1.03 (1.05)
95% CI of LS mean	(-2.72, 1.40)	(-3.10, 1.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-3.29, 2.55)
Week 16 (MMRM)		
n	236	230
LS mean (SE)	84.77 (1.04)	85.75 (1.05)
95% CI of LS mean	(82.74, 86.81)	(83.69, 87.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.98 (-1.92, 3.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 16 (MMRM)		
n	229	227
LS mean (SE)	-0.92 (1.02)	-0.63 (1.02)
95% CI of LS mean	(-2.92, 1.07)	(-2.64, 1.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-2.54, 3.12)
Week 24 (MMRM)		
n	238	226
LS mean (SE)	83.24 (1.01)	83.80 (1.03)
95% CI of LS mean	(81.26, 85.21)	(81.78, 85.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.56 (-2.26, 3.39)
Absolute Change at Week 24 (MMRM)		
n	231	223
LS mean (SE)	-2.47 (0.99)	-2.39 (1.01)
95% CI of LS mean	(-4.42, -0.52)	(-4.37, -0.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-2.70, 2.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Week 52		
n	241	224
Mean (SD)	84.62 (17.16)	87.42 (12.85)
Absolute Change at Week 52		
n	234	220
Mean (SD)	-1.21 (17.75)	1.19 (13.21)
Week 52 (MMRM)		
n	235	221
LS mean (SE)	84.63 (0.96)	87.29 (0.99)
95% CI of LS mean	(82.74, 86.52)	(85.35, 89.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.66 (-0.05, 5.38)
Absolute Change at Week 52 (MMRM)		
n	228	217
LS mean (SE)	-1.13 (1.04)	0.99 (1.06)
95% CI of LS mean	(-3.17, 0.92)	(-1.09, 3.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-0.80, 5.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change through Week 52 (MMRM)		
n	233	229
LS mean (SE)	-1.51 (0.80)	-0.67 (0.80)
95% CI of LS mean	(-3.07, 0.06)	(-2.26, 0.91)
P-value within Treatment	0.0590	0.4024
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.83 (-1.39, 3.06)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4631
Hedges' G (SE)		0.07 (0.09)
Hedges' 95% CI		(-0.11, 0.25)
Hedges' P-value		0.4630

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Baseline		
n	39	43
Mean (SD)	85.11 (12.91)	82.88 (15.50)
Week 8 (MMRM)		
n	37	39
LS mean (SE)	85.15 (2.83)	80.96 (2.74)
95% CI of LS mean	(79.49, 90.80)	(75.49, 86.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.18 (-12.14, 3.77)
Absolute Change at Week 8 (MMRM)		
n	37	39
LS mean (SE)	-0.95 (2.72)	-1.25 (2.64)
95% CI of LS mean	(-6.39, 4.49)	(-6.52, 4.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-7.96, 7.36)
Week 16 (MMRM)		
n	36	38
LS mean (SE)	87.78 (2.74)	82.16 (2.66)
95% CI of LS mean	(82.31, 93.25)	(76.85, 87.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.62 (-13.33, 2.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 16 (MMRM)		
n	36	38
LS mean (SE)	1.77 (2.82)	0.23 (2.74)
95% CI of LS mean	(-3.85, 7.40)	(-5.24, 5.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.55 (-9.48, 6.39)
Week 24 (MMRM)		
n	36	39
LS mean (SE)	86.01 (2.50)	83.87 (2.40)
95% CI of LS mean	(81.03, 90.98)	(79.08, 88.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.13 (-9.17, 4.90)
Absolute Change at Week 24 (MMRM)		
n	36	39
LS mean (SE)	0.14 (2.29)	2.13 (2.20)
95% CI of LS mean	(-4.42, 4.70)	(-2.26, 6.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.00 (-4.47, 8.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Week 52		
n	36	40
Mean (SD)	86.57 (15.34)	86.24 (14.88)
Absolute Change at Week 52		
n	36	40
Mean (SD)	1.93 (13.93)	3.53 (14.50)
Week 52 (MMRM)		
n	34	37
LS mean (SE)	86.52 (2.52)	85.57 (2.42)
95% CI of LS mean	(81.48, 91.56)	(80.73, 90.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-8.06, 6.15)
Absolute Change at Week 52 (MMRM)		
n	34	37
LS mean (SE)	0.68 (2.60)	3.87 (2.49)
95% CI of LS mean	(-4.51, 5.87)	(-1.11, 8.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.19 (-4.12, 10.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change through Week 52 (MMRM)		
n	37	39
LS mean (SE)	0.86 (1.97)	2.08 (1.91)
95% CI of LS mean	(-3.08, 4.80)	(-1.73, 5.88)
P-value within Treatment	0.6630	0.2798
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-4.41, 6.84)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6683
Hedges' G (SE)		0.10 (0.23)
Hedges' 95% CI		(-0.35, 0.55)
Hedges' P-value		0.6600

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: F/F

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Baseline		
n	219	219
Mean (SD)	86.70 (12.97)	86.12 (12.75)
Week 8 (MMRM)		
n	215	215
LS mean (SE)	85.22 (1.08)	85.34 (1.08)
95% CI of LS mean	(83.10, 87.33)	(83.23, 87.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-2.87, 3.11)
Absolute Change at Week 8 (MMRM)		
n	210	213
LS mean (SE)	-1.46 (1.14)	-1.07 (1.14)
95% CI of LS mean	(-3.71, 0.79)	(-3.31, 1.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.39 (-2.78, 3.56)
Week 16 (MMRM)		
n	210	212
LS mean (SE)	85.58 (1.09)	85.94 (1.08)
95% CI of LS mean	(83.44, 87.71)	(83.81, 88.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-2.66, 3.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 16 (MMRM)		
n	205	210
LS mean (SE)	-1.16 (1.10)	-0.45 (1.09)
95% CI of LS mean	(-3.32, 1.00)	(-2.59, 1.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.71 (-2.33, 3.75)
Week 24 (MMRM)		
n	212	211
LS mean (SE)	84.05 (1.05)	84.20 (1.05)
95% CI of LS mean	(81.99, 86.11)	(82.14, 86.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-2.76, 3.06)
Absolute Change at Week 24 (MMRM)		
n	207	208
LS mean (SE)	-2.63 (1.04)	-2.08 (1.04)
95% CI of LS mean	(-4.68, -0.59)	(-4.12, -0.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-2.34, 3.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Week 52		
n	212	208
Mean (SD)	85.43 (17.06)	87.49 (13.20)
Absolute Change at Week 52		
n	207	205
Mean (SD)	-1.28 (17.44)	1.18 (13.46)
Week 52 (MMRM)		
n	207	205
LS mean (SE)	85.37 (1.02)	87.41 (1.03)
95% CI of LS mean	(83.35, 87.38)	(85.39, 89.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.04 (-0.81, 4.89)
Absolute Change at Week 52 (MMRM)		
n	202	202
LS mean (SE)	-1.29 (1.10)	0.96 (1.10)
95% CI of LS mean	(-3.45, 0.88)	(-1.20, 3.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.25 (-0.81, 5.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change through Week 52 (MMRM)		
n	210	212
LS mean (SE)	-1.70 (0.84)	-0.52 (0.84)
95% CI of LS mean	(-3.35, -0.04)	(-2.17, 1.12)
P-value within Treatment	0.0448	0.5323
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-1.17, 3.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3250
Hedges' G (SE)		0.10 (0.10)
Hedges' 95% CI		(-0.10, 0.29)
Hedges' P-value		0.3248

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: F/G

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	18	19
Mean (SD)	79.01 (13.14)	85.09 (14.94)
Week 8 (MMRM)		
n	19	18
LS mean (SE)	86.89 (2.48)	85.44 (2.55)
95% CI of LS mean	(81.84, 91.95)	(80.24, 90.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.45 (-8.72, 5.81)
Absolute Change at Week 8 (MMRM)		
n	17	18
LS mean (SE)	7.87 (3.02)	0.59 (2.93)
95% CI of LS mean	(1.71, 14.03)	(-5.40, 6.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.28 (-15.92, 1.37)
Week 16 (MMRM)		
n	19	16
LS mean (SE)	83.68 (2.83)	87.42 (3.06)
95% CI of LS mean	(77.92, 89.44)	(81.21, 93.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.74 (-4.75, 12.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 16 (MMRM)		
n	17	16
LS mean (SE)	5.91 (3.15)	2.68 (3.21)
95% CI of LS mean	(-0.54, 12.36)	(-3.87, 9.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.23 (-12.48, 6.02)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	84.85 (3.29)	81.07 (3.56)
95% CI of LS mean	(78.16, 91.54)	(73.82, 88.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.78 (-13.65, 6.09)
Absolute Change at Week 24 (MMRM)		
n	17	16
LS mean (SE)	6.89 (3.92)	-3.20 (3.98)
95% CI of LS mean	(-1.11, 14.89)	(-11.32, 4.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.08 (-21.52, 1.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Week 52		
n	20	16
Mean (SD)	84.17 (12.65)	87.85 (8.17)
Absolute Change at Week 52		
n	18	16
Mean (SD)	4.01 (14.74)	3.13 (13.75)
Week 52 (MMRM)		
n	19	15
LS mean (SE)	84.85 (2.52)	87.65 (2.79)
95% CI of LS mean	(79.71, 89.98)	(81.98, 93.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.80 (-4.86, 10.46)
Absolute Change at Week 52 (MMRM)		
n	17	15
LS mean (SE)	5.58 (3.47)	3.34 (3.56)
95% CI of LS mean	(-1.52, 12.69)	(-3.91, 10.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.24 (-12.44, 7.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change through Week 52 (MMRM)		
n	17	17
LS mean (SE)	6.13 (2.99)	0.94 (3.02)
95% CI of LS mean	(0.01, 12.25)	(-5.20, 7.09)
P-value within Treatment	0.0498	0.7570
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.19 (-13.91, 3.54)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2348
Hedges' G (SE)		-0.41 (0.34)
Hedges' 95% CI		(-1.10, 0.28)
Hedges' P-value		0.2364

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: F/RF

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Baseline		
n	23	22
Mean (SD)	81.16 (15.24)	84.60 (14.54)
Week 8 (MMRM)		
n	23	23
LS mean (SE)	81.40 (3.95)	76.74 (3.95)
95% CI of LS mean	(73.43, 89.38)	(68.76, 84.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.67 (-15.97, 6.63)
Absolute Change at Week 8 (MMRM)		
n	23	22
LS mean (SE)	-0.23 (3.35)	-7.91 (3.42)
95% CI of LS mean	(-6.99, 6.53)	(-14.83, -1.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.68 (-17.36, 2.00)
Week 16 (MMRM)		
n	23	23
LS mean (SE)	83.22 (4.16)	78.86 (4.16)
95% CI of LS mean	(74.81, 91.62)	(70.46, 87.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.36 (-16.25, 7.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 16 (MMRM)		
n	23	22
LS mean (SE)	1.58 (3.49)	-5.69 (3.56)
95% CI of LS mean	(-5.47, 8.62)	(-12.89, 1.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.27 (-17.36, 2.82)
Week 24 (MMRM)		
n	23	22
LS mean (SE)	79.11 (3.46)	79.26 (3.50)
95% CI of LS mean	(72.12, 86.10)	(72.19, 86.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-9.81, 10.11)
Absolute Change at Week 24 (MMRM)		
n	23	22
LS mean (SE)	-2.53 (2.50)	-4.68 (2.56)
95% CI of LS mean	(-7.58, 2.52)	(-9.85, 0.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.15 (-9.39, 5.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Week 52		
n	23	23
Mean (SD)	77.54 (20.48)	84.30 (14.38)
Absolute Change at Week 52		
n	23	22
Mean (SD)	-3.62 (19.22)	0.76 (8.62)
Week 52 (MMRM)		
n	23	23
LS mean (SE)	78.14 (3.61)	83.69 (3.61)
95% CI of LS mean	(70.85, 85.44)	(76.39, 90.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.55 (-4.79, 15.89)
Absolute Change at Week 52 (MMRM)		
n	23	22
LS mean (SE)	-3.49 (3.27)	0.62 (3.34)
95% CI of LS mean	(-10.09, 3.11)	(-6.13, 7.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.12 (-5.34, 13.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change through Week 52 (MMRM)		
n	23	22
LS mean (SE)	-1.48 (2.16)	-3.25 (2.21)
95% CI of LS mean	(-5.84, 2.88)	(-7.71, 1.21)
P-value within Treatment	0.4971	0.1490
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.77 (-8.03, 4.49)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5712
Hedges' G (SE)		-0.17 (0.29)
Hedges' 95% CI		(-0.76, 0.42)
Hedges' P-value		0.5706

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: TCR/non-F

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	20
Mean (SD)	84.97 (11.59)	83.00 (15.20)
Week 8 (MMRM)		
n	20	18
LS mean (SE)	87.81 (3.28)	85.15 (3.47)
95% CI of LS mean	(81.13, 94.49)	(78.10, 92.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.66 (-12.53, 7.22)
Absolute Change at Week 8 (MMRM)		
n	20	18
LS mean (SE)	2.18 (2.89)	2.89 (3.05)
95% CI of LS mean	(-3.70, 8.06)	(-3.33, 9.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.71 (-8.02, 9.43)
Week 16 (MMRM)		
n	20	17
LS mean (SE)	86.14 (3.61)	80.96 (3.92)
95% CI of LS mean	(78.78, 93.50)	(72.97, 88.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.18 (-16.19, 5.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 16 (MMRM)		
n	20	17
LS mean (SE)	0.51 (3.69)	-0.83 (4.02)
95% CI of LS mean	(-7.04, 8.07)	(-9.03, 7.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.34 (-12.63, 9.96)
Week 24 (MMRM)		
n	20	16
LS mean (SE)	84.47 (3.86)	85.27 (4.21)
95% CI of LS mean	(76.63, 92.32)	(76.73, 93.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.80 (-10.95, 12.55)
Absolute Change at Week 24 (MMRM)		
n	20	16
LS mean (SE)	-1.15 (3.68)	3.21 (4.03)
95% CI of LS mean	(-8.66, 6.35)	(-4.99, 11.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.37 (-6.89, 15.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Week 52		
n	22	17
Mean (SD)	87.88 (13.46)	87.58 (15.15)
Absolute Change at Week 52		
n	22	17
Mean (SD)	2.90 (15.49)	5.56 (17.46)
Week 52 (MMRM)		
n	20	15
LS mean (SE)	88.92 (3.27)	84.62 (3.67)
95% CI of LS mean	(82.27, 95.56)	(77.17, 92.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.30 (-14.43, 5.83)
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	3.29 (3.95)	1.99 (4.41)
95% CI of LS mean	(-4.77, 11.35)	(-6.97, 10.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.30 (-13.49, 10.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	0.88 (3.23)	1.46 (3.52)
95% CI of LS mean	(-5.73, 7.50)	(-5.73, 8.65)
P-value within Treatment	0.7866	0.6816
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-9.35, 10.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9066
Hedges' G (SE)		0.04 (0.32)
Hedges' 95% CI		(-0.62, 0.69)
Hedges' P-value		0.9048

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.2.9.2.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.4359
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.2.9.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, and as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	96.30 (4.54)	87.04 (11.56)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	93.75 (6.11)	87.04 (8.65)
95% CI of LS mean	(78.32, 109.18)	(65.58, 108.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.71 (-33.47, 20.05)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	N/C	N/C
95% CI of LS mean	N/C	N/C
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	N/C
Week 16 (MMRM)		
n	4	3
LS mean (SE)	90.09 (10.18)	83.50 (14.25)
95% CI of LS mean	(64.97, 115.21)	(48.78, 118.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.59 (-49.65, 36.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	N/C	N/C
95% CI of LS mean	N/C	N/C
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	N/C
Week 24 (MMRM)		
n	6	5
LS mean (SE)	95.05 (4.98)	83.55 (5.57)
95% CI of LS mean	(83.77, 106.33)	(70.97, 96.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-11.50 (-28.89, 5.89)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	N/C	N/C
95% CI of LS mean	N/C	N/C
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	94.92 (6.38)	95.37 (4.18)
Absolute Change at Week 52		
n	5	3
Mean (SD)	-0.44 (9.18)	5.56 (11.11)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	95.61 (2.47)	95.69 (2.47)
95% CI of LS mean	(89.73, 101.48)	(89.81, 101.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-9.10, 9.26)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	N/C	N/C
95% CI of LS mean	N/C	N/C
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	N/C	N/C
95% CI of LS mean	N/C	N/C
P-value within Treatment	N/C	N/C
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	N/C
Hedges' G (SE)		-
Hedges' 95% CI		-
Hedges' P-value		-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	93.33 (8.16)	91.85 (9.23)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	92.20 (4.71)	91.49 (3.83)
95% CI of LS mean	(81.47, 102.94)	(82.76, 100.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.71 (-14.66, 13.25)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-0.53 (6.15)	-0.76 (5.01)
95% CI of LS mean	(-14.07, 13.01)	(-11.80, 10.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-17.77, 17.32)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	92.15 (4.37)	90.81 (3.45)
95% CI of LS mean	(82.41, 101.88)	(83.04, 98.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.34 (-14.00, 11.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	0.02 (3.85)	-1.28 (3.09)
95% CI of LS mean	(-8.80, 8.84)	(-8.37, 5.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.30 (-12.81, 10.21)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	92.39 (10.01)	83.44 (8.34)
95% CI of LS mean	(70.70, 114.08)	(65.44, 101.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.94 (-37.19, 19.31)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-0.34 (9.20)	-8.24 (7.94)
95% CI of LS mean	(-20.36, 19.67)	(-25.43, 8.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.89 (-34.33, 18.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	98.61 (2.78)	94.44 (8.49)
Absolute Change at Week 52		
n	4	7
Mean (SD)	1.67 (3.33)	0.95 (6.10)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	99.59 (3.83)	93.26 (3.01)
95% CI of LS mean	(90.63, 108.54)	(86.15, 100.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.33 (-17.94, 5.29)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	5.04 (4.71)	-1.16 (3.77)
95% CI of LS mean	(-5.56, 15.64)	(-9.66, 7.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.20 (-19.91, 7.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	1.57 (4.92)	-3.56 (4.11)
95% CI of LS mean	(-9.35, 12.49)	(-12.63, 5.52)
P-value within Treatment	0.7556	0.4059
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.13 (-19.45, 9.18)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4453
Hedges' G (SE)		-0.39 (0.50)
Hedges' 95% CI		(-1.48, 0.69)
Hedges' P-value		0.4450

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Genotype group: F/F

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Genotype group: F/G

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.2.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6319
Age at screening (<18 years vs. ≥18 years) [2]	0.2999
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0528
Sex (Male vs. Female) [1]	0.0161
Region (North America vs. Rest of the World) [1]	0.8232

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.2019
Age at screening (<18 years vs. ≥18 years) [2]	0.8180
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.2752
Sex (Male vs. Female) [1]	0.5075
Region (North America vs. Rest of the World) [1]	0.0949

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6339
Age at screening (<18 years vs. ≥18 years) [2]	0.1101
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5833
Sex (Male vs. Female) [1]	0.4969
Region (North America vs. Rest of the World) [1]	0.1146

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.2508
Age at screening (<18 years vs. ≥18 years) [2]	0.6351
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5208
Sex (Male vs. Female) [1]	0.7593
Region (North America vs. Rest of the World) [1]	0.2486

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.7356
Age at screening (<18 years vs. ≥18 years) [2]	0.6487
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.3043
Sex (Male vs. Female) [1]	0.3521
Region (North America vs. Rest of the World) [1]	0.1670

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.2161
Age at screening (<18 years vs. ≥18 years) [2]	0.2101
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.2073
Sex (Male vs. Female) [1]	0.9410
Region (North America vs. Rest of the World) [1]	0.2415

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.6302
Age at screening (<18 years vs. ≥18 years) [2]	0.6326
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.6606
Sex (Male vs. Female) [1]	0.6202
Region (North America vs. Rest of the World) [1]	0.6124

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4732
Age at screening (<18 years vs. ≥18 years) [2]	0.3240
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.8155
Sex (Male vs. Female) [1]	0.7819
Region (North America vs. Rest of the World) [1]	0.7232

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.8734
Age at screening (<18 years vs. ≥18 years) [2]	0.0150
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.5255
Sex (Male vs. Female) [1]	0.6513
Region (North America vs. Rest of the World) [1]	0.8885

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4107
Age at screening (<18 years vs. ≥18 years) [2]	0.3491
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.6407
Sex (Male vs. Female) [1]	0.7303
Region (North America vs. Rest of the World) [1]	0.2823

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1121
Age at screening (<18 years vs. ≥18 years) [2]	0.8145
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.7648
Sex (Male vs. Female) [1]	0.5029
Region (North America vs. Rest of the World) [1]	0.0303

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.1701
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.1383

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.9759
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.3287

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.1402
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.0881

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.0475
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.9141

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.2351
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.5061

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.9207
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.7673

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.8401
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.6724

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.6887
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.3033

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.1839
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.4287

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.2580
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.6860

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	0.6623
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	0.4155

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype and age at screening (<18 vs ≥18 years) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, age at screening (<18 vs ≥18 years) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	75.27 (24.35)	78.65 (21.07)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	76.75 (1.86)	78.49 (1.91)
95% CI of LS mean	(73.10, 80.41)	(74.74, 82.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.74 (-3.50, 6.98)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	1.86 (1.24)	0.12 (1.27)
95% CI of LS mean	(-0.59, 4.31)	(-2.39, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.74 (-5.25, 1.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 16 (MMRM)		
n	158	148
LS mean (SE)	77.07 (1.66)	79.95 (1.71)
95% CI of LS mean	(73.79, 80.34)	(76.59, 83.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.88 (-1.82, 7.59)
Absolute Change at Week 16 (MMRM)		
n	155	146
LS mean (SE)	1.75 (1.19)	1.33 (1.22)
95% CI of LS mean	(-0.59, 4.09)	(-1.08, 3.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-3.78, 2.93)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	78.40 (1.72)	79.56 (1.77)
95% CI of LS mean	(75.02, 81.78)	(76.09, 83.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-3.69, 6.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	3.18 (1.22)	1.09 (1.25)
95% CI of LS mean	(0.77, 5.58)	(-1.38, 3.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.09 (-5.54, 1.36)
Week 52		
n	159	145
Mean (SD)	77.99 (21.85)	79.62 (22.57)
Absolute Change at Week 52		
n	156	143
Mean (SD)	2.28 (17.97)	1.40 (17.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52 (MMRM)		
n	155	144
LS mean (SE)	77.14 (1.76)	79.82 (1.82)
95% CI of LS mean	(73.67, 80.61)	(76.24, 83.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.68 (-2.31, 7.67)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	1.70 (1.43)	1.47 (1.47)
95% CI of LS mean	(-1.10, 4.51)	(-1.43, 4.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-4.27, 3.80)
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	2.21 (1.08)	1.29 (1.11)
95% CI of LS mean	(0.08, 4.34)	(-0.89, 3.48)
P-value within Treatment	0.0419	0.2451
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-3.97, 2.14)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5550

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Hedges' G (SE)		-0.07 (0.11)
Hedges' 95% CI		(-0.29, 0.16)
Hedges' P-value		0.5548

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	77.29 (22.44)	79.04 (21.63)
Week 8 (MMRM)		
n	116	120
LS mean (SE)	80.94 (1.88)	80.34 (1.84)
95% CI of LS mean	(77.23, 84.65)	(76.72, 83.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.60 (-5.80, 4.60)
Absolute Change at Week 8 (MMRM)		
n	112	119
LS mean (SE)	3.23 (1.25)	1.12 (1.21)
95% CI of LS mean	(0.78, 5.69)	(-1.26, 3.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.12 (-5.54, 1.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 16 (MMRM)		
n	115	119
LS mean (SE)	80.28 (1.91)	79.09 (1.87)
95% CI of LS mean	(76.52, 84.04)	(75.41, 82.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.19 (-6.47, 4.10)
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	2.64 (1.24)	-0.06 (1.20)
95% CI of LS mean	(0.19, 5.09)	(-2.43, 2.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.70 (-6.12, 0.72)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	80.43 (2.02)	79.90 (1.99)
95% CI of LS mean	(76.44, 84.42)	(75.98, 83.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-6.14, 5.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	3.06 (1.44)	0.82 (1.41)
95% CI of LS mean	(0.23, 5.89)	(-1.95, 3.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.24 (-6.21, 1.73)
Week 52		
n	115	116
Mean (SD)	80.10 (19.94)	79.89 (20.82)
Absolute Change at Week 52		
n	111	114
Mean (SD)	2.70 (15.87)	1.36 (15.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52 (MMRM)		
n	114	115
LS mean (SE)	80.30 (1.88)	80.43 (1.85)
95% CI of LS mean	(76.59, 84.01)	(76.78, 84.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-5.09, 5.35)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	2.95 (1.49)	1.31 (1.46)
95% CI of LS mean	(0.01, 5.89)	(-1.57, 4.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.64 (-5.76, 2.48)
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	2.88 (1.17)	0.69 (1.13)
95% CI of LS mean	(0.59, 5.18)	(-1.55, 2.93)
P-value within Treatment	0.0141	0.5440
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.19 (-5.41, 1.02)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1800

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Hedges' G (SE)		-0.18 (0.13)
Hedges' 95% CI		(-0.43, 0.08)
Hedges' P-value		0.1796

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	77.48 (27.78)	83.89 (23.19)
Week 8 (MMRM)		
n	34	36
LS mean (SE)	82.31 (3.89)	84.58 (3.71)
95% CI of LS mean	(74.55, 90.07)	(77.18, 91.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.27 (-8.52, 13.06)
Absolute Change at Week 8 (MMRM)		
n	33	36
LS mean (SE)	4.32 (2.47)	0.07 (2.35)
95% CI of LS mean	(-0.61, 9.25)	(-4.61, 4.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.24 (-11.09, 2.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 16 (MMRM)		
n	32	36
LS mean (SE)	80.60 (4.02)	83.53 (3.80)
95% CI of LS mean	(72.59, 88.62)	(75.94, 91.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.92 (-8.19, 14.04)
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	2.99 (2.70)	-0.91 (2.53)
95% CI of LS mean	(-2.40, 8.37)	(-5.96, 4.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.90 (-11.33, 3.54)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	81.10 (4.33)	82.43 (4.12)
95% CI of LS mean	(72.45, 89.75)	(74.20, 90.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.33 (-10.67, 13.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	3.96 (3.23)	-1.96 (3.07)
95% CI of LS mean	(-2.48, 10.40)	(-8.10, 4.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.92 (-14.86, 3.02)
Week 52		
n	33	35
Mean (SD)	80.47 (20.98)	83.17 (22.45)
Absolute Change at Week 52		
n	32	34
Mean (SD)	1.74 (24.30)	-1.63 (20.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52 (MMRM)		
n	32	35
LS mean (SE)	78.99 (3.77)	83.51 (3.60)
95% CI of LS mean	(71.46, 86.53)	(76.32, 90.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.51 (-5.97, 15.00)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	1.60 (4.09)	-1.29 (3.89)
95% CI of LS mean	(-6.56, 9.77)	(-9.05, 6.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.90 (-14.19, 8.40)
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	2.85 (2.93)	-1.39 (2.77)
95% CI of LS mean	(-3.00, 8.70)	(-6.92, 4.14)
P-value within Treatment	0.3341	0.6176
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.24 (-12.34, 3.86)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2997

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		-0.25 (0.24)
Hedges' 95% CI		(-0.72, 0.22)
Hedges' P-value		0.2990

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	75.56 (23.02)	77.73 (21.02)
Week 8 (MMRM)		
n	243	237
LS mean (SE)	77.98 (1.42)	78.47 (1.44)
95% CI of LS mean	(75.19, 80.76)	(75.64, 81.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-3.48, 4.46)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	2.16 (0.95)	0.66 (0.95)
95% CI of LS mean	(0.29, 4.02)	(-1.21, 2.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.50 (-4.14, 1.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 16 (MMRM)		
n	241	231
LS mean (SE)	78.01 (1.32)	78.89 (1.34)
95% CI of LS mean	(75.42, 80.60)	(76.25, 81.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-2.82, 4.58)
Absolute Change at Week 16 (MMRM)		
n	235	228
LS mean (SE)	2.00 (0.90)	0.94 (0.91)
95% CI of LS mean	(0.22, 3.77)	(-0.86, 2.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.06 (-3.58, 1.47)
Week 24 (MMRM)		
n	240	229
LS mean (SE)	78.88 (1.37)	79.27 (1.39)
95% CI of LS mean	(76.19, 81.57)	(76.53, 82.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.39 (-3.46, 4.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 24 (MMRM)		
n	234	227
LS mean (SE)	2.98 (0.96)	1.44 (0.97)
95% CI of LS mean	(1.10, 4.86)	(-0.47, 3.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.54 (-4.23, 1.14)
Week 52		
n	244	230
Mean (SD)	78.37 (21.12)	79.03 (21.74)
Absolute Change at Week 52		
n	238	227
Mean (SD)	2.61 (15.92)	1.76 (15.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52 (MMRM)		
n	237	224
LS mean (SE)	78.35 (1.37)	79.52 (1.39)
95% CI of LS mean	(75.66, 81.04)	(76.78, 82.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-2.67, 5.01)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	2.29 (1.04)	1.81 (1.06)
95% CI of LS mean	(0.24, 4.34)	(-0.27, 3.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.48 (-3.40, 2.45)
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	2.42 (0.81)	1.40 (0.82)
95% CI of LS mean	(0.83, 4.01)	(-0.21, 3.01)
P-value within Treatment	0.0029	0.0885
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.03 (-3.29, 1.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3738

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Hedges' G (SE)		-0.08 (0.09)
Hedges' 95% CI		(-0.26, 0.10)
Hedges' P-value		0.3734

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	75.64 (21.94)	83.26 (20.22)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	80.76 (2.56)	79.30 (2.75)
95% CI of LS mean	(75.70, 85.82)	(73.88, 84.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.45 (-8.89, 5.98)
Absolute Change at Week 8 (MMRM)		
n	77	67
LS mean (SE)	4.24 (1.74)	-3.56 (1.86)
95% CI of LS mean	(0.81, 7.67)	(-7.23, 0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.80 (-12.85, -2.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 16 (MMRM)		
n	77	67
LS mean (SE)	80.09 (2.22)	83.59 (2.38)
95% CI of LS mean	(75.71, 84.48)	(78.88, 88.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.49 (-2.95, 9.94)
Absolute Change at Week 16 (MMRM)		
n	75	66
LS mean (SE)	3.68 (1.63)	0.86 (1.74)
95% CI of LS mean	(0.46, 6.89)	(-2.57, 4.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.82 (-7.54, 1.90)
Week 24 (MMRM)		
n	79	63
LS mean (SE)	79.07 (2.35)	82.33 (2.56)
95% CI of LS mean	(74.42, 83.72)	(77.28, 87.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.26 (-3.62, 10.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 24 (MMRM)		
n	77	63
LS mean (SE)	2.80 (1.88)	-0.38 (2.05)
95% CI of LS mean	(-0.92, 6.52)	(-4.42, 3.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.18 (-8.68, 2.33)
Week 52		
n	78	67
Mean (SD)	79.91 (20.89)	82.09 (22.22)
Absolute Change at Week 52		
n	76	66
Mean (SD)	4.24 (17.77)	-0.51 (17.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52 (MMRM)		
n	77	64
LS mean (SE)	80.21 (2.40)	83.05 (2.60)
95% CI of LS mean	(75.46, 84.96)	(77.91, 88.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.83 (-4.18, 9.85)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	3.84 (2.08)	0.54 (2.25)
95% CI of LS mean	(-0.28, 7.95)	(-3.91, 5.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.29 (-9.37, 2.78)
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	3.44 (1.64)	0.34 (1.77)
95% CI of LS mean	(0.20, 6.68)	(-3.15, 3.83)
P-value within Treatment	0.0377	0.8467
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.10 (-7.88, 1.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2024

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Hedges' G (SE)		-0.21 (0.17)
Hedges' 95% CI		(-0.55, 0.12)
Hedges' P-value		0.2020

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	75.75 (24.25)	77.03 (21.61)
Week 8 (MMRM)		
n	198	205
LS mean (SE)	77.63 (1.57)	79.28 (1.54)
95% CI of LS mean	(74.55, 80.71)	(76.26, 82.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.65 (-2.67, 5.97)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	1.64 (1.02)	1.98 (1.00)
95% CI of LS mean	(-0.36, 3.65)	(0.02, 3.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (-2.47, 3.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 16 (MMRM)		
n	196	200
LS mean (SE)	77.73 (1.52)	78.23 (1.49)
95% CI of LS mean	(74.75, 80.72)	(75.29, 81.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-3.69, 4.69)
Absolute Change at Week 16 (MMRM)		
n	191	198
LS mean (SE)	1.42 (1.01)	0.72 (0.99)
95% CI of LS mean	(-0.57, 3.41)	(-1.23, 2.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-3.49, 2.09)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	79.32 (1.57)	78.85 (1.54)
95% CI of LS mean	(76.23, 82.40)	(75.82, 81.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-4.79, 3.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	3.19 (1.07)	1.51 (1.04)
95% CI of LS mean	(1.09, 5.29)	(-0.54, 3.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.68 (-4.62, 1.26)
Week 52		
n	194	196
Mean (SD)	77.84 (21.08)	78.68 (21.74)
Absolute Change at Week 52		
n	189	193
Mean (SD)	1.53 (16.77)	1.90 (16.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52 (MMRM)		
n	192	195
LS mean (SE)	77.78 (1.53)	79.12 (1.51)
95% CI of LS mean	(74.77, 80.79)	(76.16, 82.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.34 (-2.88, 5.57)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	1.50 (1.19)	1.80 (1.17)
95% CI of LS mean	(-0.84, 3.85)	(-0.51, 4.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-3.00, 3.59)
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	2.04 (0.90)	1.34 (0.88)
95% CI of LS mean	(0.26, 3.81)	(-0.39, 3.08)
P-value within Treatment	0.0245	0.1289
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-3.18, 1.79)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5826

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Hedges' G (SE)		-0.06 (0.10)
Hedges' 95% CI		(-0.25, 0.14)
Hedges' P-value		0.5825

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	73.97 (24.89)	78.23 (22.90)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	77.70 (2.01)	76.59 (1.95)
95% CI of LS mean	(73.74, 81.67)	(72.76, 80.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.11 (-6.66, 4.44)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	3.46 (1.13)	-1.73 (1.08)
95% CI of LS mean	(1.24, 5.68)	(-3.86, 0.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.18 (-8.28, -2.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 16 (MMRM)		
n	130	138
LS mean (SE)	77.09 (1.93)	77.99 (1.87)
95% CI of LS mean	(73.28, 80.89)	(74.30, 81.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.90 (-4.43, 6.24)
Absolute Change at Week 16 (MMRM)		
n	126	136
LS mean (SE)	3.02 (1.16)	-0.55 (1.11)
95% CI of LS mean	(0.74, 5.29)	(-2.74, 1.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.57 (-6.74, -0.39)
Week 24 (MMRM)		
n	133	140
LS mean (SE)	78.04 (2.03)	78.40 (1.97)
95% CI of LS mean	(74.05, 82.04)	(74.53, 82.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-5.24, 5.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 24 (MMRM)		
n	129	137
LS mean (SE)	4.22 (1.32)	0.11 (1.28)
95% CI of LS mean	(1.62, 6.81)	(-2.41, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.11 (-7.74, -0.49)
Week 52		
n	139	143
Mean (SD)	78.34 (21.04)	78.40 (23.73)
Absolute Change at Week 52		
n	135	140
Mean (SD)	4.44 (15.49)	0.79 (15.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52 (MMRM)		
n	132	139
LS mean (SE)	78.02 (1.95)	79.19 (1.90)
95% CI of LS mean	(74.17, 81.87)	(75.46, 82.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-4.23, 6.57)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	4.02 (1.38)	0.91 (1.34)
95% CI of LS mean	(1.31, 6.74)	(-1.73, 3.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.12 (-6.91, 0.68)
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	3.75 (1.09)	0.15 (1.05)
95% CI of LS mean	(1.61, 5.90)	(-1.92, 2.23)
P-value within Treatment	0.0007	0.8835
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.60 (-6.60, -0.60)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0190

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Hedges' G (SE)		-0.29 (0.12)
Hedges' 95% CI		(-0.53, -0.05)
Hedges' P-value		0.0190

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	77.62 (22.30)	79.02 (19.73)
Week 8 (MMRM)		
n	143	130
LS mean (SE)	79.54 (1.78)	81.97 (1.86)
95% CI of LS mean	(76.03, 83.05)	(78.30, 85.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.43 (-2.68, 7.53)
Absolute Change at Week 8 (MMRM)		
n	140	129
LS mean (SE)	1.48 (1.36)	2.96 (1.42)
95% CI of LS mean	(-1.20, 4.17)	(0.17, 5.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.48 (-2.41, 5.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 16 (MMRM)		
n	143	129
LS mean (SE)	79.85 (1.64)	81.03 (1.71)
95% CI of LS mean	(76.63, 83.07)	(77.67, 84.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.18 (-3.51, 5.87)
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	1.32 (1.28)	1.98 (1.33)
95% CI of LS mean	(-1.19, 3.84)	(-0.64, 4.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-3.00, 4.31)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	80.62 (1.69)	80.91 (1.77)
95% CI of LS mean	(77.30, 83.94)	(77.43, 84.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.29 (-4.55, 5.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	2.16 (1.33)	1.85 (1.38)
95% CI of LS mean	(-0.45, 4.77)	(-0.87, 4.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-4.10, 3.48)
Week 52		
n	138	122
Mean (SD)	78.90 (21.20)	80.97 (19.40)
Absolute Change at Week 52		
n	135	121
Mean (SD)	0.58 (18.38)	1.93 (17.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52 (MMRM)		
n	137	120
LS mean (SE)	79.11 (1.72)	80.79 (1.81)
95% CI of LS mean	(75.72, 82.49)	(77.23, 84.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-3.26, 6.63)
Absolute Change at Week 52 (MMRM)		
n	134	119
LS mean (SE)	0.59 (1.56)	1.82 (1.63)
95% CI of LS mean	(-2.48, 3.65)	(-1.40, 5.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-3.22, 5.70)
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	1.36 (1.16)	1.88 (1.21)
95% CI of LS mean	(-0.94, 3.65)	(-0.50, 4.27)
P-value within Treatment	0.2452	0.1215
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-2.81, 3.86)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7559

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Hedges' G (SE)		0.04 (0.12)
Hedges' 95% CI		(-0.20, 0.28)
Hedges' P-value		0.7543

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	75.82 (21.74)	80.98 (20.23)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	78.43 (2.27)	80.66 (2.12)
95% CI of LS mean	(73.95, 82.90)	(76.47, 84.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.23 (-3.91, 8.37)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	2.47 (1.55)	-0.36 (1.46)
95% CI of LS mean	(-0.58, 5.53)	(-3.24, 2.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.83 (-7.04, 1.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 16 (MMRM)		
n	96	108
LS mean (SE)	77.94 (2.06)	82.34 (1.94)
95% CI of LS mean	(73.87, 82.00)	(78.53, 86.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.40 (-1.18, 9.99)
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	2.03 (1.40)	1.07 (1.33)
95% CI of LS mean	(-0.74, 4.80)	(-1.56, 3.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.96 (-4.78, 2.86)
Week 24 (MMRM)		
n	98	108
LS mean (SE)	78.70 (2.11)	80.99 (1.98)
95% CI of LS mean	(74.55, 82.86)	(77.08, 84.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.28 (-3.43, 8.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 24 (MMRM)		
n	97	106
LS mean (SE)	2.92 (1.44)	-0.18 (1.37)
95% CI of LS mean	(0.09, 5.75)	(-2.88, 2.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.10 (-7.01, 0.82)
Week 52		
n	101	104
Mean (SD)	77.45 (21.69)	80.56 (20.35)
Absolute Change at Week 52		
n	100	101
Mean (SD)	1.56 (18.08)	0.22 (15.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52 (MMRM)		
n	97	104
LS mean (SE)	77.31 (2.11)	81.44 (2.00)
95% CI of LS mean	(73.15, 81.46)	(77.49, 85.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.13 (-1.61, 9.87)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	1.27 (1.70)	0.57 (1.64)
95% CI of LS mean	(-2.08, 4.62)	(-2.66, 3.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-5.36, 3.96)
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	2.07 (1.23)	0.49 (1.17)
95% CI of LS mean	(-0.35, 4.49)	(-1.82, 2.79)
P-value within Treatment	0.0928	0.6777
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-4.93, 1.76)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3519

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Hedges' G (SE)		-0.13 (0.14)
Hedges' 95% CI		(-0.41, 0.14)
Hedges' P-value		0.3515

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	75.80 (24.72)	77.05 (22.06)
Week 8 (MMRM)		
n	179	161
LS mean (SE)	78.48 (1.65)	78.42 (1.73)
95% CI of LS mean	(75.24, 81.72)	(75.01, 81.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-4.77, 4.65)
Absolute Change at Week 8 (MMRM)		
n	173	161
LS mean (SE)	2.44 (1.08)	1.16 (1.12)
95% CI of LS mean	(0.31, 4.58)	(-1.04, 3.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.28 (-4.35, 1.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 16 (MMRM)		
n	177	159
LS mean (SE)	78.55 (1.57)	77.76 (1.65)
95% CI of LS mean	(75.47, 81.64)	(74.52, 81.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.79 (-5.27, 3.69)
Absolute Change at Week 16 (MMRM)		
n	171	159
LS mean (SE)	2.17 (1.10)	0.45 (1.13)
95% CI of LS mean	(0.01, 4.33)	(-1.78, 2.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.71 (-4.82, 1.39)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	79.43 (1.67)	78.97 (1.76)
95% CI of LS mean	(76.14, 82.73)	(75.51, 82.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-5.25, 4.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	3.22 (1.22)	1.75 (1.27)
95% CI of LS mean	(0.82, 5.62)	(-0.74, 4.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.47 (-4.93, 2.00)
Week 52		
n	176	161
Mean (SD)	79.29 (20.76)	78.95 (22.79)
Absolute Change at Week 52		
n	170	160
Mean (SD)	3.07 (16.49)	2.01 (17.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	172	155
LS mean (SE)	79.03 (1.62)	79.28 (1.70)
95% CI of LS mean	(75.84, 82.22)	(75.93, 82.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-4.38, 4.88)
Absolute Change at Week 52 (MMRM)		
n	166	154
LS mean (SE)	2.78 (1.31)	1.96 (1.36)
95% CI of LS mean	(0.20, 5.36)	(-0.71, 4.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.82 (-4.53, 2.90)
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	2.72 (1.04)	1.39 (1.08)
95% CI of LS mean	(0.67, 4.77)	(-0.73, 3.51)
P-value within Treatment	0.0093	0.1984
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.33 (-4.29, 1.62)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3754

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Hedges' G (SE)		-0.10 (0.11)
Hedges' 95% CI		(-0.31, 0.12)
Hedges' P-value		0.3749

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	79.95 (16.87)	82.97 (18.44)
Week 8 (MMRM)		
n	161	152
LS mean (SE)	79.97 (1.48)	81.52 (1.52)
95% CI of LS mean	(77.06, 82.88)	(78.52, 84.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.54 (-2.63, 5.72)
Absolute Change at Week 8 (MMRM)		
n	158	150
LS mean (SE)	0.72 (1.22)	-1.34 (1.25)
95% CI of LS mean	(-1.67, 3.11)	(-3.80, 1.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.07 (-5.49, 1.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 16 (MMRM)		
n	157	149
LS mean (SE)	78.66 (1.50)	80.97 (1.54)
95% CI of LS mean	(75.71, 81.62)	(77.94, 84.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.31 (-1.93, 6.55)
Absolute Change at Week 16 (MMRM)		
n	154	147
LS mean (SE)	-0.72 (1.24)	-1.99 (1.27)
95% CI of LS mean	(-3.17, 1.72)	(-4.50, 0.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.27 (-4.77, 2.23)
Week 24 (MMRM)		
n	155	147
LS mean (SE)	80.04 (1.46)	80.72 (1.50)
95% CI of LS mean	(77.16, 82.92)	(77.76, 83.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.68 (-3.45, 4.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 24 (MMRM)		
n	152	145
LS mean (SE)	0.99 (1.24)	-2.24 (1.27)
95% CI of LS mean	(-1.44, 3.43)	(-4.73, 0.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.23 (-6.71, 0.26)
Week 52		
n	159	144
Mean (SD)	78.48 (19.99)	80.02 (17.85)
Absolute Change at Week 52		
n	156	142
Mean (SD)	-0.93 (16.45)	-2.90 (15.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52 (MMRM)		
n	155	143
LS mean (SE)	78.08 (1.50)	80.19 (1.55)
95% CI of LS mean	(75.13, 81.04)	(77.14, 83.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.11 (-2.14, 6.36)
Absolute Change at Week 52 (MMRM)		
n	152	141
LS mean (SE)	-1.19 (1.30)	-2.71 (1.34)
95% CI of LS mean	(-3.75, 1.36)	(-5.35, -0.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.51 (-5.19, 2.17)
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	-0.31 (1.07)	-2.31 (1.10)
95% CI of LS mean	(-2.41, 1.79)	(-4.47, -0.16)
P-value within Treatment	0.7726	0.0356
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.00 (-5.02, 1.01)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1917

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Hedges' G (SE)		-0.15 (0.11)
Hedges' 95% CI		(-0.38, 0.08)
Hedges' P-value		0.1919

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	83.00 (17.31)	80.94 (18.58)
Week 8 (MMRM)		
n	116	121
LS mean (SE)	82.76 (1.70)	81.09 (1.66)
95% CI of LS mean	(79.42, 86.11)	(77.82, 84.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.68 (-6.37, 3.02)
Absolute Change at Week 8 (MMRM)		
n	112	120
LS mean (SE)	-0.69 (1.29)	0.10 (1.25)
95% CI of LS mean	(-3.24, 1.86)	(-2.36, 2.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.79 (-2.77, 4.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 16 (MMRM)		
n	115	119
LS mean (SE)	83.75 (1.66)	81.75 (1.63)
95% CI of LS mean	(80.47, 87.02)	(78.55, 84.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.99 (-6.59, 2.61)
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	0.54 (1.37)	0.67 (1.33)
95% CI of LS mean	(-2.16, 3.23)	(-1.94, 3.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-3.63, 3.90)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	82.18 (1.90)	79.44 (1.87)
95% CI of LS mean	(78.44, 85.92)	(75.77, 83.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.74 (-8.00, 2.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	-1.23 (1.37)	-1.60 (1.34)
95% CI of LS mean	(-3.93, 1.47)	(-4.24, 1.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-4.16, 3.42)
Week 52		
n	115	116
Mean (SD)	80.97 (20.85)	79.69 (20.63)
Absolute Change at Week 52		
n	111	114
Mean (SD)	-2.70 (14.54)	-1.56 (17.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52 (MMRM)		
n	114	115
LS mean (SE)	80.42 (1.95)	79.82 (1.92)
95% CI of LS mean	(76.59, 84.26)	(76.04, 83.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.60 (-6.01, 4.80)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	-2.91 (1.53)	-1.34 (1.50)
95% CI of LS mean	(-5.92, 0.10)	(-4.30, 1.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.57 (-2.66, 5.80)
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	-1.20 (1.18)	-0.76 (1.15)
95% CI of LS mean	(-3.54, 1.13)	(-3.03, 1.52)
P-value within Treatment	0.3105	0.5122
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-2.82, 3.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7880

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Hedges' G (SE)		0.04 (0.13)
Hedges' 95% CI		(-0.22, 0.29)
Hedges' P-value		0.7874

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	87.39 (15.97)	83.06 (21.79)
Week 8 (MMRM)		
n	34	37
LS mean (SE)	89.51 (3.10)	85.69 (2.95)
95% CI of LS mean	(83.34, 95.69)	(79.81, 91.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.82 (-12.41, 4.76)
Absolute Change at Week 8 (MMRM)		
n	33	37
LS mean (SE)	1.79 (2.83)	2.41 (2.68)
95% CI of LS mean	(-3.86, 7.43)	(-2.93, 7.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-7.21, 8.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 16 (MMRM)		
n	32	36
LS mean (SE)	92.42 (2.94)	89.39 (2.79)
95% CI of LS mean	(86.55, 98.30)	(83.82, 94.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.03 (-11.20, 5.13)
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	5.00 (3.15)	6.10 (2.95)
95% CI of LS mean	(-1.27, 11.28)	(0.21, 11.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.10 (-7.57, 9.76)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	89.22 (3.28)	84.72 (3.14)
95% CI of LS mean	(82.68, 95.76)	(78.46, 90.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.50 (-13.61, 4.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	1.98 (3.01)	1.16 (2.89)
95% CI of LS mean	(-4.03, 7.99)	(-4.60, 6.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.82 (-9.19, 7.56)
Week 52		
n	33	34
Mean (SD)	87.54 (17.29)	85.62 (18.66)
Absolute Change at Week 52		
n	32	33
Mean (SD)	0.69 (13.22)	-0.67 (24.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52 (MMRM)		
n	32	34
LS mean (SE)	86.47 (3.37)	84.25 (3.24)
95% CI of LS mean	(79.72, 93.22)	(77.77, 90.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.22 (-11.63, 7.18)
Absolute Change at Week 52 (MMRM)		
n	31	33
LS mean (SE)	-1.01 (3.55)	0.49 (3.40)
95% CI of LS mean	(-8.11, 6.10)	(-6.31, 7.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.49 (-8.38, 11.37)
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	1.99 (2.79)	2.58 (2.64)
95% CI of LS mean	(-3.57, 7.55)	(-2.69, 7.85)
P-value within Treatment	0.4772	0.3319
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-7.13, 8.31)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8791

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		0.04 (0.24)
Hedges' 95% CI		(-0.43, 0.51)
Hedges' P-value		0.8783

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	80.14 (17.14)	81.90 (17.81)
Week 8 (MMRM)		
n	243	236
LS mean (SE)	79.90 (1.19)	80.63 (1.21)
95% CI of LS mean	(77.55, 82.25)	(78.25, 83.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.74 (-2.61, 4.08)
Absolute Change at Week 8 (MMRM)		
n	237	233
LS mean (SE)	-0.21 (0.93)	-1.11 (0.94)
95% CI of LS mean	(-2.05, 1.62)	(-2.96, 0.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.90 (-3.51, 1.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 16 (MMRM)		
n	240	232
LS mean (SE)	79.06 (1.21)	79.97 (1.22)
95% CI of LS mean	(76.69, 81.43)	(77.57, 82.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-2.47, 4.30)
Absolute Change at Week 16 (MMRM)		
n	234	229
LS mean (SE)	-1.07 (0.95)	-1.83 (0.96)
95% CI of LS mean	(-2.94, 0.80)	(-3.72, 0.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.76 (-3.42, 1.91)
Week 24 (MMRM)		
n	239	229
LS mean (SE)	79.67 (1.25)	79.37 (1.27)
95% CI of LS mean	(77.21, 82.12)	(76.88, 81.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-3.80, 3.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 24 (MMRM)		
n	233	227
LS mean (SE)	-0.34 (0.96)	-2.44 (0.97)
95% CI of LS mean	(-2.22, 1.54)	(-4.34, -0.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.10 (-4.78, 0.58)
Week 52		
n	244	230
Mean (SD)	78.51 (20.47)	78.94 (19.03)
Absolute Change at Week 52		
n	238	227
Mean (SD)	-1.77 (16.04)	-2.69 (14.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52 (MMRM)		
n	237	224
LS mean (SE)	77.93 (1.28)	79.32 (1.31)
95% CI of LS mean	(75.42, 80.45)	(76.75, 81.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-2.21, 4.98)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	-2.20 (1.01)	-2.42 (1.03)
95% CI of LS mean	(-4.18, -0.21)	(-4.44, -0.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-3.06, 2.61)
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	-1.20 (0.81)	-2.23 (0.82)
95% CI of LS mean	(-2.80, 0.40)	(-3.85, -0.61)
P-value within Treatment	0.1403	0.0072
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.02 (-3.30, 1.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3776

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Hedges' G (SE)		-0.08 (0.09)
Hedges' 95% CI		(-0.26, 0.10)
Hedges' P-value		0.3771

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	80.91 (17.81)	82.79 (18.67)
Week 8 (MMRM)		
n	79	69
LS mean (SE)	81.81 (2.15)	80.57 (2.30)
95% CI of LS mean	(77.56, 86.06)	(76.02, 85.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.24 (-7.48, 5.00)
Absolute Change at Week 8 (MMRM)		
n	77	68
LS mean (SE)	0.61 (1.69)	-1.50 (1.80)
95% CI of LS mean	(-2.74, 3.95)	(-5.07, 2.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.11 (-7.02, 2.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 16 (MMRM)		
n	76	67
LS mean (SE)	81.02 (2.31)	79.42 (2.47)
95% CI of LS mean	(76.45, 85.58)	(74.53, 84.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.60 (-8.30, 5.11)
Absolute Change at Week 16 (MMRM)		
n	74	66
LS mean (SE)	-0.32 (1.97)	-2.87 (2.10)
95% CI of LS mean	(-4.23, 3.58)	(-7.03, 1.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.55 (-8.27, 3.17)
Week 24 (MMRM)		
n	79	63
LS mean (SE)	82.51 (2.27)	80.50 (2.46)
95% CI of LS mean	(78.03, 87.00)	(75.64, 85.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.01 (-8.64, 4.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 24 (MMRM)		
n	77	63
LS mean (SE)	1.18 (1.93)	-1.74 (2.08)
95% CI of LS mean	(-2.63, 4.99)	(-5.86, 2.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.92 (-8.55, 2.71)
Week 52		
n	78	66
Mean (SD)	81.48 (20.55)	80.13 (18.54)
Absolute Change at Week 52		
n	76	65
Mean (SD)	-0.15 (15.77)	-3.59 (15.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52 (MMRM)		
n	77	63
LS mean (SE)	81.37 (2.20)	79.93 (2.39)
95% CI of LS mean	(77.01, 85.73)	(75.21, 84.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-7.88, 5.00)
Absolute Change at Week 52 (MMRM)		
n	75	62
LS mean (SE)	-0.05 (1.87)	-2.52 (2.03)
95% CI of LS mean	(-3.74, 3.64)	(-6.53, 1.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.47 (-7.94, 2.99)
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	0.27 (1.68)	-2.38 (1.80)
95% CI of LS mean	(-3.04, 3.58)	(-5.93, 1.18)
P-value within Treatment	0.8720	0.1884
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.65 (-7.53, 2.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2853

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\global\clinstat_prod\20251111\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13NOV2025 16:20

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Hedges' G (SE)		-0.18 (0.17)
Hedges' 95% CI		(-0.51, 0.15)
Hedges' P-value		0.2845

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	80.82 (16.97)	81.75 (18.38)
Week 8 (MMRM)		
n	198	204
LS mean (SE)	80.93 (1.31)	81.55 (1.29)
95% CI of LS mean	(78.35, 83.52)	(79.01, 84.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-3.01, 4.24)
Absolute Change at Week 8 (MMRM)		
n	193	202
LS mean (SE)	-0.12 (1.04)	-0.36 (1.02)
95% CI of LS mean	(-2.17, 1.93)	(-2.37, 1.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-3.12, 2.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 16 (MMRM)		
n	196	201
LS mean (SE)	80.72 (1.27)	81.91 (1.25)
95% CI of LS mean	(78.22, 83.21)	(79.46, 84.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.20 (-2.30, 4.70)
Absolute Change at Week 16 (MMRM)		
n	191	199
LS mean (SE)	-0.24 (1.04)	-0.01 (1.02)
95% CI of LS mean	(-2.29, 1.80)	(-2.01, 1.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-2.63, 3.09)
Week 24 (MMRM)		
n	194	202
LS mean (SE)	80.31 (1.36)	80.07 (1.33)
95% CI of LS mean	(77.64, 82.99)	(77.44, 82.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-3.99, 3.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 24 (MMRM)		
n	189	199
LS mean (SE)	-0.47 (1.04)	-1.88 (1.01)
95% CI of LS mean	(-2.51, 1.57)	(-3.87, 0.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.41 (-4.26, 1.44)
Week 52		
n	194	196
Mean (SD)	78.41 (20.27)	79.65 (19.32)
Absolute Change at Week 52		
n	189	193
Mean (SD)	-2.18 (15.83)	-2.01 (16.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52 (MMRM)		
n	192	195
LS mean (SE)	78.19 (1.42)	80.11 (1.40)
95% CI of LS mean	(75.40, 80.98)	(77.35, 82.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.91 (-2.01, 5.83)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	-2.70 (1.17)	-1.79 (1.15)
95% CI of LS mean	(-5.00, -0.40)	(-4.06, 0.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-2.32, 4.14)
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	-1.14 (0.90)	-1.23 (0.88)
95% CI of LS mean	(-2.90, 0.62)	(-2.95, 0.49)
P-value within Treatment	0.2049	0.1615
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-2.56, 2.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9417

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Program: GMA\VX121\global\clinstat_prod\20251111\t-qs-mmrm-abs-cfqr-nonrd-ag12-52wks-sub-103.sas Creation: 13NOV2025 16:20

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Hedges' G (SE)		-0.01 (0.10)
Hedges' 95% CI		(-0.20, 0.19)
Hedges' P-value		0.9417

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	81.59 (16.47)	82.88 (17.99)
Week 8 (MMRM)		
n	134	142
LS mean (SE)	82.35 (1.49)	83.06 (1.45)
95% CI of LS mean	(79.42, 85.29)	(80.21, 85.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.70 (-3.41, 4.82)
Absolute Change at Week 8 (MMRM)		
n	130	140
LS mean (SE)	1.09 (1.27)	0.00 (1.22)
95% CI of LS mean	(-1.40, 3.59)	(-2.41, 2.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.10 (-4.58, 2.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 16 (MMRM)		
n	129	139
LS mean (SE)	80.66 (1.46)	82.66 (1.41)
95% CI of LS mean	(77.78, 83.53)	(79.87, 85.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.00 (-2.03, 6.02)
Absolute Change at Week 16 (MMRM)		
n	125	137
LS mean (SE)	-0.45 (1.30)	-0.41 (1.25)
95% CI of LS mean	(-3.01, 2.11)	(-2.87, 2.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.04 (-3.53, 3.61)
Week 24 (MMRM)		
n	132	140
LS mean (SE)	80.58 (1.49)	82.70 (1.45)
95% CI of LS mean	(77.64, 83.52)	(79.85, 85.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-2.00, 6.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 24 (MMRM)		
n	128	137
LS mean (SE)	-0.52 (1.21)	-0.44 (1.17)
95% CI of LS mean	(-2.91, 1.87)	(-2.75, 1.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-3.26, 3.42)
Week 52		
n	139	143
Mean (SD)	80.02 (19.11)	81.74 (17.16)
Absolute Change at Week 52		
n	135	140
Mean (SD)	-1.48 (15.23)	-0.95 (15.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52 (MMRM)		
n	132	139
LS mean (SE)	79.02 (1.57)	82.66 (1.53)
95% CI of LS mean	(75.92, 82.12)	(79.65, 85.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.64 (-0.70, 7.98)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	-2.26 (1.37)	-0.36 (1.33)
95% CI of LS mean	(-4.96, 0.43)	(-2.97, 2.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.90 (-1.86, 5.67)
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	-1.08 (1.07)	-0.40 (1.03)
95% CI of LS mean	(-3.18, 1.02)	(-2.43, 1.63)
P-value within Treatment	0.3136	0.6951
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.67 (-2.27, 3.61)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6525

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Hedges' G (SE)		0.06 (0.12)
Hedges' 95% CI		(-0.18, 0.29)
Hedges' P-value		0.6507

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	80.59 (17.82)	81.18 (18.84)
Week 8 (MMRM)		
n	143	131
LS mean (SE)	79.88 (1.66)	79.62 (1.73)
95% CI of LS mean	(76.61, 83.16)	(76.21, 83.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.26 (-5.02, 4.50)
Absolute Change at Week 8 (MMRM)		
n	140	130
LS mean (SE)	-1.00 (1.25)	-1.13 (1.29)
95% CI of LS mean	(-3.46, 1.45)	(-3.67, 1.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-3.68, 3.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 16 (MMRM)		
n	143	129
LS mean (SE)	80.74 (1.70)	80.01 (1.78)
95% CI of LS mean	(77.39, 84.09)	(76.51, 83.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-5.61, 4.15)
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	-0.21 (1.31)	-0.91 (1.36)
95% CI of LS mean	(-2.79, 2.37)	(-3.59, 1.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-4.44, 3.04)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	81.07 (1.80)	77.61 (1.89)
95% CI of LS mean	(77.53, 84.61)	(73.90, 81.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.46 (-8.62, 1.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	0.30 (1.37)	-3.27 (1.43)
95% CI of LS mean	(-2.39, 3.00)	(-6.09, -0.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.58 (-7.50, 0.34)
Week 52		
n	138	121
Mean (SD)	79.15 (21.50)	77.50 (20.96)
Absolute Change at Week 52		
n	135	120
Mean (SD)	-1.48 (16.28)	-4.17 (16.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52 (MMRM)		
n	137	119
LS mean (SE)	78.93 (1.80)	77.25 (1.90)
95% CI of LS mean	(75.38, 82.49)	(73.51, 81.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.68 (-6.87, 3.51)
Absolute Change at Week 52 (MMRM)		
n	134	118
LS mean (SE)	-1.83 (1.42)	-3.74 (1.50)
95% CI of LS mean	(-4.63, 0.97)	(-6.69, -0.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.91 (-5.99, 2.17)
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	-0.58 (1.16)	-2.64 (1.21)
95% CI of LS mean	(-2.87, 1.72)	(-5.03, -0.25)
P-value within Treatment	0.6203	0.0304
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.06 (-5.40, 1.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2240

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Hedges' G (SE)		-0.15 (0.12)
Hedges' 95% CI		(-0.39, 0.09)
Hedges' P-value		0.2217

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	79.52 (17.74)	83.58 (18.46)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	79.37 (1.85)	84.65 (1.73)
95% CI of LS mean	(75.73, 83.02)	(81.24, 88.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.28 (0.28, 10.28)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	-0.34 (1.34)	1.05 (1.27)
95% CI of LS mean	(-2.99, 2.30)	(-1.45, 3.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.39 (-2.25, 5.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 16 (MMRM)		
n	96	108
LS mean (SE)	79.15 (1.78)	84.79 (1.68)
95% CI of LS mean	(75.63, 82.66)	(81.49, 88.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.65 (0.81, 10.48)
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	-0.39 (1.50)	0.91 (1.43)
95% CI of LS mean	(-3.35, 2.58)	(-1.91, 3.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.29 (-2.80, 5.39)
Week 24 (MMRM)		
n	98	108
LS mean (SE)	80.24 (1.93)	83.85 (1.82)
95% CI of LS mean	(76.43, 84.05)	(80.26, 87.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.61 (-1.63, 8.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 24 (MMRM)		
n	97	106
LS mean (SE)	0.77 (1.47)	-0.04 (1.40)
95% CI of LS mean	(-2.12, 3.67)	(-2.80, 2.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-4.82, 3.19)
Week 52		
n	101	104
Mean (SD)	77.89 (20.21)	83.65 (17.51)
Absolute Change at Week 52		
n	100	101
Mean (SD)	-1.78 (16.01)	0.22 (15.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52 (MMRM)		
n	97	104
LS mean (SE)	77.24 (1.91)	84.24 (1.82)
95% CI of LS mean	(73.47, 81.01)	(80.66, 87.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.00 (1.80, 12.20)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	-2.51 (1.57)	0.53 (1.52)
95% CI of LS mean	(-5.61, 0.58)	(-2.46, 3.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.04 (-1.27, 7.35)
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	-0.71 (1.26)	0.47 (1.21)
95% CI of LS mean	(-3.20, 1.79)	(-1.91, 2.85)
P-value within Treatment	0.5761	0.6999
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-2.28, 4.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5033

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Hedges' G (SE)		0.09 (0.14)
Hedges' 95% CI		(-0.18, 0.37)
Hedges' P-value		0.5028

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	81.98 (16.78)	81.07 (18.33)
Week 8 (MMRM)		
n	179	161
LS mean (SE)	82.15 (1.39)	78.99 (1.46)
95% CI of LS mean	(79.41, 84.89)	(76.11, 81.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.16 (-7.14, 0.82)
Absolute Change at Week 8 (MMRM)		
n	173	161
LS mean (SE)	0.38 (1.15)	-1.82 (1.20)
95% CI of LS mean	(-1.89, 2.65)	(-4.17, 0.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.20 (-5.47, 1.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 16 (MMRM)		
n	176	160
LS mean (SE)	81.76 (1.42)	78.90 (1.49)
95% CI of LS mean	(78.97, 84.55)	(75.97, 81.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.86 (-6.92, 1.19)
Absolute Change at Week 16 (MMRM)		
n	170	160
LS mean (SE)	-0.12 (1.14)	-1.90 (1.18)
95% CI of LS mean	(-2.37, 2.13)	(-4.23, 0.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.79 (-5.03, 1.45)
Week 24 (MMRM)		
n	175	157
LS mean (SE)	81.33 (1.46)	77.61 (1.53)
95% CI of LS mean	(78.47, 84.19)	(74.60, 80.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.72 (-7.87, 0.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 24 (MMRM)		
n	169	156
LS mean (SE)	-0.42 (1.15)	-3.22 (1.20)
95% CI of LS mean	(-2.69, 1.84)	(-5.57, -0.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.79 (-6.06, 0.48)
Week 52		
n	176	160
Mean (SD)	80.56 (20.35)	77.29 (19.68)
Absolute Change at Week 52		
n	170	159
Mean (SD)	-1.31 (15.61)	-4.12 (16.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	172	154
LS mean (SE)	80.12 (1.51)	77.13 (1.59)
95% CI of LS mean	(77.15, 83.09)	(74.00, 80.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.99 (-7.31, 1.32)
Absolute Change at Week 52 (MMRM)		
n	166	153
LS mean (SE)	-1.61 (1.25)	-3.79 (1.30)
95% CI of LS mean	(-4.07, 0.85)	(-6.35, -1.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.18 (-5.73, 1.38)
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	-0.72 (0.99)	-2.97 (1.02)
95% CI of LS mean	(-2.66, 1.23)	(-4.98, -0.95)
P-value within Treatment	0.4691	0.0040
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.25 (-5.06, 0.56)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1156

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Hedges' G (SE)		-0.17 (0.11)
Hedges' 95% CI		(-0.39, 0.04)
Hedges' P-value		0.1156

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	92.78 (13.34)	94.15 (12.13)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	91.88 (1.09)	93.87 (1.12)
95% CI of LS mean	(89.74, 94.03)	(91.67, 96.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.99 (-1.09, 5.06)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	-0.42 (0.87)	-0.34 (0.89)
95% CI of LS mean	(-2.12, 1.29)	(-2.08, 1.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-2.36, 2.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 16 (MMRM)		
n	158	149
LS mean (SE)	91.93 (1.10)	93.27 (1.13)
95% CI of LS mean	(89.76, 94.11)	(91.03, 95.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.33 (-1.79, 4.45)
Absolute Change at Week 16 (MMRM)		
n	155	147
LS mean (SE)	-0.29 (0.87)	-0.93 (0.89)
95% CI of LS mean	(-2.01, 1.42)	(-2.69, 0.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-3.09, 1.81)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	92.24 (1.13)	93.01 (1.16)
95% CI of LS mean	(90.01, 94.46)	(90.72, 95.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.78 (-2.42, 3.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	0.07 (0.83)	-1.17 (0.85)
95% CI of LS mean	(-1.55, 1.70)	(-2.84, 0.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.24 (-3.58, 1.09)
Week 52		
n	159	145
Mean (SD)	93.01 (14.55)	93.26 (13.50)
Absolute Change at Week 52		
n	156	143
Mean (SD)	0.75 (13.16)	-0.93 (10.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52 (MMRM)		
n	155	144
LS mean (SE)	92.83 (1.12)	93.31 (1.16)
95% CI of LS mean	(90.63, 95.03)	(91.04, 95.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-2.68, 3.65)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	0.47 (0.99)	-0.88 (1.02)
95% CI of LS mean	(-1.47, 2.41)	(-2.88, 1.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.35 (-4.13, 1.44)
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	0.08 (0.70)	-0.99 (0.72)
95% CI of LS mean	(-1.29, 1.45)	(-2.40, 0.41)
P-value within Treatment	0.9055	0.1661
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.08 (-3.04, 0.89)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2827

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Hedges' G (SE)		-0.12 (0.11)
Hedges' 95% CI		(-0.35, 0.10)
Hedges' P-value		0.2826

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	92.66 (16.11)	94.17 (11.96)
Week 8 (MMRM)		
n	116	121
LS mean (SE)	93.44 (1.27)	94.30 (1.24)
95% CI of LS mean	(90.93, 95.94)	(91.85, 96.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-2.65, 4.37)
Absolute Change at Week 8 (MMRM)		
n	112	120
LS mean (SE)	0.93 (1.04)	0.13 (1.00)
95% CI of LS mean	(-1.12, 2.98)	(-1.85, 2.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.80 (-3.66, 2.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 16 (MMRM)		
n	115	119
LS mean (SE)	93.58 (1.42)	93.05 (1.39)
95% CI of LS mean	(90.79, 96.37)	(90.31, 95.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-4.45, 3.40)
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	0.99 (1.24)	-1.15 (1.20)
95% CI of LS mean	(-1.45, 3.44)	(-3.52, 1.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.14 (-5.55, 1.27)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	92.79 (1.55)	92.01 (1.54)
95% CI of LS mean	(89.73, 95.85)	(88.99, 95.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.78 (-5.09, 3.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	-0.07 (1.36)	-2.22 (1.34)
95% CI of LS mean	(-2.74, 2.61)	(-4.85, 0.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.15 (-5.91, 1.61)
Week 52		
n	115	116
Mean (SD)	92.95 (15.60)	93.39 (13.74)
Absolute Change at Week 52		
n	111	114
Mean (SD)	0.30 (13.52)	-1.22 (12.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52 (MMRM)		
n	114	115
LS mean (SE)	92.91 (1.34)	93.59 (1.33)
95% CI of LS mean	(90.26, 95.56)	(90.98, 96.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.68 (-3.05, 4.41)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	0.18 (1.22)	-0.62 (1.20)
95% CI of LS mean	(-2.22, 2.59)	(-2.98, 1.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.80 (-4.18, 2.57)
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	0.37 (1.01)	-1.33 (0.99)
95% CI of LS mean	(-1.62, 2.36)	(-3.27, 0.61)
P-value within Treatment	0.7152	0.1785
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.70 (-4.49, 1.09)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2311

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Hedges' G (SE)		-0.16 (0.13)
Hedges' 95% CI		(-0.41, 0.10)
Hedges' P-value		0.2306

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	95.50 (8.87)	93.89 (13.06)
Week 8 (MMRM)		
n	34	37
LS mean (SE)	95.39 (1.80)	95.11 (1.73)
95% CI of LS mean	(91.79, 98.99)	(91.66, 98.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-5.28, 4.71)
Absolute Change at Week 8 (MMRM)		
n	33	37
LS mean (SE)	-0.02 (2.02)	1.16 (1.91)
95% CI of LS mean	(-4.05, 4.02)	(-2.65, 4.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.18 (-4.39, 6.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 16 (MMRM)		
n	32	36
LS mean (SE)	94.37 (1.78)	96.13 (1.68)
95% CI of LS mean	(90.81, 97.93)	(92.76, 99.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.76 (-3.16, 6.68)
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	-0.95 (1.73)	2.42 (1.62)
95% CI of LS mean	(-4.41, 2.51)	(-0.83, 5.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.37 (-1.41, 8.15)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	93.13 (2.25)	95.28 (2.17)
95% CI of LS mean	(88.63, 97.63)	(90.95, 99.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.14 (-4.11, 8.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	-1.89 (1.72)	1.33 (1.67)
95% CI of LS mean	(-5.33, 1.55)	(-2.00, 4.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-1.60, 8.03)
Week 52		
n	33	35
Mean (SD)	96.97 (7.99)	96.83 (6.36)
Absolute Change at Week 52		
n	32	34
Mean (SD)	1.74 (8.52)	1.31 (13.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52 (MMRM)		
n	32	35
LS mean (SE)	96.73 (1.23)	96.33 (1.19)
95% CI of LS mean	(94.28, 99.19)	(93.96, 98.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.40 (-3.84, 3.04)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	0.67 (2.03)	2.41 (1.94)
95% CI of LS mean	(-3.39, 4.73)	(-1.46, 6.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.74 (-3.89, 7.38)
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	-0.72 (1.36)	2.05 (1.29)
95% CI of LS mean	(-3.44, 1.99)	(-0.54, 4.64)
P-value within Treatment	0.5956	0.1179
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.78 (-1.01, 6.56)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1478

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		0.35 (0.24)
Hedges' 95% CI		(-0.13, 0.82)
Hedges' P-value		0.1470

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	92.36 (15.10)	94.28 (11.78)
Week 8 (MMRM)		
n	243	237
LS mean (SE)	92.13 (0.91)	93.86 (0.93)
95% CI of LS mean	(90.34, 93.93)	(92.04, 95.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-0.83, 4.29)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	0.16 (0.69)	-0.40 (0.70)
95% CI of LS mean	(-1.20, 1.53)	(-1.78, 0.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.57 (-2.51, 1.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 16 (MMRM)		
n	241	232
LS mean (SE)	92.42 (0.96)	92.65 (0.98)
95% CI of LS mean	(90.52, 94.32)	(90.72, 94.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-2.48, 2.93)
Absolute Change at Week 16 (MMRM)		
n	235	229
LS mean (SE)	0.42 (0.78)	-1.57 (0.79)
95% CI of LS mean	(-1.12, 1.96)	(-3.12, -0.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.99 (-4.18, 0.20)
Week 24 (MMRM)		
n	240	229
LS mean (SE)	92.38 (1.01)	92.11 (1.03)
95% CI of LS mean	(90.39, 94.36)	(90.09, 94.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-3.11, 2.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 24 (MMRM)		
n	234	227
LS mean (SE)	0.29 (0.82)	-2.11 (0.83)
95% CI of LS mean	(-1.31, 1.90)	(-3.74, -0.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.41 (-4.70, -0.12)
Week 52		
n	244	230
Mean (SD)	92.40 (15.56)	92.85 (14.21)
Absolute Change at Week 52		
n	238	227
Mean (SD)	0.30 (13.81)	-1.40 (11.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52 (MMRM)		
n	237	224
LS mean (SE)	92.45 (0.96)	92.91 (0.98)
95% CI of LS mean	(90.56, 94.34)	(90.98, 94.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.46 (-2.25, 3.16)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	0.32 (0.82)	-1.28 (0.84)
95% CI of LS mean	(-1.30, 1.93)	(-2.93, 0.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.60 (-3.91, 0.72)
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	0.34 (0.64)	-1.65 (0.64)
95% CI of LS mean	(-0.91, 1.59)	(-2.92, -0.39)
P-value within Treatment	0.5891	0.0106
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.00 (-3.78, -0.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0280

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Hedges' G (SE)		-0.20 (0.09)
Hedges' 95% CI		(-0.39, -0.02)
Hedges' P-value		0.0282

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	90.67 (17.83)	94.37 (12.72)
Week 8 (MMRM)		
n	79	69
LS mean (SE)	91.57 (1.65)	94.51 (1.77)
95% CI of LS mean	(88.31, 94.83)	(91.02, 98.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.94 (-1.85, 7.73)
Absolute Change at Week 8 (MMRM)		
n	77	68
LS mean (SE)	0.82 (1.26)	0.13 (1.35)
95% CI of LS mean	(-1.68, 3.32)	(-2.53, 2.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.70 (-4.36, 2.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 16 (MMRM)		
n	77	67
LS mean (SE)	91.50 (1.65)	92.56 (1.77)
95% CI of LS mean	(88.24, 94.76)	(89.06, 96.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.05 (-3.74, 5.84)
Absolute Change at Week 16 (MMRM)		
n	75	66
LS mean (SE)	1.08 (1.11)	-1.79 (1.19)
95% CI of LS mean	(-1.12, 3.28)	(-4.13, 0.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.87 (-6.10, 0.36)
Week 24 (MMRM)		
n	79	63
LS mean (SE)	90.73 (1.77)	92.70 (1.93)
95% CI of LS mean	(87.23, 94.22)	(88.89, 96.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.98 (-3.21, 7.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 24 (MMRM)		
n	77	63
LS mean (SE)	-0.04 (1.40)	-1.63 (1.54)
95% CI of LS mean	(-2.82, 2.74)	(-4.67, 1.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.59 (-5.71, 2.54)
Week 52		
n	78	67
Mean (SD)	92.31 (15.33)	93.03 (14.32)
Absolute Change at Week 52		
n	76	66
Mean (SD)	1.68 (11.30)	-1.52 (9.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52 (MMRM)		
n	77	64
LS mean (SE)	92.29 (1.70)	92.85 (1.84)
95% CI of LS mean	(88.92, 95.66)	(89.21, 96.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.57 (-4.40, 5.54)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	1.62 (1.21)	-1.45 (1.31)
95% CI of LS mean	(-0.78, 4.01)	(-4.04, 1.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.07 (-6.61, 0.47)
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	0.89 (1.06)	-1.62 (1.14)
95% CI of LS mean	(-1.21, 2.98)	(-3.88, 0.64)
P-value within Treatment	0.4041	0.1577
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.51 (-5.60, 0.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1111

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Hedges' G (SE)		-0.27 (0.17)
Hedges' 95% CI		(-0.60, 0.06)
Hedges' P-value		0.1112

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	93.46 (13.03)	94.12 (11.75)
Week 8 (MMRM)		
n	198	205
LS mean (SE)	92.91 (0.96)	93.92 (0.94)
95% CI of LS mean	(91.03, 94.79)	(92.07, 95.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.00 (-1.63, 3.64)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	-0.07 (0.77)	-0.28 (0.76)
95% CI of LS mean	(-1.59, 1.45)	(-1.76, 1.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-2.34, 1.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 16 (MMRM)		
n	196	201
LS mean (SE)	93.10 (1.04)	93.37 (1.02)
95% CI of LS mean	(91.07, 95.14)	(91.36, 95.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-2.59, 3.12)
Absolute Change at Week 16 (MMRM)		
n	191	199
LS mean (SE)	-0.01 (0.90)	-0.84 (0.89)
95% CI of LS mean	(-1.79, 1.77)	(-2.58, 0.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.83 (-3.32, 1.66)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	93.18 (1.09)	92.53 (1.07)
95% CI of LS mean	(91.03, 95.33)	(90.42, 94.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.65 (-3.66, 2.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	0.11 (0.88)	-1.69 (0.86)
95% CI of LS mean	(-1.62, 1.85)	(-3.38, 0.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.80 (-4.23, 0.62)
Week 52		
n	194	196
Mean (SD)	93.24 (14.71)	93.65 (13.03)
Absolute Change at Week 52		
n	189	193
Mean (SD)	0.12 (14.08)	-0.66 (11.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52 (MMRM)		
n	192	195
LS mean (SE)	93.12 (1.00)	93.63 (0.98)
95% CI of LS mean	(91.16, 95.08)	(91.70, 95.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.51 (-2.24, 3.27)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	-0.08 (0.95)	-0.60 (0.94)
95% CI of LS mean	(-1.95, 1.78)	(-2.44, 1.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-3.14, 2.10)
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	0.01 (0.70)	-1.04 (0.68)
95% CI of LS mean	(-1.37, 1.38)	(-2.39, 0.30)
P-value within Treatment	0.9919	0.1278
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.05 (-2.98, 0.87)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2834

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Hedges' G (SE)		-0.11 (0.10)
Hedges' 95% CI		(-0.31, 0.09)
Hedges' P-value		0.2835

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	93.25 (13.90)	94.52 (12.19)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	93.21 (1.06)	94.88 (1.03)
95% CI of LS mean	(91.12, 95.30)	(92.86, 96.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.67 (-1.26, 4.59)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	0.01 (0.85)	0.49 (0.82)
95% CI of LS mean	(-1.67, 1.69)	(-1.12, 2.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-1.86, 2.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 16 (MMRM)		
n	130	139
LS mean (SE)	93.89 (1.10)	93.17 (1.06)
95% CI of LS mean	(91.73, 96.05)	(91.08, 95.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.72 (-3.74, 2.31)
Absolute Change at Week 16 (MMRM)		
n	126	137
LS mean (SE)	0.89 (0.84)	-1.20 (0.81)
95% CI of LS mean	(-0.76, 2.55)	(-2.79, 0.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.09 (-4.40, 0.22)
Week 24 (MMRM)		
n	133	140
LS mean (SE)	93.19 (1.20)	93.25 (1.16)
95% CI of LS mean	(90.83, 95.55)	(90.96, 95.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-3.24, 3.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 24 (MMRM)		
n	129	137
LS mean (SE)	0.08 (0.91)	-1.14 (0.88)
95% CI of LS mean	(-1.71, 1.87)	(-2.87, 0.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.22 (-3.72, 1.28)
Week 52		
n	139	143
Mean (SD)	93.05 (14.61)	94.09 (12.36)
Absolute Change at Week 52		
n	135	140
Mean (SD)	0.08 (14.14)	-0.32 (10.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52 (MMRM)		
n	132	139
LS mean (SE)	93.07 (1.19)	94.00 (1.15)
95% CI of LS mean	(90.73, 95.41)	(91.72, 96.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-2.35, 4.20)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	-0.13 (1.14)	-0.35 (1.11)
95% CI of LS mean	(-2.38, 2.13)	(-2.53, 1.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-3.37, 2.92)
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	0.28 (0.80)	-0.90 (0.77)
95% CI of LS mean	(-1.29, 1.85)	(-2.41, 0.62)
P-value within Treatment	0.7232	0.2459
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.18 (-3.37, 1.02)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2911

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Hedges' G (SE)		-0.13 (0.12)
Hedges' 95% CI		(-0.37, 0.11)
Hedges' P-value		0.2891

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	92.29 (15.03)	93.91 (11.72)
Week 8 (MMRM)		
n	143	131
LS mean (SE)	92.07 (1.28)	92.96 (1.33)
95% CI of LS mean	(89.56, 94.58)	(90.33, 95.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-2.77, 4.54)
Absolute Change at Week 8 (MMRM)		
n	140	130
LS mean (SE)	0.43 (1.02)	-1.01 (1.05)
95% CI of LS mean	(-1.58, 2.43)	(-3.09, 1.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-4.34, 1.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 16 (MMRM)		
n	143	129
LS mean (SE)	91.60 (1.37)	92.97 (1.43)
95% CI of LS mean	(88.91, 94.30)	(90.15, 95.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.37 (-2.55, 5.29)
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	-0.21 (1.17)	-1.05 (1.22)
95% CI of LS mean	(-2.51, 2.09)	(-3.45, 1.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.84 (-4.18, 2.50)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	91.95 (1.43)	91.65 (1.51)
95% CI of LS mean	(89.13, 94.76)	(88.68, 94.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-4.40, 3.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	0.08 (1.19)	-2.37 (1.25)
95% CI of LS mean	(-2.27, 2.43)	(-4.83, 0.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.45 (-5.86, 0.96)
Week 52		
n	138	122
Mean (SD)	92.83 (15.30)	92.53 (14.74)
Absolute Change at Week 52		
n	135	121
Mean (SD)	0.86 (12.42)	-1.88 (11.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52 (MMRM)		
n	137	120
LS mean (SE)	92.78 (1.27)	92.48 (1.34)
95% CI of LS mean	(90.28, 95.28)	(89.84, 95.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-3.95, 3.36)
Absolute Change at Week 52 (MMRM)		
n	134	119
LS mean (SE)	0.85 (1.04)	-1.61 (1.10)
95% CI of LS mean	(-1.21, 2.90)	(-3.77, 0.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.45 (-5.45, 0.55)
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	0.24 (0.87)	-1.68 (0.91)
95% CI of LS mean	(-1.48, 1.96)	(-3.47, 0.12)
P-value within Treatment	0.7844	0.0670
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.91 (-4.42, 0.59)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1328

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Hedges' G (SE)		-0.18 (0.12)
Hedges' 95% CI		(-0.42, 0.06)
Hedges' P-value		0.1313

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	91.07 (15.16)	93.59 (13.28)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	89.49 (1.40)	94.69 (1.31)
95% CI of LS mean	(86.73, 92.25)	(92.11, 97.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.20 (1.42, 8.98)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	-1.03 (1.07)	1.09 (1.00)
95% CI of LS mean	(-3.14, 1.07)	(-0.90, 3.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-0.77, 5.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 16 (MMRM)		
n	96	108
LS mean (SE)	89.81 (1.46)	93.52 (1.37)
95% CI of LS mean	(86.93, 92.68)	(90.82, 96.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.71 (-0.24, 7.66)
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	-0.79 (1.04)	-0.10 (0.99)
95% CI of LS mean	(-2.84, 1.25)	(-2.05, 1.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.69 (-2.14, 3.51)
Week 24 (MMRM)		
n	98	108
LS mean (SE)	90.92 (1.65)	92.94 (1.55)
95% CI of LS mean	(87.67, 94.16)	(89.87, 96.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.02 (-2.45, 6.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 24 (MMRM)		
n	97	106
LS mean (SE)	0.42 (1.02)	-0.74 (0.98)
95% CI of LS mean	(-1.60, 2.44)	(-2.67, 1.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.16 (-3.95, 1.63)
Week 52		
n	101	104
Mean (SD)	90.98 (16.61)	93.38 (13.00)
Absolute Change at Week 52		
n	100	101
Mean (SD)	0.33 (12.58)	-0.22 (12.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52 (MMRM)		
n	97	104
LS mean (SE)	91.03 (1.50)	93.39 (1.43)
95% CI of LS mean	(88.07, 93.99)	(90.57, 96.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.36 (-1.74, 6.45)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	0.55 (1.25)	-0.12 (1.21)
95% CI of LS mean	(-1.92, 3.02)	(-2.52, 2.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-4.11, 2.77)
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	0.06 (0.83)	-0.32 (0.79)
95% CI of LS mean	(-1.58, 1.70)	(-1.89, 1.24)
P-value within Treatment	0.9449	0.6847
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-2.65, 1.89)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7414

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Hedges' G (SE)		-0.05 (0.14)
Hedges' 95% CI		(-0.32, 0.23)
Hedges' P-value		0.7410

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	93.73 (14.00)	94.64 (11.01)
Week 8 (MMRM)		
n	179	162
LS mean (SE)	94.25 (1.01)	93.58 (1.06)
95% CI of LS mean	(92.26, 96.24)	(91.49, 95.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-3.56, 2.22)
Absolute Change at Week 8 (MMRM)		
n	173	162
LS mean (SE)	0.83 (0.84)	-0.98 (0.87)
95% CI of LS mean	(-0.83, 2.48)	(-2.69, 0.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.81 (-4.19, 0.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 16 (MMRM)		
n	177	160
LS mean (SE)	94.20 (1.08)	92.88 (1.14)
95% CI of LS mean	(92.07, 96.33)	(90.64, 95.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.31 (-4.41, 1.78)
Absolute Change at Week 16 (MMRM)		
n	171	160
LS mean (SE)	0.81 (0.98)	-1.68 (1.01)
95% CI of LS mean	(-1.12, 2.74)	(-3.68, 0.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.50 (-5.27, 0.28)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	93.37 (1.11)	92.26 (1.17)
95% CI of LS mean	(91.18, 95.55)	(89.95, 94.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.11 (-4.29, 2.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	-0.25 (1.03)	-2.30 (1.07)
95% CI of LS mean	(-2.27, 1.78)	(-4.41, -0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.05 (-4.98, 0.87)
Week 52		
n	176	161
Mean (SD)	94.07 (13.80)	93.37 (13.85)
Absolute Change at Week 52		
n	170	160
Mean (SD)	0.56 (13.72)	-1.56 (11.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	172	155
LS mean (SE)	93.93 (1.04)	93.46 (1.09)
95% CI of LS mean	(91.89, 95.97)	(91.31, 95.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-3.43, 2.50)
Absolute Change at Week 52 (MMRM)		
n	166	154
LS mean (SE)	0.24 (0.97)	-1.18 (1.01)
95% CI of LS mean	(-1.67, 2.15)	(-3.16, 0.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.43 (-4.18, 1.33)
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	0.27 (0.80)	-1.72 (0.83)
95% CI of LS mean	(-1.30, 1.84)	(-3.35, -0.10)
P-value within Treatment	0.7355	0.0377
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.99 (-4.25, 0.27)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0838

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Hedges' G (SE)		-0.19 (0.11)
Hedges' 95% CI		(-0.41, 0.03)
Hedges' P-value		0.0840

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	80.28 (17.20)	83.16 (17.96)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	81.07 (1.40)	83.41 (1.43)
95% CI of LS mean	(78.32, 83.82)	(80.59, 86.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.34 (-1.60, 6.28)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	1.02 (0.86)	0.44 (0.88)
95% CI of LS mean	(-0.67, 2.71)	(-1.30, 2.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.58 (-3.01, 1.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 16 (MMRM)		
n	158	149
LS mean (SE)	80.83 (1.39)	81.89 (1.43)
95% CI of LS mean	(78.09, 83.58)	(79.07, 84.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.06 (-2.88, 4.99)
Absolute Change at Week 16 (MMRM)		
n	155	147
LS mean (SE)	0.91 (0.92)	-1.03 (0.94)
95% CI of LS mean	(-0.90, 2.72)	(-2.89, 0.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.94 (-4.54, 0.66)
Week 24 (MMRM)		
n	155	147
LS mean (SE)	81.06 (1.39)	82.28 (1.42)
95% CI of LS mean	(78.33, 83.79)	(79.48, 85.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.22 (-2.69, 5.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 24 (MMRM)		
n	152	145
LS mean (SE)	0.97 (0.97)	-0.67 (0.99)
95% CI of LS mean	(-0.93, 2.87)	(-2.62, 1.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.64 (-4.36, 1.08)
Week 52		
n	159	145
Mean (SD)	80.42 (18.58)	81.79 (19.25)
Absolute Change at Week 52		
n	156	143
Mean (SD)	0.09 (15.24)	-0.79 (14.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52 (MMRM)		
n	155	144
LS mean (SE)	80.16 (1.49)	81.89 (1.54)
95% CI of LS mean	(77.22, 83.10)	(78.86, 84.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-2.49, 5.96)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	-0.02 (1.22)	-0.99 (1.25)
95% CI of LS mean	(-2.41, 2.38)	(-3.46, 1.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.98 (-4.42, 2.47)
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	0.62 (0.86)	-0.90 (0.88)
95% CI of LS mean	(-1.06, 2.30)	(-2.63, 0.83)
P-value within Treatment	0.4688	0.3069
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.52 (-3.93, 0.89)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2166

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Hedges' G (SE)		-0.14 (0.11)
Hedges' 95% CI		(-0.37, 0.08)
Hedges' P-value		0.2168

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	83.81 (14.95)	80.20 (17.65)
Week 8 (MMRM)		
n	115	121
LS mean (SE)	84.23 (1.48)	81.98 (1.44)
95% CI of LS mean	(81.32, 87.14)	(79.14, 84.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.25 (-6.33, 1.83)
Absolute Change at Week 8 (MMRM)		
n	112	120
LS mean (SE)	0.13 (1.11)	1.91 (1.07)
95% CI of LS mean	(-2.05, 2.32)	(-0.20, 4.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.78 (-1.27, 4.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 16 (MMRM)		
n	115	119
LS mean (SE)	84.98 (1.50)	80.10 (1.46)
95% CI of LS mean	(82.03, 87.93)	(77.22, 82.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.88 (-9.02, -0.74)
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	1.17 (1.16)	0.08 (1.12)
95% CI of LS mean	(-1.11, 3.45)	(-2.13, 2.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.09 (-4.28, 2.09)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	82.86 (1.60)	79.51 (1.57)
95% CI of LS mean	(79.72, 86.01)	(76.42, 82.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.35 (-7.78, 1.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	-1.15 (1.25)	-0.54 (1.23)
95% CI of LS mean	(-3.62, 1.32)	(-2.96, 1.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.61 (-2.86, 4.08)
Week 52		
n	115	116
Mean (SD)	83.37 (14.52)	81.75 (17.25)
Absolute Change at Week 52		
n	111	114
Mean (SD)	-0.87 (12.27)	1.43 (14.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52 (MMRM)		
n	114	115
LS mean (SE)	83.35 (1.50)	81.45 (1.47)
95% CI of LS mean	(80.40, 86.29)	(78.55, 84.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.90 (-6.04, 2.25)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	-0.79 (1.27)	1.44 (1.24)
95% CI of LS mean	(-3.28, 1.71)	(-1.00, 3.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.23 (-1.27, 5.72)
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	-0.26 (1.05)	0.33 (1.02)
95% CI of LS mean	(-2.33, 1.82)	(-1.69, 2.34)
P-value within Treatment	0.8086	0.7510
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-2.32, 3.49)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6939

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Hedges' G (SE)		0.05 (0.13)
Hedges' 95% CI		(-0.21, 0.31)
Hedges' P-value		0.6930

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	84.91 (15.02)	79.60 (18.72)
Week 8 (MMRM)		
n	34	37
LS mean (SE)	86.62 (2.53)	81.21 (2.41)
95% CI of LS mean	(81.58, 91.67)	(76.41, 86.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.41 (-12.44, 1.61)
Absolute Change at Week 8 (MMRM)		
n	33	37
LS mean (SE)	1.82 (1.77)	1.37 (1.67)
95% CI of LS mean	(-1.71, 5.35)	(-1.96, 4.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-5.34, 4.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 16 (MMRM)		
n	32	36
LS mean (SE)	85.09 (2.97)	80.69 (2.81)
95% CI of LS mean	(79.17, 91.01)	(75.09, 86.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.40 (-12.60, 3.81)
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	0.45 (2.30)	0.98 (2.15)
95% CI of LS mean	(-4.13, 5.04)	(-3.32, 5.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-5.79, 6.84)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	86.25 (2.69)	81.23 (2.56)
95% CI of LS mean	(80.87, 91.63)	(76.11, 86.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.03 (-12.50, 2.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	1.69 (2.02)	1.39 (1.92)
95% CI of LS mean	(-2.34, 5.73)	(-2.45, 5.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-5.90, 5.30)
Week 52		
n	33	35
Mean (SD)	84.07 (16.83)	84.07 (16.47)
Absolute Change at Week 52		
n	32	34
Mean (SD)	-1.46 (17.06)	1.86 (18.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52 (MMRM)		
n	32	35
LS mean (SE)	83.21 (3.01)	82.19 (2.86)
95% CI of LS mean	(77.19, 89.22)	(76.47, 87.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.02 (-9.36, 7.33)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	-2.19 (3.24)	2.16 (3.07)
95% CI of LS mean	(-8.65, 4.27)	(-3.98, 8.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.35 (-4.59, 13.28)
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	-0.01 (2.29)	1.51 (2.16)
95% CI of LS mean	(-4.59, 4.56)	(-2.81, 5.83)
P-value within Treatment	0.9949	0.4874
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-4.80, 7.85)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6314

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		0.11 (0.24)
Hedges' 95% CI		(-0.36, 0.58)
Hedges' P-value		0.6303

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	81.35 (16.49)	82.11 (17.61)
Week 8 (MMRM)		
n	242	237
LS mean (SE)	81.65 (1.11)	83.10 (1.12)
95% CI of LS mean	(79.47, 83.84)	(80.89, 85.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-1.66, 4.55)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	0.52 (0.74)	0.94 (0.74)
95% CI of LS mean	(-0.93, 1.97)	(-0.52, 2.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-1.65, 2.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 16 (MMRM)		
n	241	232
LS mean (SE)	82.05 (1.10)	81.25 (1.12)
95% CI of LS mean	(79.89, 84.22)	(79.05, 83.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.80 (-3.89, 2.28)
Absolute Change at Week 16 (MMRM)		
n	235	229
LS mean (SE)	1.09 (0.76)	-0.85 (0.76)
95% CI of LS mean	(-0.39, 2.58)	(-2.35, 0.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.94 (-4.06, 0.17)
Week 24 (MMRM)		
n	239	229
LS mean (SE)	81.01 (1.14)	81.13 (1.16)
95% CI of LS mean	(78.78, 83.25)	(78.86, 83.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-3.08, 3.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 24 (MMRM)		
n	233	227
LS mean (SE)	-0.16 (0.84)	-1.00 (0.85)
95% CI of LS mean	(-1.80, 1.49)	(-2.66, 0.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.85 (-3.18, 1.49)
Week 52		
n	244	230
Mean (SD)	81.37 (17.01)	81.57 (18.53)
Absolute Change at Week 52		
n	238	227
Mean (SD)	-0.21 (13.57)	0.12 (13.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52 (MMRM)		
n	237	224
LS mean (SE)	81.10 (1.15)	81.76 (1.17)
95% CI of LS mean	(78.85, 83.35)	(79.46, 84.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.66 (-2.56, 3.88)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	-0.16 (0.91)	-0.27 (0.92)
95% CI of LS mean	(-1.94, 1.62)	(-2.08, 1.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-2.65, 2.44)
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	0.26 (0.69)	-0.71 (0.70)
95% CI of LS mean	(-1.10, 1.62)	(-2.08, 0.67)
P-value within Treatment	0.7079	0.3126
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-2.90, 0.97)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3268

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Hedges' G (SE)		-0.09 (0.09)
Hedges' 95% CI		(-0.27, 0.09)
Hedges' P-value		0.3265

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	82.08 (17.29)	82.98 (16.84)
Week 8 (MMRM)		
n	79	69
LS mean (SE)	84.00 (1.95)	83.90 (2.09)
95% CI of LS mean	(80.14, 87.86)	(79.77, 88.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-5.77, 5.57)
Absolute Change at Week 8 (MMRM)		
n	77	68
LS mean (SE)	2.16 (1.29)	1.24 (1.37)
95% CI of LS mean	(-0.39, 4.71)	(-1.47, 3.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-4.65, 2.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 16 (MMRM)		
n	77	67
LS mean (SE)	81.22 (2.02)	82.89 (2.17)
95% CI of LS mean	(77.22, 85.22)	(78.60, 87.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.67 (-4.21, 7.55)
Absolute Change at Week 16 (MMRM)		
n	75	66
LS mean (SE)	-0.34 (1.27)	0.29 (1.35)
95% CI of LS mean	(-2.84, 2.17)	(-2.38, 2.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-3.05, 4.31)
Week 24 (MMRM)		
n	78	63
LS mean (SE)	79.74 (2.01)	82.51 (2.18)
95% CI of LS mean	(75.76, 83.72)	(78.19, 86.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.77 (-3.11, 8.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 24 (MMRM)		
n	76	63
LS mean (SE)	-2.32 (1.42)	-0.10 (1.55)
95% CI of LS mean	(-5.14, 0.50)	(-3.16, 2.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.22 (-1.95, 6.40)
Week 52		
n	78	67
Mean (SD)	81.01 (17.43)	84.91 (17.30)
Absolute Change at Week 52		
n	76	66
Mean (SD)	-1.18 (12.67)	2.18 (16.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52 (MMRM)		
n	77	64
LS mean (SE)	81.05 (1.98)	84.21 (2.14)
95% CI of LS mean	(77.15, 84.96)	(79.98, 88.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.15 (-2.61, 8.92)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	-1.18 (1.64)	1.60 (1.77)
95% CI of LS mean	(-4.42, 2.06)	(-1.91, 5.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.78 (-2.00, 7.56)
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	-1.28 (1.21)	0.60 (1.30)
95% CI of LS mean	(-3.67, 1.11)	(-1.98, 3.17)
P-value within Treatment	0.2916	0.6462
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.88 (-1.65, 5.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2940

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Hedges' G (SE)		0.18 (0.17)
Hedges' 95% CI		(-0.15, 0.51)
Hedges' P-value		0.2932

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	81.59 (15.84)	81.32 (18.09)
Week 8 (MMRM)		
n	197	205
LS mean (SE)	81.67 (1.20)	82.47 (1.18)
95% CI of LS mean	(79.31, 84.03)	(80.16, 84.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.80 (-2.50, 4.10)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	0.05 (0.80)	1.02 (0.78)
95% CI of LS mean	(-1.53, 1.62)	(-0.52, 2.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-1.23, 3.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 16 (MMRM)		
n	196	201
LS mean (SE)	83.03 (1.19)	80.57 (1.17)
95% CI of LS mean	(80.69, 85.37)	(78.27, 82.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.46 (-5.74, 0.82)
Absolute Change at Week 16 (MMRM)		
n	191	199
LS mean (SE)	1.56 (0.87)	-0.83 (0.85)
95% CI of LS mean	(-0.14, 3.27)	(-2.50, 0.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.39 (-4.78, 0.00)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	82.55 (1.22)	80.65 (1.20)
95% CI of LS mean	(80.15, 84.96)	(78.29, 83.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.90 (-5.27, 1.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	1.04 (0.90)	-0.81 (0.88)
95% CI of LS mean	(-0.74, 2.82)	(-2.55, 0.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.85 (-4.34, 0.63)
Week 52		
n	194	196
Mean (SD)	81.87 (16.88)	80.82 (18.54)
Absolute Change at Week 52		
n	189	193
Mean (SD)	-0.02 (14.61)	-0.32 (13.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52 (MMRM)		
n	192	195
LS mean (SE)	81.62 (1.26)	80.93 (1.25)
95% CI of LS mean	(79.13, 84.11)	(78.48, 83.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.69 (-4.18, 2.81)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	0.01 (1.04)	-0.42 (1.02)
95% CI of LS mean	(-2.03, 2.06)	(-2.43, 1.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-3.30, 2.44)
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	0.87 (0.79)	-0.69 (0.77)
95% CI of LS mean	(-0.67, 2.42)	(-2.20, 0.83)
P-value within Treatment	0.2676	0.3730
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.56 (-3.72, 0.60)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1574

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Hedges' G (SE)		-0.14 (0.10)
Hedges' 95% CI		(-0.34, 0.06)
Hedges' P-value		0.1577

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	83.05 (16.23)	83.89 (18.23)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	83.50 (1.43)	84.80 (1.38)
95% CI of LS mean	(80.69, 86.31)	(82.08, 87.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.30 (-2.64, 5.23)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	0.92 (0.99)	1.08 (0.96)
95% CI of LS mean	(-1.04, 2.87)	(-0.80, 2.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-2.56, 2.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 16 (MMRM)		
n	130	139
LS mean (SE)	83.83 (1.43)	84.06 (1.39)
95% CI of LS mean	(81.01, 86.65)	(81.33, 86.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-3.71, 4.19)
Absolute Change at Week 16 (MMRM)		
n	126	137
LS mean (SE)	1.60 (1.02)	0.45 (0.98)
95% CI of LS mean	(-0.40, 3.60)	(-1.48, 2.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.15 (-3.94, 1.63)
Week 24 (MMRM)		
n	132	140
LS mean (SE)	83.65 (1.41)	84.30 (1.37)
95% CI of LS mean	(80.87, 86.42)	(81.61, 86.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-3.24, 4.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 24 (MMRM)		
n	128	137
LS mean (SE)	1.14 (1.00)	0.67 (0.96)
95% CI of LS mean	(-0.83, 3.10)	(-1.23, 2.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-3.21, 2.28)
Week 52		
n	139	143
Mean (SD)	83.87 (14.98)	83.96 (18.25)
Absolute Change at Week 52		
n	135	140
Mean (SD)	0.78 (12.13)	0.77 (14.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52 (MMRM)		
n	132	139
LS mean (SE)	83.63 (1.47)	84.08 (1.42)
95% CI of LS mean	(80.75, 86.52)	(81.28, 86.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-3.60, 4.49)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	0.94 (1.19)	0.59 (1.15)
95% CI of LS mean	(-1.40, 3.27)	(-1.67, 2.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-3.61, 2.91)
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	1.23 (0.90)	0.57 (0.87)
95% CI of LS mean	(-0.55, 3.01)	(-1.15, 2.29)
P-value within Treatment	0.1765	0.5166
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.66 (-3.15, 1.83)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6033

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Hedges' G (SE)		-0.06 (0.12)
Hedges' 95% CI		(-0.30, 0.18)
Hedges' P-value		0.6013

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	80.60 (16.38)	79.43 (17.00)
Week 8 (MMRM)		
n	142	131
LS mean (SE)	81.39 (1.45)	80.48 (1.51)
95% CI of LS mean	(78.53, 84.25)	(77.50, 83.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-5.07, 3.24)
Absolute Change at Week 8 (MMRM)		
n	140	130
LS mean (SE)	0.58 (0.95)	0.87 (0.99)
95% CI of LS mean	(-1.30, 2.45)	(-1.07, 2.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.30 (-2.42, 3.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 16 (MMRM)		
n	143	129
LS mean (SE)	81.43 (1.46)	77.79 (1.53)
95% CI of LS mean	(78.55, 84.31)	(74.79, 80.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.64 (-7.82, 0.55)
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	0.64 (1.03)	-1.82 (1.07)
95% CI of LS mean	(-1.38, 2.66)	(-3.93, 0.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.46 (-5.39, 0.47)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	80.12 (1.53)	77.43 (1.61)
95% CI of LS mean	(77.11, 83.13)	(74.27, 80.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.69 (-7.08, 1.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	-0.74 (1.17)	-2.23 (1.22)
95% CI of LS mean	(-3.03, 1.56)	(-4.63, 0.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.49 (-4.83, 1.85)
Week 52		
n	138	122
Mean (SD)	79.49 (18.57)	79.47 (18.05)
Absolute Change at Week 52		
n	135	121
Mean (SD)	-1.49 (15.61)	-0.15 (15.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52 (MMRM)		
n	137	120
LS mean (SE)	79.54 (1.54)	79.02 (1.62)
95% CI of LS mean	(76.51, 82.57)	(75.83, 82.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-4.95, 3.90)
Absolute Change at Week 52 (MMRM)		
n	134	119
LS mean (SE)	-1.35 (1.31)	-0.61 (1.37)
95% CI of LS mean	(-3.93, 1.22)	(-3.31, 2.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-3.00, 4.49)
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	-0.49 (0.97)	-1.55 (1.01)
95% CI of LS mean	(-2.40, 1.43)	(-3.55, 0.44)
P-value within Treatment	0.6180	0.1267
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.07 (-3.85, 1.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4505

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Hedges' G (SE)		-0.09 (0.12)
Hedges' 95% CI		(-0.33, 0.15)
Hedges' P-value		0.4482

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	81.23 (17.43)	83.31 (17.95)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	80.47 (1.87)	84.08 (1.75)
95% CI of LS mean	(76.78, 84.16)	(80.62, 87.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (-1.46, 8.66)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	-0.27 (1.15)	0.84 (1.08)
95% CI of LS mean	(-2.53, 1.99)	(-1.29, 2.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.11 (-2.00, 4.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 16 (MMRM)		
n	96	108
LS mean (SE)	81.86 (1.71)	83.57 (1.61)
95% CI of LS mean	(78.48, 85.23)	(80.41, 86.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.72 (-2.92, 6.35)
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	1.21 (1.13)	0.39 (1.07)
95% CI of LS mean	(-1.02, 3.44)	(-1.73, 2.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.82 (-3.90, 2.25)
Week 24 (MMRM)		
n	97	108
LS mean (SE)	79.82 (1.72)	84.58 (1.62)
95% CI of LS mean	(76.42, 83.22)	(81.39, 87.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.76 (0.09, 9.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 24 (MMRM)		
n	96	106
LS mean (SE)	-0.84 (1.13)	1.29 (1.07)
95% CI of LS mean	(-3.06, 1.39)	(-0.83, 3.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.13 (-0.95, 5.20)
Week 52		
n	101	104
Mean (SD)	79.88 (17.62)	83.04 (17.79)
Absolute Change at Week 52		
n	100	101
Mean (SD)	-1.24 (13.72)	0.29 (13.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52 (MMRM)		
n	97	104
LS mean (SE)	79.56 (1.78)	83.30 (1.69)
95% CI of LS mean	(76.05, 83.07)	(79.97, 86.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.74 (-1.10, 8.58)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	-1.12 (1.40)	0.16 (1.36)
95% CI of LS mean	(-3.89, 1.65)	(-2.52, 2.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.27 (-2.58, 5.12)
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	-0.25 (1.03)	0.61 (0.98)
95% CI of LS mean	(-2.27, 1.77)	(-1.32, 2.54)
P-value within Treatment	0.8090	0.5330
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-1.94, 3.66)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5458

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Hedges' G (SE)		0.08 (0.14)
Hedges' 95% CI		(-0.19, 0.36)
Hedges' P-value		0.5452

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	82.15 (15.71)	80.73 (17.61)
Week 8 (MMRM)		
n	178	162
LS mean (SE)	83.26 (1.19)	82.06 (1.25)
95% CI of LS mean	(80.92, 85.61)	(79.60, 84.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.20 (-4.61, 2.20)
Absolute Change at Week 8 (MMRM)		
n	173	162
LS mean (SE)	1.20 (0.86)	1.21 (0.88)
95% CI of LS mean	(-0.48, 2.88)	(-0.53, 2.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-2.42, 2.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 16 (MMRM)		
n	177	160
LS mean (SE)	82.79 (1.28)	79.62 (1.34)
95% CI of LS mean	(80.27, 85.30)	(76.98, 82.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.17 (-6.82, 0.48)
Absolute Change at Week 16 (MMRM)		
n	171	160
LS mean (SE)	0.94 (0.93)	-1.21 (0.96)
95% CI of LS mean	(-0.89, 2.77)	(-3.11, 0.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.15 (-4.79, 0.48)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	82.69 (1.31)	78.87 (1.38)
95% CI of LS mean	(80.12, 85.27)	(76.16, 81.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.82 (-7.56, -0.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	0.60 (1.03)	-1.96 (1.07)
95% CI of LS mean	(-1.42, 2.62)	(-4.06, 0.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.56 (-5.47, 0.36)
Week 52		
n	176	161
Mean (SD)	82.73 (16.56)	81.15 (18.58)
Absolute Change at Week 52		
n	170	160
Mean (SD)	0.16 (14.18)	0.38 (15.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	172	155
LS mean (SE)	82.38 (1.33)	80.79 (1.40)
95% CI of LS mean	(79.75, 85.00)	(78.03, 83.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.59 (-5.39, 2.22)
Absolute Change at Week 52 (MMRM)		
n	166	154
LS mean (SE)	0.14 (1.13)	-0.01 (1.18)
95% CI of LS mean	(-2.10, 2.37)	(-2.32, 2.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-3.36, 3.07)
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	0.56 (0.87)	-1.06 (0.90)
95% CI of LS mean	(-1.15, 2.26)	(-2.83, 0.70)
P-value within Treatment	0.5204	0.2375
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.62 (-4.08, 0.84)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1957

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Hedges' G (SE)		-0.14 (0.11)
Hedges' 95% CI		(-0.36, 0.07)
Hedges' P-value		0.1956

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	77.35 (21.33)	80.92 (19.11)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	74.79 (1.60)	79.51 (1.64)
95% CI of LS mean	(71.63, 77.94)	(76.27, 82.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.72 (0.20, 9.24)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	-2.49 (1.33)	-1.23 (1.36)
95% CI of LS mean	(-5.12, 0.13)	(-3.91, 1.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.27 (-2.49, 5.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 16 (MMRM)		
n	158	149
LS mean (SE)	76.29 (1.64)	80.12 (1.69)
95% CI of LS mean	(73.06, 79.53)	(76.80, 83.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.83 (-0.81, 8.47)
Absolute Change at Week 16 (MMRM)		
n	155	147
LS mean (SE)	-0.73 (1.29)	-0.43 (1.33)
95% CI of LS mean	(-3.28, 1.81)	(-3.04, 2.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-3.34, 3.95)
Week 24 (MMRM)		
n	155	147
LS mean (SE)	75.53 (1.68)	79.22 (1.73)
95% CI of LS mean	(72.22, 78.84)	(75.82, 82.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.69 (-1.06, 8.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 24 (MMRM)		
n	152	145
LS mean (SE)	-1.78 (1.29)	-1.34 (1.32)
95% CI of LS mean	(-4.31, 0.75)	(-3.93, 1.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.44 (-3.18, 4.06)
Week 52		
n	159	145
Mean (SD)	76.54 (21.91)	81.79 (18.22)
Absolute Change at Week 52		
n	156	143
Mean (SD)	-0.11 (16.86)	0.99 (12.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52 (MMRM)		
n	155	144
LS mean (SE)	77.11 (1.53)	81.36 (1.58)
95% CI of LS mean	(74.10, 80.12)	(78.26, 84.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.25 (-0.08, 8.58)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	-0.17 (1.21)	0.80 (1.25)
95% CI of LS mean	(-2.55, 2.21)	(-1.66, 3.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-2.45, 4.39)
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	-0.89 (0.98)	-0.32 (1.00)
95% CI of LS mean	(-2.81, 1.02)	(-2.29, 1.64)
P-value within Treatment	0.3595	0.7463
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.57 (-2.18, 3.32)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6834

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Hedges' G (SE)		0.05 (0.11)
Hedges' 95% CI		(-0.18, 0.27)
Hedges' P-value		0.6831

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	85.34 (18.08)	85.56 (17.85)
Week 8 (MMRM)		
n	115	121
LS mean (SE)	87.61 (1.76)	85.45 (1.72)
95% CI of LS mean	(84.14, 91.08)	(82.06, 88.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.16 (-7.02, 2.70)
Absolute Change at Week 8 (MMRM)		
n	112	120
LS mean (SE)	1.96 (1.33)	-0.31 (1.29)
95% CI of LS mean	(-0.67, 4.59)	(-2.85, 2.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.27 (-5.94, 1.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 16 (MMRM)		
n	115	119
LS mean (SE)	88.24 (1.66)	85.62 (1.62)
95% CI of LS mean	(84.97, 91.50)	(82.42, 88.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.62 (-7.21, 1.97)
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	2.79 (1.25)	-0.11 (1.22)
95% CI of LS mean	(0.32, 5.27)	(-2.50, 2.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.90 (-6.35, 0.55)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	87.19 (1.71)	85.66 (1.68)
95% CI of LS mean	(83.82, 90.56)	(82.35, 88.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.53 (-6.27, 3.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	1.56 (1.27)	0.17 (1.24)
95% CI of LS mean	(-0.94, 4.05)	(-2.27, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.38 (-4.89, 2.13)
Week 52		
n	115	116
Mean (SD)	88.00 (16.14)	87.52 (18.06)
Absolute Change at Week 52		
n	111	114
Mean (SD)	2.47 (15.93)	1.66 (12.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52 (MMRM)		
n	114	115
LS mean (SE)	87.76 (1.63)	87.02 (1.61)
95% CI of LS mean	(84.54, 90.99)	(83.85, 90.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.74 (-5.28, 3.79)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	2.34 (1.39)	1.30 (1.36)
95% CI of LS mean	(-0.40, 5.09)	(-1.38, 3.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.04 (-4.89, 2.81)
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	2.23 (1.11)	0.46 (1.08)
95% CI of LS mean	(0.05, 4.41)	(-1.67, 2.58)
P-value within Treatment	0.0453	0.6725
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.77 (-4.83, 1.28)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2542

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Hedges' G (SE)		-0.15 (0.13)
Hedges' 95% CI		(-0.41, 0.11)
Hedges' P-value		0.2534

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	86.99 (16.74)	88.27 (13.46)
Week 8 (MMRM)		
n	34	37
LS mean (SE)	90.74 (2.72)	87.71 (2.59)
95% CI of LS mean	(85.32, 96.17)	(82.54, 92.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.03 (-10.57, 4.50)
Absolute Change at Week 8 (MMRM)		
n	33	37
LS mean (SE)	3.85 (2.35)	-1.31 (2.22)
95% CI of LS mean	(-0.84, 8.53)	(-5.74, 3.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.16 (-11.65, 1.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 16 (MMRM)		
n	32	36
LS mean (SE)	89.94 (2.65)	88.69 (2.50)
95% CI of LS mean	(84.65, 95.24)	(83.69, 93.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.25 (-8.58, 6.08)
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	3.33 (2.38)	0.09 (2.23)
95% CI of LS mean	(-1.41, 8.07)	(-4.36, 4.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.24 (-9.78, 3.31)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	88.72 (2.49)	90.91 (2.38)
95% CI of LS mean	(83.74, 93.70)	(86.16, 95.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.18 (-4.74, 9.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	2.11 (2.32)	2.57 (2.21)
95% CI of LS mean	(-2.54, 6.75)	(-1.86, 6.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.46 (-6.00, 6.92)
Week 52		
n	33	35
Mean (SD)	94.02 (9.61)	92.58 (12.50)
Absolute Change at Week 52		
n	32	34
Mean (SD)	7.10 (17.84)	2.06 (13.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52 (MMRM)		
n	32	35
LS mean (SE)	93.00 (2.18)	91.42 (2.07)
95% CI of LS mean	(88.64, 97.36)	(87.27, 95.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-7.65, 4.49)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	5.68 (2.77)	2.04 (2.62)
95% CI of LS mean	(0.13, 11.23)	(-3.22, 7.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.64 (-11.33, 4.04)
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	3.70 (2.30)	1.56 (2.17)
95% CI of LS mean	(-0.90, 8.31)	(-2.78, 5.91)
P-value within Treatment	0.1126	0.4739
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.14 (-8.51, 4.23)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5042

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		-0.16 (0.24)
Hedges' 95% CI		(-0.63, 0.31)
Hedges' P-value		0.5019

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	79.71 (20.65)	81.92 (19.20)
Week 8 (MMRM)		
n	242	237
LS mean (SE)	78.66 (1.31)	81.21 (1.32)
95% CI of LS mean	(76.09, 81.24)	(78.61, 83.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.55 (-1.12, 6.21)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	-1.30 (1.03)	-0.72 (1.04)
95% CI of LS mean	(-3.33, 0.72)	(-2.76, 1.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-2.29, 3.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 16 (MMRM)		
n	241	232
LS mean (SE)	80.08 (1.30)	81.52 (1.32)
95% CI of LS mean	(77.53, 82.63)	(78.93, 84.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-2.19, 5.09)
Absolute Change at Week 16 (MMRM)		
n	235	229
LS mean (SE)	0.33 (0.98)	-0.28 (1.00)
95% CI of LS mean	(-1.60, 2.27)	(-2.24, 1.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.61 (-3.37, 2.14)
Week 24 (MMRM)		
n	239	229
LS mean (SE)	79.22 (1.34)	80.63 (1.36)
95% CI of LS mean	(76.60, 81.85)	(77.96, 83.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-2.34, 5.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 24 (MMRM)		
n	233	227
LS mean (SE)	-0.78 (0.98)	-1.15 (1.00)
95% CI of LS mean	(-2.72, 1.15)	(-3.11, 0.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-3.12, 2.39)
Week 52		
n	244	230
Mean (SD)	79.73 (20.86)	83.12 (18.67)
Absolute Change at Week 52		
n	238	227
Mean (SD)	0.21 (16.10)	1.33 (12.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52 (MMRM)		
n	237	224
LS mean (SE)	80.00 (1.23)	82.75 (1.26)
95% CI of LS mean	(77.57, 82.42)	(80.27, 85.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.75 (-0.72, 6.22)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	0.12 (0.95)	1.02 (0.97)
95% CI of LS mean	(-1.74, 1.99)	(-0.88, 2.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.90 (-1.77, 3.56)
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	-0.11 (0.76)	-0.14 (0.77)
95% CI of LS mean	(-1.60, 1.38)	(-1.65, 1.38)
P-value within Treatment	0.8860	0.8603
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-2.16, 2.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9804

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Hedges' G (SE)		0.00 (0.09)
Hedges' 95% CI		(-0.18, 0.18)
Hedges' P-value		0.9804

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	75.45 (22.39)	81.98 (17.93)
Week 8 (MMRM)		
n	79	69
LS mean (SE)	78.34 (2.25)	81.73 (2.41)
95% CI of LS mean	(73.89, 82.79)	(76.96, 86.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.39 (-3.16, 9.93)
Absolute Change at Week 8 (MMRM)		
n	77	68
LS mean (SE)	2.49 (1.58)	-0.48 (1.68)
95% CI of LS mean	(-0.64, 5.61)	(-3.81, 2.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.97 (-7.55, 1.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 16 (MMRM)		
n	77	67
LS mean (SE)	78.28 (2.44)	80.91 (2.61)
95% CI of LS mean	(73.46, 83.11)	(75.74, 86.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-4.46, 9.72)
Absolute Change at Week 16 (MMRM)		
n	75	66
LS mean (SE)	2.86 (1.67)	-1.30 (1.77)
95% CI of LS mean	(-0.43, 6.15)	(-4.81, 2.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.16 (-8.99, 0.66)
Week 24 (MMRM)		
n	78	63
LS mean (SE)	75.69 (2.57)	80.50 (2.79)
95% CI of LS mean	(70.61, 80.78)	(74.99, 86.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.81 (-2.70, 12.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 24 (MMRM)		
n	76	63
LS mean (SE)	-0.18 (1.58)	-1.32 (1.73)
95% CI of LS mean	(-3.31, 2.96)	(-4.74, 2.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.14 (-5.79, 3.51)
Week 52		
n	78	67
Mean (SD)	78.31 (21.49)	83.62 (18.12)
Absolute Change at Week 52		
n	76	66
Mean (SD)	3.38 (14.02)	1.99 (13.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52 (MMRM)		
n	77	64
LS mean (SE)	78.86 (2.18)	82.88 (2.36)
95% CI of LS mean	(74.55, 83.18)	(78.21, 87.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.02 (-2.35, 10.39)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	3.42 (1.58)	1.02 (1.72)
95% CI of LS mean	(0.30, 6.55)	(-2.37, 4.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.40 (-7.03, 2.22)
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	2.04 (1.27)	-0.53 (1.36)
95% CI of LS mean	(-0.47, 4.54)	(-3.23, 2.16)
P-value within Treatment	0.1102	0.6966
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.57 (-6.26, 1.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1716

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Hedges' G (SE)		-0.23 (0.17)
Hedges' 95% CI		(-0.56, 0.10)
Hedges' P-value		0.1712

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	82.67 (19.17)	83.05 (18.91)
Week 8 (MMRM)		
n	197	205
LS mean (SE)	80.99 (1.41)	82.27 (1.38)
95% CI of LS mean	(78.22, 83.76)	(79.55, 84.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.28 (-2.60, 5.16)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	-1.76 (1.17)	-1.05 (1.14)
95% CI of LS mean	(-4.05, 0.54)	(-3.29, 1.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.70 (-2.51, 3.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 16 (MMRM)		
n	196	201
LS mean (SE)	82.62 (1.35)	83.12 (1.33)
95% CI of LS mean	(79.97, 85.27)	(80.52, 85.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-3.21, 4.22)
Absolute Change at Week 16 (MMRM)		
n	191	199
LS mean (SE)	0.07 (1.10)	-0.07 (1.07)
95% CI of LS mean	(-2.09, 2.22)	(-2.18, 2.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.13 (-3.15, 2.88)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	82.38 (1.36)	82.57 (1.34)
95% CI of LS mean	(79.70, 85.05)	(79.94, 85.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.19 (-3.56, 3.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	-0.32 (1.11)	-0.55 (1.08)
95% CI of LS mean	(-2.50, 1.85)	(-2.67, 1.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.23 (-3.27, 2.81)
Week 52		
n	194	196
Mean (SD)	82.83 (19.73)	84.64 (18.34)
Absolute Change at Week 52		
n	189	193
Mean (SD)	0.18 (17.29)	1.31 (12.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52 (MMRM)		
n	192	195
LS mean (SE)	82.79 (1.30)	84.33 (1.28)
95% CI of LS mean	(80.24, 85.35)	(81.80, 86.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-2.06, 5.13)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	0.09 (1.09)	1.06 (1.07)
95% CI of LS mean	(-2.05, 2.23)	(-1.04, 3.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.98 (-2.03, 3.98)
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	-0.06 (0.88)	0.15 (0.86)
95% CI of LS mean	(-1.79, 1.68)	(-1.55, 1.84)
P-value within Treatment	0.9480	0.8637
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.21 (-2.22, 2.63)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8677

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Hedges' G (SE)		0.02 (0.10)
Hedges' 95% CI		(-0.18, 0.21)
Hedges' P-value		0.8676

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	84.00 (18.26)	86.96 (17.04)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	82.99 (1.63)	86.16 (1.57)
95% CI of LS mean	(79.79, 86.19)	(83.06, 89.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.17 (-1.31, 7.64)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	-1.28 (1.39)	-1.03 (1.34)
95% CI of LS mean	(-4.02, 1.46)	(-3.66, 1.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-3.56, 4.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 16 (MMRM)		
n	130	139
LS mean (SE)	85.83 (1.40)	87.38 (1.36)
95% CI of LS mean	(83.06, 88.59)	(84.70, 90.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-2.32, 5.42)
Absolute Change at Week 16 (MMRM)		
n	126	137
LS mean (SE)	2.00 (1.18)	0.47 (1.14)
95% CI of LS mean	(-0.33, 4.32)	(-1.76, 2.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.52 (-4.76, 1.72)
Week 24 (MMRM)		
n	132	140
LS mean (SE)	84.63 (1.43)	87.60 (1.39)
95% CI of LS mean	(81.80, 87.45)	(84.85, 90.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.97 (-0.99, 6.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 24 (MMRM)		
n	128	137
LS mean (SE)	0.49 (1.15)	0.79 (1.12)
95% CI of LS mean	(-1.78, 2.76)	(-1.41, 2.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.30 (-2.88, 3.47)
Week 52		
n	139	143
Mean (SD)	84.38 (18.68)	87.62 (17.49)
Absolute Change at Week 52		
n	135	140
Mean (SD)	0.84 (14.92)	0.89 (11.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52 (MMRM)		
n	132	139
LS mean (SE)	84.56 (1.50)	87.78 (1.46)
95% CI of LS mean	(81.61, 87.50)	(84.91, 90.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-0.91, 7.36)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	0.67 (1.16)	0.84 (1.12)
95% CI of LS mean	(-1.61, 2.95)	(-1.37, 3.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-3.02, 3.36)
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	1.05 (0.95)	0.70 (0.92)
95% CI of LS mean	(-0.82, 2.92)	(-1.11, 2.51)
P-value within Treatment	0.2693	0.4458
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-2.96, 2.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7924

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Hedges' G (SE)		-0.03 (0.12)
Hedges' 95% CI		(-0.27, 0.21)
Hedges' P-value		0.7912

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	77.37 (21.70)	78.33 (19.24)
Week 8 (MMRM)		
n	142	131
LS mean (SE)	77.83 (1.74)	77.47 (1.81)
95% CI of LS mean	(74.40, 81.26)	(73.90, 81.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-5.34, 4.62)
Absolute Change at Week 8 (MMRM)		
n	140	130
LS mean (SE)	-0.27 (1.31)	-0.34 (1.36)
95% CI of LS mean	(-2.85, 2.31)	(-3.01, 2.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.07 (-3.81, 3.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 16 (MMRM)		
n	143	129
LS mean (SE)	77.48 (1.84)	76.96 (1.92)
95% CI of LS mean	(73.86, 81.11)	(73.17, 80.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-5.79, 4.75)
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	-0.55 (1.41)	-0.91 (1.46)
95% CI of LS mean	(-3.32, 2.21)	(-3.79, 1.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-4.36, 3.66)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	76.77 (1.88)	75.70 (1.98)
95% CI of LS mean	(73.07, 80.48)	(71.81, 79.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.07 (-6.47, 4.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	-1.42 (1.41)	-1.99 (1.48)
95% CI of LS mean	(-4.21, 1.36)	(-4.90, 0.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.57 (-4.62, 3.48)
Week 52		
n	138	122
Mean (SD)	78.45 (21.62)	80.57 (18.45)
Absolute Change at Week 52		
n	135	121
Mean (SD)	1.21 (17.88)	2.04 (13.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52 (MMRM)		
n	137	120
LS mean (SE)	79.17 (1.65)	79.44 (1.73)
95% CI of LS mean	(75.93, 82.42)	(76.03, 82.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-4.47, 5.01)
Absolute Change at Week 52 (MMRM)		
n	134	119
LS mean (SE)	0.99 (1.39)	1.65 (1.46)
95% CI of LS mean	(-1.74, 3.73)	(-1.22, 4.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.65 (-3.33, 4.63)
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	-0.33 (1.11)	-0.42 (1.16)
95% CI of LS mean	(-2.52, 1.87)	(-2.70, 1.87)
P-value within Treatment	0.7692	0.7201
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-3.28, 3.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9562

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Hedges' G (SE)		-0.01 (0.12)
Hedges' 95% CI		(-0.25, 0.23)
Hedges' P-value		0.9559

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	81.06 (20.58)	84.45 (18.41)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	77.95 (2.06)	83.69 (1.93)
95% CI of LS mean	(73.89, 82.02)	(79.89, 87.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.74 (0.17, 11.32)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	-2.94 (1.57)	-1.50 (1.48)
95% CI of LS mean	(-6.03, 0.15)	(-4.41, 1.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-2.80, 5.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 16 (MMRM)		
n	96	108
LS mean (SE)	79.80 (1.88)	84.66 (1.77)
95% CI of LS mean	(76.09, 83.51)	(81.17, 88.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.86 (-0.24, 9.96)
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	-1.06 (1.29)	-0.26 (1.22)
95% CI of LS mean	(-3.59, 1.48)	(-2.67, 2.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.80 (-2.70, 4.30)
Week 24 (MMRM)		
n	97	108
LS mean (SE)	79.31 (2.01)	83.87 (1.89)
95% CI of LS mean	(75.36, 83.27)	(80.13, 87.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.55 (-0.89, 10.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 24 (MMRM)		
n	96	106
LS mean (SE)	-1.59 (1.24)	-1.00 (1.18)
95% CI of LS mean	(-4.02, 0.85)	(-3.31, 1.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-2.78, 3.96)
Week 52		
n	101	104
Mean (SD)	80.75 (21.50)	85.99 (16.99)
Absolute Change at Week 52		
n	100	101
Mean (SD)	-0.12 (11.82)	1.47 (9.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52 (MMRM)		
n	97	104
LS mean (SE)	80.55 (1.86)	85.99 (1.76)
95% CI of LS mean	(76.89, 84.22)	(82.52, 89.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.43 (0.38, 10.49)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	-0.30 (1.10)	1.28 (1.07)
95% CI of LS mean	(-2.47, 1.87)	(-0.82, 3.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.58 (-1.44, 4.61)
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	-0.98 (0.93)	0.01 (0.89)
95% CI of LS mean	(-2.82, 0.86)	(-1.75, 1.76)
P-value within Treatment	0.2931	0.9925
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.99 (-1.56, 3.54)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4441

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Hedges' G (SE)		0.11 (0.14)
Hedges' 95% CI		(-0.17, 0.38)
Hedges' P-value		0.4434

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	80.44 (20.20)	81.76 (18.70)
Week 8 (MMRM)		
n	178	162
LS mean (SE)	81.41 (1.47)	81.19 (1.54)
95% CI of LS mean	(78.53, 84.29)	(78.17, 84.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-4.40, 3.96)
Absolute Change at Week 8 (MMRM)		
n	173	162
LS mean (SE)	0.80 (1.20)	-0.49 (1.24)
95% CI of LS mean	(-1.56, 3.16)	(-2.93, 1.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.30 (-4.69, 2.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 16 (MMRM)		
n	177	160
LS mean (SE)	82.17 (1.52)	81.21 (1.60)
95% CI of LS mean	(79.18, 85.16)	(78.07, 84.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.96 (-5.30, 3.39)
Absolute Change at Week 16 (MMRM)		
n	171	160
LS mean (SE)	1.91 (1.24)	-0.45 (1.28)
95% CI of LS mean	(-0.53, 4.35)	(-2.97, 2.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.36 (-5.87, 1.16)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	80.99 (1.52)	80.94 (1.60)
95% CI of LS mean	(78.00, 83.98)	(77.79, 84.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-4.40, 4.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	0.38 (1.25)	-0.57 (1.30)
95% CI of LS mean	(-2.07, 2.83)	(-3.12, 1.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-4.49, 2.59)
Week 52		
n	176	161
Mean (SD)	81.82 (19.77)	83.32 (18.99)
Absolute Change at Week 52		
n	170	160
Mean (SD)	1.70 (18.62)	1.40 (13.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	172	155
LS mean (SE)	82.18 (1.41)	82.61 (1.48)
95% CI of LS mean	(79.40, 84.96)	(79.69, 85.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-3.60, 4.47)
Absolute Change at Week 52 (MMRM)		
n	166	154
LS mean (SE)	1.73 (1.28)	0.87 (1.33)
95% CI of LS mean	(-0.80, 4.25)	(-1.75, 3.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.86 (-4.50, 2.78)
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	1.34 (1.02)	-0.05 (1.05)
95% CI of LS mean	(-0.66, 3.34)	(-2.12, 2.02)
P-value within Treatment	0.1881	0.9633
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.39 (-4.27, 1.49)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3440

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Hedges' G (SE)		-0.10 (0.11)
Hedges' 95% CI		(-0.32, 0.11)
Hedges' P-value		0.3435

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	71.48 (18.66)	75.22 (17.41)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	72.18 (1.39)	75.39 (1.43)
95% CI of LS mean	(69.44, 74.93)	(72.57, 78.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.21 (-0.73, 7.14)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	0.64 (1.13)	0.14 (1.16)
95% CI of LS mean	(-1.59, 2.86)	(-2.14, 2.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.49 (-3.68, 2.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 16 (MMRM)		
n	158	148
LS mean (SE)	74.25 (1.40)	75.19 (1.44)
95% CI of LS mean	(71.49, 77.00)	(72.35, 78.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.95 (-3.01, 4.90)
Absolute Change at Week 16 (MMRM)		
n	155	146
LS mean (SE)	2.77 (1.13)	0.08 (1.16)
95% CI of LS mean	(0.55, 5.00)	(-2.21, 2.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.69 (-5.89, 0.50)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	72.26 (1.43)	76.67 (1.48)
95% CI of LS mean	(69.44, 75.09)	(73.76, 79.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.40 (0.35, 8.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	0.78 (1.15)	1.56 (1.18)
95% CI of LS mean	(-1.49, 3.05)	(-0.77, 3.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.78 (-2.47, 4.03)
Week 52		
n	159	145
Mean (SD)	74.33 (19.53)	78.43 (18.19)
Absolute Change at Week 52		
n	156	143
Mean (SD)	3.28 (14.24)	3.11 (13.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52 (MMRM)		
n	155	144
LS mean (SE)	74.30 (1.48)	78.03 (1.53)
95% CI of LS mean	(71.38, 77.22)	(75.02, 81.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.73 (-0.47, 7.92)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	2.94 (1.13)	2.95 (1.16)
95% CI of LS mean	(0.71, 5.16)	(0.66, 5.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-3.18, 3.21)
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	2.16 (0.95)	1.53 (0.98)
95% CI of LS mean	(0.29, 4.04)	(-0.39, 3.45)
P-value within Treatment	0.0238	0.1187
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-3.32, 2.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6429

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Hedges' G (SE)		-0.05 (0.11)
Hedges' 95% CI		(-0.28, 0.17)
Hedges' P-value		0.6426

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	74.22 (16.61)	75.19 (18.57)
Week 8 (MMRM)		
n	116	120
LS mean (SE)	76.06 (1.60)	76.00 (1.57)
95% CI of LS mean	(72.90, 79.22)	(72.91, 79.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-4.49, 4.38)
Absolute Change at Week 8 (MMRM)		
n	112	119
LS mean (SE)	1.27 (1.21)	0.83 (1.17)
95% CI of LS mean	(-1.11, 3.65)	(-1.47, 3.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-3.76, 2.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 16 (MMRM)		
n	115	119
LS mean (SE)	75.26 (1.61)	77.20 (1.58)
95% CI of LS mean	(72.09, 78.44)	(74.09, 80.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.94 (-2.52, 6.39)
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	0.92 (1.30)	2.03 (1.26)
95% CI of LS mean	(-1.64, 3.48)	(-0.46, 4.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.11 (-2.46, 4.68)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	75.22 (1.52)	77.84 (1.50)
95% CI of LS mean	(72.21, 78.22)	(74.88, 80.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.62 (-1.61, 6.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	0.71 (1.29)	2.73 (1.27)
95% CI of LS mean	(-1.84, 3.26)	(0.23, 5.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.02 (-1.56, 5.59)
Week 52		
n	115	116
Mean (SD)	79.44 (15.42)	81.09 (16.87)
Absolute Change at Week 52		
n	111	114
Mean (SD)	4.92 (15.04)	5.59 (14.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52 (MMRM)		
n	114	115
LS mean (SE)	79.38 (1.49)	80.90 (1.46)
95% CI of LS mean	(76.45, 82.31)	(78.02, 83.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.52 (-2.60, 5.65)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	4.67 (1.40)	5.64 (1.37)
95% CI of LS mean	(1.92, 7.42)	(2.94, 8.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-2.89, 4.83)
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	2.10 (1.11)	3.47 (1.08)
95% CI of LS mean	(-0.08, 4.28)	(1.34, 5.59)
P-value within Treatment	0.0592	0.0015
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.36 (-1.69, 4.42)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3802

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Hedges' G (SE)		0.11 (0.13)
Hedges' 95% CI		(-0.14, 0.37)
Hedges' P-value		0.3792

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	78.29 (17.13)	76.90 (17.08)
Week 8 (MMRM)		
n	34	36
LS mean (SE)	79.90 (2.50)	79.66 (2.40)
95% CI of LS mean	(74.91, 84.89)	(74.87, 84.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-7.19, 6.72)
Absolute Change at Week 8 (MMRM)		
n	33	36
LS mean (SE)	0.30 (2.65)	1.96 (2.51)
95% CI of LS mean	(-4.98, 5.58)	(-3.05, 6.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.66 (-5.67, 9.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 16 (MMRM)		
n	32	36
LS mean (SE)	78.29 (2.63)	81.00 (2.49)
95% CI of LS mean	(73.05, 83.53)	(76.03, 85.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.71 (-4.56, 9.98)
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	-0.64 (2.70)	3.21 (2.53)
95% CI of LS mean	(-6.03, 4.76)	(-1.85, 8.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.84 (-3.61, 11.30)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	81.58 (2.52)	82.09 (2.42)
95% CI of LS mean	(76.55, 86.60)	(77.26, 86.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.51 (-6.49, 7.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	2.66 (2.86)	4.34 (2.74)
95% CI of LS mean	(-3.06, 8.37)	(-1.13, 9.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.68 (-6.28, 9.64)
Week 52		
n	33	35
Mean (SD)	83.91 (16.66)	85.37 (13.54)
Absolute Change at Week 52		
n	32	34
Mean (SD)	5.43 (19.14)	6.14 (17.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52 (MMRM)		
n	32	35
LS mean (SE)	83.26 (2.68)	84.52 (2.57)
95% CI of LS mean	(77.90, 88.62)	(79.39, 89.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.26 (-6.19, 8.71)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	3.69 (3.32)	6.07 (3.16)
95% CI of LS mean	(-2.94, 10.31)	(-0.24, 12.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-6.81, 11.57)
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	1.90 (2.51)	4.54 (2.38)
95% CI of LS mean	(-3.11, 6.92)	(-0.22, 9.29)
P-value within Treatment	0.4514	0.0611
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.64 (-4.33, 9.60)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4527

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		0.18 (0.24)
Hedges' 95% CI		(-0.29, 0.65)
Hedges' P-value		0.4504

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	71.63 (17.78)	74.72 (17.99)
Week 8 (MMRM)		
n	243	237
LS mean (SE)	72.83 (1.15)	75.09 (1.17)
95% CI of LS mean	(70.57, 75.10)	(72.80, 77.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.25 (-0.97, 5.48)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	0.99 (0.87)	0.18 (0.87)
95% CI of LS mean	(-0.71, 2.69)	(-1.53, 1.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-3.22, 1.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 16 (MMRM)		
n	241	231
LS mean (SE)	73.99 (1.15)	75.36 (1.17)
95% CI of LS mean	(71.73, 76.25)	(73.06, 77.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.37 (-1.86, 4.60)
Absolute Change at Week 16 (MMRM)		
n	235	228
LS mean (SE)	2.30 (0.90)	0.58 (0.91)
95% CI of LS mean	(0.54, 4.06)	(-1.20, 2.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.72 (-4.23, 0.79)
Week 24 (MMRM)		
n	240	229
LS mean (SE)	72.26 (1.14)	76.48 (1.16)
95% CI of LS mean	(70.02, 74.51)	(74.19, 78.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.22 (1.01, 7.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 24 (MMRM)		
n	234	227
LS mean (SE)	0.47 (0.89)	1.70 (0.90)
95% CI of LS mean	(-1.28, 2.23)	(-0.07, 3.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-1.27, 3.73)
Week 52		
n	244	230
Mean (SD)	75.48 (18.03)	78.70 (17.93)
Absolute Change at Week 52		
n	238	227
Mean (SD)	3.90 (13.94)	4.02 (13.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52 (MMRM)		
n	237	224
LS mean (SE)	75.38 (1.16)	78.61 (1.18)
95% CI of LS mean	(73.11, 77.65)	(76.29, 80.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.23 (-0.02, 6.48)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	3.60 (0.89)	3.86 (0.90)
95% CI of LS mean	(1.86, 5.35)	(2.09, 5.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-2.23, 2.75)
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	2.12 (0.74)	2.05 (0.75)
95% CI of LS mean	(0.67, 3.58)	(0.57, 3.52)
P-value within Treatment	0.0043	0.0066
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-2.15, 2.00)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9424

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Hedges' G (SE)		-0.01 (0.09)
Hedges' 95% CI		(-0.19, 0.17)
Hedges' P-value		0.9423

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	69.96 (19.16)	73.87 (16.52)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	72.92 (1.90)	75.56 (2.04)
95% CI of LS mean	(69.16, 76.68)	(71.53, 79.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.64 (-2.89, 8.17)
Absolute Change at Week 8 (MMRM)		
n	77	67
LS mean (SE)	2.23 (1.40)	2.05 (1.49)
95% CI of LS mean	(-0.54, 4.99)	(-0.90, 5.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-4.23, 3.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 16 (MMRM)		
n	77	67
LS mean (SE)	73.35 (1.97)	75.21 (2.11)
95% CI of LS mean	(69.46, 77.24)	(71.03, 79.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.86 (-3.86, 7.58)
Absolute Change at Week 16 (MMRM)		
n	75	66
LS mean (SE)	2.99 (1.60)	1.72 (1.71)
95% CI of LS mean	(-0.17, 6.16)	(-1.65, 5.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.27 (-5.91, 3.37)
Week 24 (MMRM)		
n	79	63
LS mean (SE)	70.23 (2.09)	75.50 (2.29)
95% CI of LS mean	(66.09, 74.37)	(70.98, 80.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.27 (-0.87, 11.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 24 (MMRM)		
n	77	63
LS mean (SE)	-0.32 (1.60)	1.93 (1.75)
95% CI of LS mean	(-3.48, 2.84)	(-1.53, 5.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.25 (-2.45, 6.95)
Week 52		
n	78	67
Mean (SD)	76.50 (20.79)	78.86 (18.43)
Absolute Change at Week 52		
n	76	66
Mean (SD)	6.34 (13.63)	4.63 (13.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52 (MMRM)		
n	77	64
LS mean (SE)	77.02 (2.19)	78.14 (2.37)
95% CI of LS mean	(72.69, 81.35)	(73.46, 82.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.13 (-5.27, 7.52)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	6.57 (1.59)	4.65 (1.72)
95% CI of LS mean	(3.43, 9.70)	(1.25, 8.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.91 (-6.55, 2.72)
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	3.08 (1.31)	2.77 (1.41)
95% CI of LS mean	(0.48, 5.68)	(-0.03, 5.56)
P-value within Treatment	0.0204	0.0526
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-4.14, 3.52)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8719

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Hedges' G (SE)		-0.03 (0.17)
Hedges' 95% CI		(-0.36, 0.30)
Hedges' P-value		0.8714

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	73.72 (17.18)	75.35 (18.30)
Week 8 (MMRM)		
n	198	205
LS mean (SE)	74.17 (1.26)	75.68 (1.23)
95% CI of LS mean	(71.70, 76.64)	(73.26, 78.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-1.95, 4.98)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	0.33 (1.02)	-0.06 (0.99)
95% CI of LS mean	(-1.67, 2.33)	(-2.01, 1.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.39 (-3.19, 2.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 16 (MMRM)		
n	196	200
LS mean (SE)	75.21 (1.24)	76.38 (1.22)
95% CI of LS mean	(72.77, 77.65)	(73.97, 78.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-2.26, 4.60)
Absolute Change at Week 16 (MMRM)		
n	191	198
LS mean (SE)	1.58 (1.01)	0.72 (0.99)
95% CI of LS mean	(-0.41, 3.57)	(-1.23, 2.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.86 (-3.65, 1.93)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	74.83 (1.20)	77.71 (1.18)
95% CI of LS mean	(72.48, 77.19)	(75.40, 80.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.88 (-0.42, 6.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	1.16 (1.02)	2.13 (0.99)
95% CI of LS mean	(-0.83, 3.16)	(0.18, 4.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-1.82, 3.76)
Week 52		
n	194	196
Mean (SD)	76.45 (16.95)	79.79 (17.27)
Absolute Change at Week 52		
n	189	193
Mean (SD)	3.00 (14.97)	4.22 (14.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52 (MMRM)		
n	192	195
LS mean (SE)	76.22 (1.20)	79.67 (1.18)
95% CI of LS mean	(73.85, 78.58)	(77.34, 82.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.45 (0.13, 6.77)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	2.48 (1.05)	4.02 (1.03)
95% CI of LS mean	(0.42, 4.54)	(1.99, 6.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.54 (-1.36, 4.43)
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	1.74 (0.86)	2.29 (0.84)
95% CI of LS mean	(0.05, 3.43)	(0.63, 3.94)
P-value within Treatment	0.0441	0.0069
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-1.82, 2.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6490

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Hedges' G (SE)		0.05 (0.10)
Hedges' 95% CI		(-0.15, 0.24)
Hedges' P-value		0.6489

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	74.21 (17.63)	77.15 (17.89)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	75.96 (1.43)	77.87 (1.38)
95% CI of LS mean	(73.14, 78.77)	(75.15, 80.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.92 (-2.02, 5.86)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	0.69 (1.15)	0.48 (1.11)
95% CI of LS mean	(-1.58, 2.96)	(-1.70, 2.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-3.37, 2.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 16 (MMRM)		
n	130	138
LS mean (SE)	75.18 (1.47)	78.37 (1.42)
95% CI of LS mean	(72.30, 78.07)	(75.57, 81.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.18 (-0.86, 7.23)
Absolute Change at Week 16 (MMRM)		
n	126	136
LS mean (SE)	0.32 (1.10)	1.15 (1.07)
95% CI of LS mean	(-1.86, 2.50)	(-0.95, 3.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.83 (-2.21, 3.86)
Week 24 (MMRM)		
n	133	140
LS mean (SE)	75.03 (1.49)	78.82 (1.45)
95% CI of LS mean	(72.09, 77.97)	(75.97, 81.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.79 (-0.33, 7.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 24 (MMRM)		
n	129	137
LS mean (SE)	0.13 (1.17)	1.73 (1.14)
95% CI of LS mean	(-2.18, 2.44)	(-0.51, 3.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.60 (-1.63, 4.83)
Week 52		
n	139	143
Mean (SD)	77.97 (17.17)	80.57 (17.51)
Absolute Change at Week 52		
n	135	140
Mean (SD)	3.70 (16.06)	3.45 (13.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52 (MMRM)		
n	132	139
LS mean (SE)	77.74 (1.50)	80.52 (1.46)
95% CI of LS mean	(74.79, 80.70)	(77.65, 83.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.77 (-1.37, 6.91)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	2.74 (1.32)	3.32 (1.28)
95% CI of LS mean	(0.15, 5.33)	(0.81, 5.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-3.04, 4.20)
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	1.06 (1.01)	2.07 (0.98)
95% CI of LS mean	(-0.93, 3.06)	(0.13, 4.00)
P-value within Treatment	0.2951	0.0363
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.00 (-1.79, 3.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4815

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Hedges' G (SE)		0.09 (0.12)
Hedges' 95% CI		(-0.15, 0.33)
Hedges' P-value		0.4792

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	70.83 (17.89)	72.73 (17.57)
Week 8 (MMRM)		
n	143	130
LS mean (SE)	71.97 (1.53)	73.05 (1.60)
95% CI of LS mean	(68.95, 74.99)	(69.90, 76.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.08 (-3.31, 5.47)
Absolute Change at Week 8 (MMRM)		
n	140	129
LS mean (SE)	0.64 (1.19)	0.90 (1.23)
95% CI of LS mean	(-1.70, 2.97)	(-1.53, 3.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-3.13, 3.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 16 (MMRM)		
n	143	129
LS mean (SE)	74.31 (1.51)	73.42 (1.58)
95% CI of LS mean	(71.34, 77.29)	(70.31, 76.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-5.21, 3.44)
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	3.07 (1.29)	1.18 (1.34)
95% CI of LS mean	(0.54, 5.61)	(-1.45, 3.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.89 (-5.56, 1.78)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	72.21 (1.48)	75.24 (1.55)
95% CI of LS mean	(69.30, 75.12)	(72.18, 78.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.03 (-1.21, 7.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	0.87 (1.26)	2.89 (1.32)
95% CI of LS mean	(-1.62, 3.35)	(0.30, 5.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.03 (-1.58, 5.64)
Week 52		
n	138	122
Mean (SD)	74.99 (18.84)	78.42 (17.57)
Absolute Change at Week 52		
n	135	121
Mean (SD)	4.47 (13.06)	5.27 (13.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52 (MMRM)		
n	137	120
LS mean (SE)	75.37 (1.53)	77.81 (1.61)
95% CI of LS mean	(72.37, 78.38)	(74.64, 80.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.43 (-1.95, 6.82)
Absolute Change at Week 52 (MMRM)		
n	134	119
LS mean (SE)	4.09 (1.15)	5.51 (1.21)
95% CI of LS mean	(1.83, 6.35)	(3.13, 7.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-1.88, 4.72)
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	2.68 (1.02)	3.20 (1.06)
95% CI of LS mean	(0.68, 4.68)	(1.11, 5.28)
P-value within Treatment	0.0089	0.0028
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-2.39, 3.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7249

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Hedges' G (SE)		0.04 (0.12)
Hedges' 95% CI		(-0.20, 0.28)
Hedges' P-value		0.7233

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	71.25 (18.32)	75.98 (18.68)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	73.15 (1.78)	76.92 (1.67)
95% CI of LS mean	(69.63, 76.66)	(73.64, 80.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.77 (-1.04, 8.59)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	1.75 (1.44)	0.50 (1.36)
95% CI of LS mean	(-1.10, 4.60)	(-2.19, 3.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.25 (-5.17, 2.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 16 (MMRM)		
n	96	108
LS mean (SE)	72.46 (1.77)	78.64 (1.67)
95% CI of LS mean	(68.96, 75.96)	(75.35, 81.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.18 (1.37, 10.99)
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	1.00 (1.40)	2.42 (1.33)
95% CI of LS mean	(-1.77, 3.77)	(-0.21, 5.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-2.40, 5.24)
Week 24 (MMRM)		
n	98	108
LS mean (SE)	71.08 (1.82)	78.38 (1.72)
95% CI of LS mean	(67.48, 74.67)	(74.98, 81.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.30 (2.35, 12.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 24 (MMRM)		
n	97	106
LS mean (SE)	-0.27 (1.42)	2.11 (1.36)
95% CI of LS mean	(-3.07, 2.53)	(-0.56, 4.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-1.50, 6.25)
Week 52		
n	101	104
Mean (SD)	76.36 (17.73)	80.73 (17.44)
Absolute Change at Week 52		
n	100	101
Mean (SD)	5.51 (13.21)	4.25 (14.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52 (MMRM)		
n	97	104
LS mean (SE)	76.30 (1.73)	80.63 (1.64)
95% CI of LS mean	(72.89, 79.71)	(77.39, 83.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.33 (-0.38, 9.04)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	5.02 (1.35)	4.35 (1.31)
95% CI of LS mean	(2.34, 7.69)	(1.77, 6.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-4.38, 3.05)
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	1.92 (1.13)	2.96 (1.08)
95% CI of LS mean	(-0.31, 4.14)	(0.83, 5.09)
P-value within Treatment	0.0913	0.0066
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-2.04, 4.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5060

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Hedges' G (SE)		0.09 (0.14)
Hedges' 95% CI		(-0.18, 0.37)
Hedges' P-value		0.5054

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	73.22 (17.53)	74.42 (17.31)
Week 8 (MMRM)		
n	179	161
LS mean (SE)	74.14 (1.31)	74.90 (1.37)
95% CI of LS mean	(71.57, 76.71)	(72.20, 77.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.76 (-2.97, 4.49)
Absolute Change at Week 8 (MMRM)		
n	173	161
LS mean (SE)	0.41 (1.00)	0.47 (1.04)
95% CI of LS mean	(-1.56, 2.39)	(-1.57, 2.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-2.79, 2.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 16 (MMRM)		
n	177	159
LS mean (SE)	75.84 (1.31)	74.42 (1.38)
95% CI of LS mean	(73.26, 78.41)	(71.71, 77.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.42 (-5.16, 2.32)
Absolute Change at Week 16 (MMRM)		
n	171	159
LS mean (SE)	2.51 (1.07)	0.00 (1.11)
95% CI of LS mean	(0.41, 4.62)	(-2.18, 2.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.51 (-5.54, 0.52)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	74.79 (1.27)	76.45 (1.34)
95% CI of LS mean	(72.29, 77.30)	(73.81, 79.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.65 (-1.99, 5.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	1.30 (1.07)	2.07 (1.11)
95% CI of LS mean	(-0.81, 3.40)	(-0.12, 4.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.78 (-2.27, 3.82)
Week 52		
n	176	161
Mean (SD)	76.56 (18.28)	78.84 (17.61)
Absolute Change at Week 52		
n	170	160
Mean (SD)	3.25 (15.36)	4.33 (13.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	172	155
LS mean (SE)	76.43 (1.35)	78.48 (1.42)
95% CI of LS mean	(73.78, 79.09)	(75.69, 81.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.04 (-1.81, 5.90)
Absolute Change at Week 52 (MMRM)		
n	166	154
LS mean (SE)	2.84 (1.13)	4.05 (1.17)
95% CI of LS mean	(0.62, 5.06)	(1.75, 6.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.21 (-1.99, 4.41)
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	2.22 (0.92)	2.04 (0.95)
95% CI of LS mean	(0.41, 4.03)	(0.17, 3.92)
P-value within Treatment	0.0165	0.0330
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-2.79, 2.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8944

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Hedges' G (SE)		-0.01 (0.11)
Hedges' 95% CI		(-0.23, 0.20)
Hedges' P-value		0.8943

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Baseline		
n	164	152
Mean (SD)	68.29 (19.31)	72.15 (18.88)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	67.63 (1.55)	73.42 (1.59)
95% CI of LS mean	(64.58, 70.69)	(70.29, 76.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.78 (1.41, 10.16)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	-0.10 (1.10)	1.57 (1.13)
95% CI of LS mean	(-2.27, 2.07)	(-0.65, 3.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.67 (-1.44, 4.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 16 (MMRM)		
n	158	149
LS mean (SE)	69.65 (1.57)	73.09 (1.61)
95% CI of LS mean	(66.56, 72.74)	(69.91, 76.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.44 (-0.99, 7.87)
Absolute Change at Week 16 (MMRM)		
n	155	147
LS mean (SE)	1.95 (1.16)	1.31 (1.19)
95% CI of LS mean	(-0.34, 4.24)	(-1.04, 3.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-3.92, 2.64)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	69.21 (1.60)	73.42 (1.65)
95% CI of LS mean	(66.05, 72.36)	(70.18, 76.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.22 (-0.31, 8.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	1.48 (1.18)	1.61 (1.21)
95% CI of LS mean	(-0.84, 3.80)	(-0.77, 3.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-3.20, 3.45)
Week 52		
n	159	145
Mean (SD)	70.93 (20.23)	74.41 (19.66)
Absolute Change at Week 52		
n	156	143
Mean (SD)	3.28 (16.85)	2.87 (14.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Week 52 (MMRM)		
n	155	144
LS mean (SE)	70.88 (1.58)	74.19 (1.63)
95% CI of LS mean	(67.77, 73.99)	(70.99, 77.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.31 (-1.16, 7.78)
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	3.26 (1.28)	2.53 (1.32)
95% CI of LS mean	(0.74, 5.77)	(-0.06, 5.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.72 (-4.33, 2.89)
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	2.23 (1.02)	1.82 (1.05)
95% CI of LS mean	(0.22, 4.24)	(-0.24, 3.88)
P-value within Treatment	0.0296	0.0834
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-3.29, 2.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7782

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167	VNZ/TEZ/D-IVA N = 154
Hedges' G (SE)		-0.03 (0.11)
Hedges' 95% CI		(-0.26, 0.19)
Hedges' P-value		0.7781

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Baseline		
n	115	123
Mean (SD)	72.85 (20.14)	71.45 (19.41)
Week 8 (MMRM)		
n	116	120
LS mean (SE)	74.84 (1.87)	73.63 (1.83)
95% CI of LS mean	(71.15, 78.53)	(70.03, 77.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.21 (-6.38, 3.97)
Absolute Change at Week 8 (MMRM)		
n	112	119
LS mean (SE)	2.06 (1.29)	2.06 (1.25)
95% CI of LS mean	(-0.47, 4.59)	(-0.40, 4.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-3.54, 3.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 16 (MMRM)		
n	115	119
LS mean (SE)	74.58 (1.81)	73.85 (1.77)
95% CI of LS mean	(71.01, 78.15)	(70.36, 77.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-5.74, 4.28)
Absolute Change at Week 16 (MMRM)		
n	111	118
LS mean (SE)	1.96 (1.33)	2.13 (1.29)
95% CI of LS mean	(-0.67, 4.59)	(-0.42, 4.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.17 (-3.50, 3.83)
Week 24 (MMRM)		
n	118	118
LS mean (SE)	72.59 (1.85)	74.13 (1.83)
95% CI of LS mean	(68.94, 76.24)	(70.53, 77.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.54 (-3.60, 6.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Absolute Change at Week 24 (MMRM)		
n	114	117
LS mean (SE)	0.20 (1.37)	2.42 (1.34)
95% CI of LS mean	(-2.50, 2.90)	(-0.22, 5.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.22 (-1.56, 6.01)
Week 52		
n	115	116
Mean (SD)	76.81 (19.05)	77.68 (19.08)
Absolute Change at Week 52		
n	111	114
Mean (SD)	3.70 (16.30)	5.95 (16.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Week 52 (MMRM)		
n	114	115
LS mean (SE)	76.53 (1.77)	77.88 (1.74)
95% CI of LS mean	(73.05, 80.01)	(74.45, 81.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-3.55, 6.25)
Absolute Change at Week 52 (MMRM)		
n	110	113
LS mean (SE)	3.88 (1.54)	6.01 (1.52)
95% CI of LS mean	(0.84, 6.93)	(3.03, 9.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.13 (-2.14, 6.40)
Absolute Change through Week 52 (MMRM)		
n	114	120
LS mean (SE)	2.01 (1.19)	3.52 (1.16)
95% CI of LS mean	(-0.34, 4.37)	(1.23, 5.81)
P-value within Treatment	0.0931	0.0028
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-1.79, 4.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3690

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119	VNZ/TEZ/D-IVA N = 125
Hedges' G (SE)		0.12 (0.13)
Hedges' 95% CI		(-0.14, 0.37)
Hedges' P-value		0.3681

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	37	40
Mean (SD)	72.07 (18.82)	76.11 (17.89)
Week 8 (MMRM)		
n	34	36
LS mean (SE)	79.33 (2.95)	76.97 (2.84)
95% CI of LS mean	(73.43, 85.22)	(71.31, 82.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.36 (-10.58, 5.86)
Absolute Change at Week 8 (MMRM)		
n	33	36
LS mean (SE)	7.43 (2.57)	0.20 (2.44)
95% CI of LS mean	(2.30, 12.57)	(-4.68, 5.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.23 (-14.36, -0.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 16 (MMRM)		
n	32	36
LS mean (SE)	77.60 (3.12)	76.70 (2.95)
95% CI of LS mean	(71.36, 83.83)	(70.81, 82.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-9.54, 7.75)
Absolute Change at Week 16 (MMRM)		
n	31	36
LS mean (SE)	6.27 (2.84)	-0.25 (2.66)
95% CI of LS mean	(0.57, 11.96)	(-5.57, 5.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.51 (-14.37, 1.34)
Week 24 (MMRM)		
n	34	36
LS mean (SE)	72.95 (3.42)	75.82 (3.28)
95% CI of LS mean	(66.13, 79.78)	(69.27, 82.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.87 (-6.64, 12.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 24 (MMRM)		
n	33	35
LS mean (SE)	1.97 (3.16)	-1.40 (3.04)
95% CI of LS mean	(-4.34, 8.29)	(-7.47, 4.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.37 (-12.17, 5.43)
Week 52		
n	33	35
Mean (SD)	79.80 (18.31)	80.63 (16.69)
Absolute Change at Week 52		
n	32	34
Mean (SD)	7.64 (19.84)	2.29 (19.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 52 (MMRM)		
n	32	35
LS mean (SE)	78.56 (3.15)	80.05 (3.00)
95% CI of LS mean	(72.27, 84.84)	(74.05, 86.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.49 (-7.24, 10.23)
Absolute Change at Week 52 (MMRM)		
n	31	34
LS mean (SE)	7.25 (3.50)	2.47 (3.33)
95% CI of LS mean	(0.26, 14.23)	(-4.17, 9.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.78 (-14.45, 4.90)
Absolute Change through Week 52 (MMRM)		
n	33	38
LS mean (SE)	5.16 (2.60)	0.28 (2.46)
95% CI of LS mean	(-0.04, 10.36)	(-4.65, 5.20)
P-value within Treatment	0.0516	0.9113
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.89 (-12.10, 2.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1806

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Hedges' G (SE)		-0.32 (0.24)
Hedges' 95% CI		(-0.79, 0.15)
Hedges' P-value		0.1803

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	70.07 (19.89)	70.93 (19.19)
Week 8 (MMRM)		
n	243	237
LS mean (SE)	69.48 (1.30)	72.90 (1.32)
95% CI of LS mean	(66.92, 72.04)	(70.31, 75.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.42 (-0.22, 7.07)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	-0.12 (0.88)	2.02 (0.88)
95% CI of LS mean	(-1.84, 1.60)	(0.29, 3.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.14 (-0.30, 4.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 16 (MMRM)		
n	241	232
LS mean (SE)	70.91 (1.28)	72.83 (1.30)
95% CI of LS mean	(68.39, 73.43)	(70.27, 75.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.91 (-1.68, 5.51)
Absolute Change at Week 16 (MMRM)		
n	235	229
LS mean (SE)	1.34 (0.90)	2.02 (0.91)
95% CI of LS mean	(-0.43, 3.12)	(0.22, 3.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.67 (-1.85, 3.20)
Week 24 (MMRM)		
n	240	229
LS mean (SE)	70.28 (1.30)	73.33 (1.32)
95% CI of LS mean	(67.72, 72.83)	(70.73, 75.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.05 (-0.60, 6.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 24 (MMRM)		
n	234	227
LS mean (SE)	0.75 (0.92)	2.50 (0.93)
95% CI of LS mean	(-1.05, 2.55)	(0.68, 4.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.75 (-0.81, 4.32)
Week 52		
n	244	230
Mean (SD)	72.63 (20.02)	75.22 (19.63)
Absolute Change at Week 52		
n	238	227
Mean (SD)	2.80 (16.06)	4.70 (14.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 52 (MMRM)		
n	237	224
LS mean (SE)	72.52 (1.28)	75.04 (1.30)
95% CI of LS mean	(70.01, 75.03)	(72.48, 77.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.52 (-1.07, 6.12)
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	2.91 (1.01)	4.33 (1.03)
95% CI of LS mean	(0.93, 4.90)	(2.31, 6.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-1.41, 4.25)
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	1.67 (0.80)	2.95 (0.81)
95% CI of LS mean	(0.10, 3.24)	(1.36, 4.54)
P-value within Treatment	0.0373	0.0003
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.28 (-0.96, 3.52)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2608

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Hedges' G (SE)		0.10 (0.09)
Hedges' 95% CI		(-0.08, 0.29)
Hedges' P-value		0.2605

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Baseline		
n	78	71
Mean (SD)	69.23 (20.57)	71.99 (20.82)
Week 8 (MMRM)		
n	79	68
LS mean (SE)	69.08 (2.42)	75.18 (2.60)
95% CI of LS mean	(64.28, 73.87)	(70.04, 80.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.11 (-0.94, 13.15)
Absolute Change at Week 8 (MMRM)		
n	77	67
LS mean (SE)	-0.03 (1.60)	3.17 (1.70)
95% CI of LS mean	(-3.19, 3.12)	(-0.20, 6.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.20 (-1.43, 7.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 16 (MMRM)		
n	77	67
LS mean (SE)	71.52 (2.35)	74.12 (2.52)
95% CI of LS mean	(66.88, 76.16)	(69.15, 79.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.60 (-4.22, 9.42)
Absolute Change at Week 16 (MMRM)		
n	75	66
LS mean (SE)	2.06 (1.70)	1.99 (1.82)
95% CI of LS mean	(-1.30, 5.43)	(-1.60, 5.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-5.01, 4.86)
Week 24 (MMRM)		
n	79	63
LS mean (SE)	70.06 (2.44)	74.51 (2.65)
95% CI of LS mean	(65.23, 74.89)	(69.26, 79.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.45 (-2.70, 11.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Absolute Change at Week 24 (MMRM)		
n	77	63
LS mean (SE)	1.27 (1.70)	2.49 (1.86)
95% CI of LS mean	(-2.10, 4.64)	(-1.19, 6.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.22 (-3.78, 6.22)
Week 52		
n	78	67
Mean (SD)	74.07 (20.86)	75.95 (19.88)
Absolute Change at Week 52		
n	76	66
Mean (SD)	4.68 (16.46)	4.88 (15.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Week 52 (MMRM)		
n	77	64
LS mean (SE)	73.88 (2.30)	75.89 (2.48)
95% CI of LS mean	(69.34, 78.41)	(70.99, 80.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.01 (-4.68, 8.71)
Absolute Change at Week 52 (MMRM)		
n	75	63
LS mean (SE)	4.56 (1.87)	3.88 (2.02)
95% CI of LS mean	(0.87, 8.25)	(-0.11, 7.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.68 (-6.13, 4.77)
Absolute Change through Week 52 (MMRM)		
n	77	66
LS mean (SE)	2.63 (1.54)	2.78 (1.65)
95% CI of LS mean	(-0.41, 5.67)	(-0.49, 6.06)
P-value within Treatment	0.0895	0.0946
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.16 (-4.33, 4.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9454

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80	VNZ/TEZ/D-IVA N = 72
Hedges' G (SE)		0.01 (0.17)
Hedges' 95% CI		(-0.32, 0.34)
Hedges' P-value		0.9452

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Baseline		
n	197	207
Mean (SD)	70.33 (19.43)	71.44 (18.46)
Week 8 (MMRM)		
n	198	205
LS mean (SE)	71.47 (1.38)	72.83 (1.35)
95% CI of LS mean	(68.76, 74.18)	(70.17, 75.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.36 (-2.44, 5.16)
Absolute Change at Week 8 (MMRM)		
n	193	203
LS mean (SE)	1.21 (0.99)	1.26 (0.97)
95% CI of LS mean	(-0.74, 3.15)	(-0.64, 3.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.05 (-2.67, 2.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 16 (MMRM)		
n	196	201
LS mean (SE)	71.99 (1.38)	73.05 (1.36)
95% CI of LS mean	(69.27, 74.70)	(70.38, 75.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.06 (-2.74, 4.87)
Absolute Change at Week 16 (MMRM)		
n	191	199
LS mean (SE)	1.97 (1.02)	1.52 (0.99)
95% CI of LS mean	(-0.03, 3.97)	(-0.44, 3.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-3.25, 2.35)
Week 24 (MMRM)		
n	195	202
LS mean (SE)	70.99 (1.40)	73.33 (1.37)
95% CI of LS mean	(68.24, 73.74)	(70.64, 76.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.34 (-1.51, 6.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Absolute Change at Week 24 (MMRM)		
n	190	199
LS mean (SE)	0.82 (1.05)	1.75 (1.03)
95% CI of LS mean	(-1.25, 2.89)	(-0.27, 3.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-1.97, 3.82)
Week 52		
n	194	196
Mean (SD)	73.14 (19.74)	75.85 (19.20)
Absolute Change at Week 52		
n	189	193
Mean (SD)	2.94 (16.82)	4.26 (15.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Week 52 (MMRM)		
n	192	195
LS mean (SE)	73.16 (1.38)	75.66 (1.36)
95% CI of LS mean	(70.44, 75.88)	(72.98, 78.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.50 (-1.32, 6.32)
Absolute Change at Week 52 (MMRM)		
n	187	192
LS mean (SE)	3.11 (1.16)	4.10 (1.15)
95% CI of LS mean	(0.82, 5.40)	(1.85, 6.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.99 (-2.22, 4.20)
Absolute Change through Week 52 (MMRM)		
n	193	202
LS mean (SE)	1.97 (0.90)	2.46 (0.88)
95% CI of LS mean	(0.20, 3.73)	(0.73, 4.18)
P-value within Treatment	0.0291	0.0054
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-1.98, 2.96)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6978

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202	VNZ/TEZ/D-IVA N = 210
Hedges' G (SE)		0.04 (0.10)
Hedges' 95% CI		(-0.16, 0.24)
Hedges' P-value		0.6977

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Baseline		
n	140	146
Mean (SD)	71.90 (19.52)	72.75 (19.97)
Week 8 (MMRM)		
n	134	143
LS mean (SE)	72.65 (1.72)	75.41 (1.66)
95% CI of LS mean	(69.27, 76.02)	(72.14, 78.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.76 (-1.97, 7.49)
Absolute Change at Week 8 (MMRM)		
n	130	141
LS mean (SE)	1.57 (1.21)	2.54 (1.17)
95% CI of LS mean	(-0.82, 3.96)	(0.24, 4.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-2.36, 4.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 16 (MMRM)		
n	130	139
LS mean (SE)	74.59 (1.75)	74.95 (1.69)
95% CI of LS mean	(71.15, 78.03)	(71.62, 78.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-4.46, 5.18)
Absolute Change at Week 16 (MMRM)		
n	126	137
LS mean (SE)	3.46 (1.13)	2.18 (1.09)
95% CI of LS mean	(1.24, 5.69)	(0.03, 4.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.29 (-4.39, 1.82)
Week 24 (MMRM)		
n	133	140
LS mean (SE)	73.04 (1.76)	75.54 (1.71)
95% CI of LS mean	(69.57, 76.50)	(72.18, 78.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.51 (-2.36, 7.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Absolute Change at Week 24 (MMRM)		
n	129	137
LS mean (SE)	2.31 (1.28)	2.64 (1.24)
95% CI of LS mean	(-0.20, 4.83)	(0.21, 5.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-3.18, 3.85)
Week 52		
n	139	143
Mean (SD)	76.50 (19.80)	77.23 (20.27)
Absolute Change at Week 52		
n	135	140
Mean (SD)	4.77 (16.49)	4.84 (14.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Week 52 (MMRM)		
n	132	139
LS mean (SE)	75.90 (1.74)	77.38 (1.69)
95% CI of LS mean	(72.47, 79.34)	(74.04, 80.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.47 (-3.34, 6.29)
Absolute Change at Week 52 (MMRM)		
n	128	136
LS mean (SE)	5.00 (1.39)	4.56 (1.35)
95% CI of LS mean	(2.26, 7.74)	(1.91, 7.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-4.26, 3.39)
Absolute Change through Week 52 (MMRM)		
n	130	139
LS mean (SE)	3.59 (1.05)	3.13 (1.01)
95% CI of LS mean	(1.53, 5.66)	(1.13, 5.12)
P-value within Treatment	0.0007	0.0023
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-3.35, 2.42)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7524

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 144	VNZ/TEZ/D-IVA N = 149
Hedges' G (SE)		-0.04 (0.12)
Hedges' 95% CI		(-0.28, 0.20)
Hedges' P-value		0.7511

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Baseline		
n	142	134
Mean (SD)	68.78 (19.89)	70.48 (18.03)
Week 8 (MMRM)		
n	143	130
LS mean (SE)	69.12 (1.68)	71.10 (1.75)
95% CI of LS mean	(65.81, 72.43)	(67.65, 74.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.98 (-2.83, 6.79)
Absolute Change at Week 8 (MMRM)		
n	140	129
LS mean (SE)	0.15 (1.19)	0.90 (1.23)
95% CI of LS mean	(-2.19, 2.48)	(-1.52, 3.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-2.63, 4.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 16 (MMRM)		
n	143	129
LS mean (SE)	69.39 (1.61)	71.41 (1.69)
95% CI of LS mean	(66.21, 72.57)	(68.09, 74.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.02 (-2.61, 6.65)
Absolute Change at Week 16 (MMRM)		
n	140	128
LS mean (SE)	0.62 (1.34)	1.15 (1.39)
95% CI of LS mean	(-2.01, 3.26)	(-1.60, 3.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-3.30, 4.34)
Week 24 (MMRM)		
n	141	125
LS mean (SE)	68.68 (1.66)	71.40 (1.74)
95% CI of LS mean	(65.40, 71.95)	(67.97, 74.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.72 (-2.05, 7.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Absolute Change at Week 24 (MMRM)		
n	138	125
LS mean (SE)	-0.35 (1.26)	1.25 (1.31)
95% CI of LS mean	(-2.83, 2.13)	(-1.34, 3.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.60 (-2.00, 5.20)
Week 52		
n	138	122
Mean (SD)	70.45 (19.66)	74.41 (18.12)
Absolute Change at Week 52		
n	135	121
Mean (SD)	1.98 (16.62)	3.86 (16.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Week 52 (MMRM)		
n	137	120
LS mean (SE)	71.08 (1.59)	73.77 (1.68)
95% CI of LS mean	(67.94, 74.21)	(70.47, 77.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.69 (-1.89, 7.27)
Absolute Change at Week 52 (MMRM)		
n	134	119
LS mean (SE)	2.11 (1.41)	3.55 (1.48)
95% CI of LS mean	(-0.66, 4.88)	(0.64, 6.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.44 (-2.59, 5.48)
Absolute Change through Week 52 (MMRM)		
n	140	129
LS mean (SE)	0.79 (1.15)	1.98 (1.20)
95% CI of LS mean	(-1.47, 3.06)	(-0.37, 4.34)
P-value within Treatment	0.4899	0.0990
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.19 (-2.10, 4.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4776

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 145	VNZ/TEZ/D-IVA N = 135
Hedges' G (SE)		0.09 (0.12)
Hedges' 95% CI		(-0.15, 0.33)
Hedges' P-value		0.4752

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Baseline		
n	102	111
Mean (SD)	70.92 (19.59)	72.37 (18.22)
Week 8 (MMRM)		
n	98	112
LS mean (SE)	70.52 (2.10)	73.42 (1.97)
95% CI of LS mean	(66.37, 74.66)	(69.54, 77.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.90 (-2.79, 8.58)
Absolute Change at Week 8 (MMRM)		
n	97	109
LS mean (SE)	-0.01 (1.15)	0.85 (1.08)
95% CI of LS mean	(-2.27, 2.24)	(-1.28, 2.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-2.25, 3.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 16 (MMRM)		
n	96	108
LS mean (SE)	70.36 (2.04)	73.17 (1.91)
95% CI of LS mean	(66.35, 74.38)	(69.41, 76.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.81 (-2.70, 8.32)
Absolute Change at Week 16 (MMRM)		
n	95	105
LS mean (SE)	0.00 (1.13)	0.49 (1.07)
95% CI of LS mean	(-2.23, 2.23)	(-1.63, 2.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-2.59, 3.57)
Week 24 (MMRM)		
n	98	108
LS mean (SE)	70.70 (2.03)	73.54 (1.91)
95% CI of LS mean	(66.70, 74.70)	(69.77, 77.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-2.67, 8.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Absolute Change at Week 24 (MMRM)		
n	97	106
LS mean (SE)	0.42 (1.38)	0.73 (1.32)
95% CI of LS mean	(-2.30, 3.13)	(-1.86, 3.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-3.45, 4.07)
Week 52		
n	101	104
Mean (SD)	70.63 (21.12)	76.28 (18.90)
Absolute Change at Week 52		
n	100	101
Mean (SD)	0.11 (17.41)	3.52 (13.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Week 52 (MMRM)		
n	97	104
LS mean (SE)	70.63 (2.02)	76.22 (1.92)
95% CI of LS mean	(66.65, 74.61)	(72.44, 80.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.59 (0.09, 11.09)
Absolute Change at Week 52 (MMRM)		
n	96	101
LS mean (SE)	0.54 (1.58)	3.62 (1.53)
95% CI of LS mean	(-2.59, 3.66)	(0.60, 6.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.08 (-1.27, 7.43)
Absolute Change through Week 52 (MMRM)		
n	98	107
LS mean (SE)	0.32 (1.12)	1.61 (1.07)
95% CI of LS mean	(-1.88, 2.52)	(-0.49, 3.72)
P-value within Treatment	0.7764	0.1322
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.30 (-1.75, 4.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4029

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 103	VNZ/TEZ/D-IVA N = 114
Hedges' G (SE)		0.12 (0.14)
Hedges' 95% CI		(-0.16, 0.39)
Hedges' P-value		0.4026

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Baseline		
n	180	169
Mean (SD)	70.00 (19.86)	71.20 (19.64)
Week 8 (MMRM)		
n	179	161
LS mean (SE)	70.77 (1.46)	73.59 (1.53)
95% CI of LS mean	(67.91, 73.64)	(70.58, 76.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.82 (-1.34, 6.98)
Absolute Change at Week 8 (MMRM)		
n	173	161
LS mean (SE)	1.25 (1.16)	2.39 (1.20)
95% CI of LS mean	(-1.02, 3.53)	(0.03, 4.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-2.14, 4.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 16 (MMRM)		
n	177	160
LS mean (SE)	72.50 (1.46)	73.61 (1.53)
95% CI of LS mean	(69.64, 75.37)	(70.60, 76.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.11 (-3.05, 5.27)
Absolute Change at Week 16 (MMRM)		
n	171	160
LS mean (SE)	3.04 (1.22)	2.43 (1.26)
95% CI of LS mean	(0.64, 5.45)	(-0.05, 4.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.61 (-4.08, 2.85)
Week 24 (MMRM)		
n	176	157
LS mean (SE)	70.58 (1.52)	73.88 (1.60)
95% CI of LS mean	(67.59, 73.58)	(70.73, 77.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.30 (-1.06, 7.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Absolute Change at Week 24 (MMRM)		
n	170	156
LS mean (SE)	1.19 (1.17)	2.83 (1.21)
95% CI of LS mean	(-1.10, 3.49)	(0.44, 5.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-1.68, 4.95)
Week 52		
n	176	161
Mean (SD)	75.13 (19.08)	75.71 (19.65)
Absolute Change at Week 52		
n	170	160
Mean (SD)	5.29 (15.82)	4.93 (16.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Week 52 (MMRM)		
n	172	155
LS mean (SE)	74.76 (1.45)	75.55 (1.52)
95% CI of LS mean	(71.91, 77.61)	(72.55, 78.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.79 (-3.35, 4.93)
Absolute Change at Week 52 (MMRM)		
n	166	154
LS mean (SE)	5.21 (1.25)	4.41 (1.30)
95% CI of LS mean	(2.74, 7.67)	(1.85, 6.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.80 (-4.35, 2.75)
Absolute Change through Week 52 (MMRM)		
n	172	161
LS mean (SE)	3.15 (1.04)	3.22 (1.08)
95% CI of LS mean	(1.10, 5.20)	(1.10, 5.35)
P-value within Treatment	0.0027	0.0030
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-2.88, 3.03)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9609
Hedges' G (SE)		0.01 (0.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 186	VNZ/TEZ/D-IVA N = 170
Hedges' 95% CI		(-0.21, 0.22)
Hedges' P-value		0.9608

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Baseline		
n	163	152
Mean (SD)	67.96 (19.85)	70.94 (19.26)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	67.64 (1.59)	69.57 (1.63)
95% CI of LS mean	(64.50, 70.77)	(66.35, 72.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.93 (-2.56, 6.43)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	0.12 (1.18)	-1.20 (1.20)
95% CI of LS mean	(-2.19, 2.44)	(-3.57, 1.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.32 (-4.64, 1.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Week 16 (MMRM)		
n	158	148
LS mean (SE)	67.87 (1.58)	69.43 (1.63)
95% CI of LS mean	(64.75, 70.98)	(66.22, 72.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.57 (-2.91, 6.05)
Absolute Change at Week 16 (MMRM)		
n	155	146
LS mean (SE)	0.65 (1.22)	-1.35 (1.26)
95% CI of LS mean	(-1.75, 3.06)	(-3.83, 1.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.01 (-5.46, 1.45)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	65.89 (1.72)	69.76 (1.77)
95% CI of LS mean	(62.51, 69.27)	(66.29, 73.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.88 (-0.97, 8.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	-1.38 (1.35)	-0.92 (1.38)
95% CI of LS mean	(-4.03, 1.27)	(-3.63, 1.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.47 (-3.33, 4.26)
Week 52		
n	159	145
Mean (SD)	69.95 (19.83)	71.19 (19.27)
Absolute Change at Week 52		
n	156	143
Mean (SD)	2.21 (16.62)	0.51 (14.32)
Week 52 (MMRM)		
n	155	144
LS mean (SE)	69.64 (1.54)	70.80 (1.59)
95% CI of LS mean	(66.60, 72.68)	(67.67, 73.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-3.21, 5.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	2.15 (1.26)	0.16 (1.30)
95% CI of LS mean	(-0.33, 4.63)	(-2.39, 2.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.99 (-5.55, 1.57)
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	0.47 (1.03)	-0.70 (1.06)
95% CI of LS mean	(-1.55, 2.50)	(-2.78, 1.38)
P-value within Treatment	0.6458	0.5074
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.18 (-4.08, 1.73)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4268
Hedges' G (SE)		-0.09 (0.11)
Hedges' 95% CI		(-0.32, 0.13)
Hedges' P-value		0.4266

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Baseline		
n	103	109
Mean (SD)	76.91 (18.19)	75.94 (20.65)
Week 8 (MMRM)		
n	106	107
LS mean (SE)	77.07 (1.77)	75.12 (1.75)
95% CI of LS mean	(73.58, 80.56)	(71.67, 78.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.95 (-6.88, 2.98)
Absolute Change at Week 8 (MMRM)		
n	103	106
LS mean (SE)	-0.27 (1.42)	-0.77 (1.39)
95% CI of LS mean	(-3.06, 2.52)	(-3.51, 1.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-4.43, 3.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Week 16 (MMRM)		
n	105	106
LS mean (SE)	76.11 (1.79)	75.47 (1.77)
95% CI of LS mean	(72.57, 79.64)	(71.98, 78.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.63 (-5.63, 4.36)
Absolute Change at Week 16 (MMRM)		
n	102	105
LS mean (SE)	-0.95 (1.50)	-0.50 (1.47)
95% CI of LS mean	(-3.91, 2.01)	(-3.40, 2.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-3.71, 4.61)
Week 24 (MMRM)		
n	106	104
LS mean (SE)	75.39 (1.84)	75.33 (1.84)
95% CI of LS mean	(71.76, 79.03)	(71.71, 78.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.06 (-5.21, 5.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Absolute Change at Week 24 (MMRM)		
n	103	104
LS mean (SE)	-1.67 (1.55)	-0.79 (1.53)
95% CI of LS mean	(-4.73, 1.38)	(-3.81, 2.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.89 (-3.42, 5.19)
Week 52		
n	104	102
Mean (SD)	80.02 (17.34)	76.36 (19.70)
Absolute Change at Week 52		
n	101	101
Mean (SD)	2.64 (14.75)	0.00 (15.63)
Week 52 (MMRM)		
n	104	101
LS mean (SE)	79.68 (1.83)	76.29 (1.83)
95% CI of LS mean	(76.08, 83.29)	(72.68, 79.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.39 (-8.51, 1.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Absolute Change at Week 52 (MMRM)		
n	101	100
LS mean (SE)	2.45 (1.53)	0.21 (1.53)
95% CI of LS mean	(-0.57, 5.47)	(-2.80, 3.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.24 (-6.51, 2.03)
Absolute Change through Week 52 (MMRM)		
n	103	106
LS mean (SE)	-0.06 (1.24)	-0.36 (1.22)
95% CI of LS mean	(-2.51, 2.39)	(-2.77, 2.05)
P-value within Treatment	0.9624	0.7698
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-3.75, 3.15)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8641
Hedges' G (SE)		-0.02 (0.14)
Hedges' 95% CI		(-0.30, 0.25)
Hedges' P-value		0.8636

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Baseline		
n	24	26
Mean (SD)	82.87 (17.02)	76.92 (25.71)
Week 8 (MMRM)		
n	24	23
LS mean (SE)	81.59 (4.61)	78.52 (4.57)
95% CI of LS mean	(72.28, 90.90)	(69.29, 87.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.07 (-16.37, 10.23)
Absolute Change at Week 8 (MMRM)		
n	24	23
LS mean (SE)	-0.96 (4.05)	0.78 (4.02)
95% CI of LS mean	(-9.17, 7.25)	(-7.37, 8.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-9.93, 13.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Week 16 (MMRM)		
n	22	23
LS mean (SE)	81.84 (4.67)	78.03 (4.57)
95% CI of LS mean	(72.36, 91.31)	(68.75, 87.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.81 (-17.25, 9.63)
Absolute Change at Week 16 (MMRM)		
n	22	23
LS mean (SE)	-0.32 (4.07)	-1.00 (3.99)
95% CI of LS mean	(-8.65, 8.00)	(-9.14, 7.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-12.43, 11.09)
Week 24 (MMRM)		
n	22	22
LS mean (SE)	81.26 (3.59)	80.83 (3.54)
95% CI of LS mean	(73.93, 88.60)	(73.60, 88.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-10.96, 10.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 24 (MMRM)		
n	22	22
LS mean (SE)	-1.19 (3.50)	-0.06 (3.47)
95% CI of LS mean	(-8.38, 6.00)	(-7.17, 7.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.13 (-9.11, 11.36)
Week 52		
n	22	21
Mean (SD)	87.88 (15.30)	77.78 (19.25)
Absolute Change at Week 52		
n	22	21
Mean (SD)	4.55 (10.66)	-5.82 (18.80)
Week 52 (MMRM)		
n	22	21
LS mean (SE)	85.15 (3.99)	77.26 (4.08)
95% CI of LS mean	(76.98, 93.32)	(68.95, 85.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.89 (-19.75, 3.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	22	21
LS mean (SE)	4.72 (3.14)	-5.10 (3.28)
95% CI of LS mean	(-1.68, 11.11)	(-11.76, 1.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.81 (-19.22, -0.41)
Absolute Change through Week 52 (MMRM)		
n	22	24
LS mean (SE)	1.07 (2.77)	-2.05 (2.76)
95% CI of LS mean	(-4.60, 6.74)	(-7.68, 3.58)
P-value within Treatment	0.7022	0.4626
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.12 (-11.28, 5.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4410
Hedges' G (SE)		-0.23 (0.29)
Hedges' 95% CI		(-0.82, 0.36)
Hedges' P-value		0.4311

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	70.34 (19.53)	72.34 (19.36)
Week 8 (MMRM)		
n	243	237
LS mean (SE)	70.27 (1.24)	71.37 (1.25)
95% CI of LS mean	(67.84, 72.69)	(68.91, 73.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.10 (-2.36, 4.56)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	0.06 (0.92)	-1.03 (0.93)
95% CI of LS mean	(-1.75, 1.87)	(-2.85, 0.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.09 (-3.66, 1.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 16 (MMRM)		
n	241	231
LS mean (SE)	69.94 (1.23)	71.39 (1.25)
95% CI of LS mean	(67.52, 72.36)	(68.93, 73.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-2.01, 4.91)
Absolute Change at Week 16 (MMRM)		
n	235	228
LS mean (SE)	-0.04 (0.97)	-0.99 (0.99)
95% CI of LS mean	(-1.95, 1.87)	(-2.93, 0.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-3.68, 1.77)
Week 24 (MMRM)		
n	240	229
LS mean (SE)	68.49 (1.34)	71.33 (1.37)
95% CI of LS mean	(65.86, 71.13)	(68.64, 74.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-0.93, 6.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 24 (MMRM)		
n	234	227
LS mean (SE)	-1.53 (1.07)	-0.95 (1.08)
95% CI of LS mean	(-3.63, 0.56)	(-3.08, 1.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-2.41, 3.58)
Week 52		
n	244	230
Mean (SD)	72.72 (19.32)	73.00 (19.68)
Absolute Change at Week 52		
n	238	227
Mean (SD)	2.19 (16.23)	1.05 (14.32)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	72.52 (1.24)	72.84 (1.27)
95% CI of LS mean	(70.08, 74.95)	(70.36, 75.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.33 (-3.16, 3.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	2.28 (1.01)	0.67 (1.03)
95% CI of LS mean	(0.30, 4.27)	(-1.35, 2.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.62 (-4.45, 1.22)
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	0.24 (0.82)	-0.43 (0.83)
95% CI of LS mean	(-1.38, 1.85)	(-2.07, 1.21)
P-value within Treatment	0.7743	0.6103
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.66 (-2.97, 1.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5732
Hedges' G (SE)		-0.05 (0.09)
Hedges' 95% CI		(-0.23, 0.13)
Hedges' P-value		0.5728

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Baseline		
n	77	70
Mean (SD)	69.55 (20.97)	74.76 (20.80)
Week 8 (MMRM)		
n	78	67
LS mean (SE)	70.83 (2.26)	72.24 (2.43)
95% CI of LS mean	(66.36, 75.29)	(67.44, 77.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.41 (-5.16, 7.98)
Absolute Change at Week 8 (MMRM)		
n	76	66
LS mean (SE)	0.45 (1.55)	-1.99 (1.65)
95% CI of LS mean	(-2.61, 3.50)	(-5.26, 1.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.43 (-6.93, 2.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Week 16 (MMRM)		
n	77	66
LS mean (SE)	69.23 (2.41)	69.44 (2.59)
95% CI of LS mean	(64.46, 73.99)	(64.31, 74.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.21 (-6.80, 7.22)
Absolute Change at Week 16 (MMRM)		
n	75	65
LS mean (SE)	-0.77 (1.90)	-4.96 (2.04)
95% CI of LS mean	(-4.53, 2.99)	(-9.00, -0.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.19 (-9.72, 1.34)
Week 24 (MMRM)		
n	78	62
LS mean (SE)	67.77 (2.42)	72.97 (2.64)
95% CI of LS mean	(62.98, 72.55)	(67.75, 78.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.20 (-1.89, 12.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Absolute Change at Week 24 (MMRM)		
n	76	62
LS mean (SE)	-2.41 (1.67)	-1.44 (1.82)
95% CI of LS mean	(-5.70, 0.89)	(-5.05, 2.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-3.93, 5.87)
Week 52		
n	77	66
Mean (SD)	72.29 (20.28)	73.40 (22.21)
Absolute Change at Week 52		
n	75	65
Mean (SD)	2.52 (12.99)	-1.37 (16.26)
Week 52 (MMRM)		
n	76	63
LS mean (SE)	72.49 (2.42)	72.35 (2.63)
95% CI of LS mean	(67.70, 77.28)	(67.16, 77.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-7.22, 6.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Absolute Change at Week 52 (MMRM)		
n	74	62
LS mean (SE)	2.27 (1.69)	-1.84 (1.84)
95% CI of LS mean	(-1.08, 5.62)	(-5.49, 1.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.12 (-9.08, 0.85)
Absolute Change through Week 52 (MMRM)		
n	76	65
LS mean (SE)	-0.30 (1.37)	-2.75 (1.48)
95% CI of LS mean	(-3.01, 2.41)	(-5.67, 0.18)
P-value within Treatment	0.8266	0.0652
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.45 (-6.45, 1.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2284
Hedges' G (SE)		-0.20 (0.17)
Hedges' 95% CI		(-0.54, 0.13)
Hedges' P-value		0.2278

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Baseline		
n	187	194
Mean (SD)	71.95 (19.01)	72.02 (19.85)
Week 8 (MMRM)		
n	189	193
LS mean (SE)	71.61 (1.41)	71.75 (1.39)
95% CI of LS mean	(68.84, 74.38)	(69.01, 74.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-3.76, 4.04)
Absolute Change at Week 8 (MMRM)		
n	185	191
LS mean (SE)	-0.22 (1.11)	-0.68 (1.09)
95% CI of LS mean	(-2.40, 1.96)	(-2.82, 1.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-3.51, 2.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Week 16 (MMRM)		
n	186	188
LS mean (SE)	71.94 (1.36)	72.82 (1.35)
95% CI of LS mean	(69.26, 74.62)	(70.17, 75.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-2.90, 4.66)
Absolute Change at Week 16 (MMRM)		
n	182	186
LS mean (SE)	0.34 (1.08)	0.39 (1.06)
95% CI of LS mean	(-1.78, 2.46)	(-1.70, 2.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.06 (-2.92, 3.04)
Week 24 (MMRM)		
n	184	189
LS mean (SE)	70.49 (1.49)	71.80 (1.47)
95% CI of LS mean	(67.56, 73.42)	(68.91, 74.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.31 (-2.81, 5.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 24 (MMRM)		
n	180	187
LS mean (SE)	-1.11 (1.25)	-0.64 (1.23)
95% CI of LS mean	(-3.57, 1.34)	(-3.05, 1.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.47 (-2.97, 3.91)
Week 52		
n	185	183
Mean (SD)	74.59 (19.00)	73.28 (18.71)
Absolute Change at Week 52		
n	181	181
Mean (SD)	2.58 (16.82)	1.07 (14.33)
Week 52 (MMRM)		
n	183	182
LS mean (SE)	74.13 (1.36)	73.38 (1.35)
95% CI of LS mean	(71.45, 76.81)	(70.71, 76.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.75 (-4.53, 3.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52 (MMRM)		
n	179	180
LS mean (SE)	2.29 (1.18)	0.95 (1.17)
95% CI of LS mean	(-0.03, 4.61)	(-1.35, 3.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.35 (-4.61, 1.92)
Absolute Change through Week 52 (MMRM)		
n	183	189
LS mean (SE)	0.51 (0.96)	0.23 (0.94)
95% CI of LS mean	(-1.38, 2.39)	(-1.62, 2.09)
P-value within Treatment	0.5978	0.8049
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.27 (-2.92, 2.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8396
Hedges' G (SE)		-0.02 (0.10)
Hedges' 95% CI		(-0.22, 0.18)
Hedges' P-value		0.8395

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Baseline		
n	133	141
Mean (SD)	72.10 (19.52)	74.59 (20.33)
Week 8 (MMRM)		
n	130	139
LS mean (SE)	70.16 (1.70)	74.35 (1.65)
95% CI of LS mean	(66.81, 73.52)	(71.10, 77.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.18 (-0.51, 8.88)
Absolute Change at Week 8 (MMRM)		
n	127	137
LS mean (SE)	-1.45 (1.27)	-0.81 (1.22)
95% CI of LS mean	(-3.95, 1.05)	(-3.21, 1.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-2.85, 4.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Week 16 (MMRM)		
n	126	134
LS mean (SE)	71.57 (1.67)	73.97 (1.61)
95% CI of LS mean	(68.29, 74.86)	(70.79, 77.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.39 (-2.20, 6.99)
Absolute Change at Week 16 (MMRM)		
n	123	132
LS mean (SE)	0.23 (1.37)	-1.13 (1.32)
95% CI of LS mean	(-2.46, 2.93)	(-3.74, 1.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.37 (-5.13, 2.40)
Week 24 (MMRM)		
n	127	134
LS mean (SE)	70.57 (1.76)	75.64 (1.71)
95% CI of LS mean	(67.10, 74.05)	(72.27, 79.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.06 (0.20, 9.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Absolute Change at Week 24 (MMRM)		
n	124	132
LS mean (SE)	-0.70 (1.49)	0.65 (1.44)
95% CI of LS mean	(-3.63, 2.24)	(-2.19, 3.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-2.75, 5.44)
Week 52		
n	132	137
Mean (SD)	73.57 (19.20)	75.02 (20.02)
Absolute Change at Week 52		
n	129	135
Mean (SD)	1.38 (17.01)	0.95 (14.69)
Week 52 (MMRM)		
n	126	133
LS mean (SE)	72.86 (1.74)	75.25 (1.69)
95% CI of LS mean	(69.43, 76.28)	(71.92, 78.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.39 (-2.41, 7.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Absolute Change at Week 52 (MMRM)		
n	123	131
LS mean (SE)	1.29 (1.45)	0.31 (1.41)
95% CI of LS mean	(-1.57, 4.16)	(-2.46, 3.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.98 (-4.98, 3.02)
Absolute Change through Week 52 (MMRM)		
n	125	134
LS mean (SE)	0.28 (1.21)	-0.06 (1.17)
95% CI of LS mean	(-2.10, 2.66)	(-2.35, 2.24)
P-value within Treatment	0.8183	0.9613
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-3.66, 2.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8432
Hedges' G (SE)		-0.02 (0.12)
Hedges' 95% CI		(-0.27, 0.22)
Hedges' P-value		0.8423

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Baseline		
n	136	125
Mean (SD)	70.83 (19.78)	70.76 (19.63)
Week 8 (MMRM)		
n	137	121
LS mean (SE)	72.79 (1.68)	68.76 (1.78)
95% CI of LS mean	(69.47, 76.10)	(65.26, 72.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.02 (-8.88, 0.84)
Absolute Change at Week 8 (MMRM)		
n	134	120
LS mean (SE)	1.44 (1.29)	-1.45 (1.36)
95% CI of LS mean	(-1.11, 3.99)	(-4.13, 1.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.89 (-6.61, 0.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Week 16 (MMRM)		
n	137	120
LS mean (SE)	71.00 (1.71)	69.36 (1.81)
95% CI of LS mean	(67.64, 74.37)	(65.79, 72.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.64 (-6.58, 3.29)
Absolute Change at Week 16 (MMRM)		
n	134	119
LS mean (SE)	-0.13 (1.32)	-1.03 (1.40)
95% CI of LS mean	(-2.74, 2.47)	(-3.78, 1.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.90 (-4.70, 2.91)
Week 24 (MMRM)		
n	135	117
LS mean (SE)	69.12 (1.82)	67.73 (1.94)
95% CI of LS mean	(65.54, 72.70)	(63.91, 71.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.40 (-6.66, 3.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Absolute Change at Week 24 (MMRM)		
n	132	117
LS mean (SE)	-2.16 (1.39)	-2.76 (1.47)
95% CI of LS mean	(-4.90, 0.58)	(-5.66, 0.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.60 (-4.60, 3.41)
Week 52		
n	134	114
Mean (SD)	74.38 (19.76)	71.44 (19.10)
Absolute Change at Week 52		
n	131	113
Mean (SD)	3.39 (14.58)	-0.10 (15.03)
Week 52 (MMRM)		
n	133	112
LS mean (SE)	74.64 (1.64)	70.43 (1.75)
95% CI of LS mean	(71.42, 77.86)	(66.98, 73.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.21 (-8.96, 0.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Absolute Change at Week 52 (MMRM)		
n	130	111
LS mean (SE)	3.28 (1.30)	-0.03 (1.40)
95% CI of LS mean	(0.71, 5.85)	(-2.79, 2.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.31 (-7.09, 0.47)
Absolute Change through Week 52 (MMRM)		
n	134	120
LS mean (SE)	0.33 (1.04)	-1.27 (1.10)
95% CI of LS mean	(-1.72, 2.38)	(-3.45, 0.90)
P-value within Treatment	0.7526	0.2490
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.60 (-4.61, 1.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2949
Hedges' G (SE)		-0.13 (0.13)
Hedges' 95% CI		(-0.38, 0.11)
Hedges' P-value		0.2924

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Baseline		
n	99	108
Mean (SD)	73.96 (19.52)	76.34 (19.52)
Week 8 (MMRM)		
n	96	109
LS mean (SE)	70.36 (1.89)	75.06 (1.76)
95% CI of LS mean	(66.64, 74.08)	(71.58, 78.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.70 (-0.40, 9.80)
Absolute Change at Week 8 (MMRM)		
n	95	106
LS mean (SE)	-2.96 (1.39)	-1.51 (1.31)
95% CI of LS mean	(-5.70, -0.23)	(-4.10, 1.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-2.32, 5.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Week 16 (MMRM)		
n	94	105
LS mean (SE)	73.18 (1.78)	77.01 (1.68)
95% CI of LS mean	(69.66, 76.69)	(73.71, 80.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.84 (-1.00, 8.67)
Absolute Change at Week 16 (MMRM)		
n	93	102
LS mean (SE)	-0.24 (1.28)	0.50 (1.22)
95% CI of LS mean	(-2.76, 2.28)	(-1.90, 2.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.73 (-2.75, 4.22)
Week 24 (MMRM)		
n	95	105
LS mean (SE)	69.69 (1.92)	76.89 (1.80)
95% CI of LS mean	(65.91, 73.46)	(73.33, 80.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.20 (2.01, 12.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Absolute Change at Week 24 (MMRM)		
n	94	103
LS mean (SE)	-3.54 (1.44)	0.52 (1.37)
95% CI of LS mean	(-6.38, -0.70)	(-2.18, 3.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.06 (0.14, 7.99)
Week 52		
n	98	101
Mean (SD)	75.06 (19.02)	75.36 (19.73)
Absolute Change at Week 52		
n	97	98
Mean (SD)	1.15 (14.39)	-0.68 (14.69)
Week 52 (MMRM)		
n	94	101
LS mean (SE)	74.43 (1.91)	75.58 (1.81)
95% CI of LS mean	(70.68, 78.19)	(72.01, 79.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-4.05, 6.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Absolute Change at Week 52 (MMRM)		
n	93	98
LS mean (SE)	1.04 (1.50)	-0.66 (1.45)
95% CI of LS mean	(-1.93, 4.00)	(-3.53, 2.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.70 (-5.83, 2.42)
Absolute Change through Week 52 (MMRM)		
n	95	104
LS mean (SE)	-0.91 (1.15)	0.12 (1.09)
95% CI of LS mean	(-3.17, 1.35)	(-2.04, 2.27)
P-value within Treatment	0.4268	0.9138
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.03 (-2.10, 4.16)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5166
Hedges' G (SE)		0.09 (0.14)
Hedges' 95% CI		(-0.19, 0.37)
Hedges' P-value		0.5161

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Baseline		
n	170	158
Mean (SD)	70.00 (19.60)	70.36 (20.12)
Week 8 (MMRM)		
n	171	151
LS mean (SE)	71.97 (1.53)	69.53 (1.63)
95% CI of LS mean	(68.95, 74.99)	(66.32, 72.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.44 (-6.85, 1.96)
Absolute Change at Week 8 (MMRM)		
n	166	151
LS mean (SE)	1.69 (1.17)	-0.76 (1.23)
95% CI of LS mean	(-0.61, 4.00)	(-3.17, 1.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.46 (-5.80, 0.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Week 16 (MMRM)		
n	169	149
LS mean (SE)	70.00 (1.56)	68.27 (1.65)
95% CI of LS mean	(66.93, 73.06)	(65.02, 71.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.73 (-6.20, 2.75)
Absolute Change at Week 16 (MMRM)		
n	164	149
LS mean (SE)	0.15 (1.31)	-2.10 (1.37)
95% CI of LS mean	(-2.42, 2.72)	(-4.80, 0.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.25 (-5.98, 1.48)
Week 24 (MMRM)		
n	167	146
LS mean (SE)	69.66 (1.67)	68.54 (1.78)
95% CI of LS mean	(66.37, 72.95)	(65.03, 72.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.13 (-5.94, 3.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Absolute Change at Week 24 (MMRM)		
n	162	146
LS mean (SE)	-0.29 (1.37)	-1.88 (1.44)
95% CI of LS mean	(-2.99, 2.41)	(-4.71, 0.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-5.50, 2.34)
Week 52		
n	168	150
Mean (SD)	73.35 (19.72)	72.07 (19.55)
Absolute Change at Week 52		
n	163	150
Mean (SD)	3.14 (16.63)	1.22 (14.91)
Week 52 (MMRM)		
n	165	144
LS mean (SE)	73.17 (1.53)	71.19 (1.63)
95% CI of LS mean	(70.16, 76.19)	(67.98, 74.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.98 (-6.39, 2.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Absolute Change at Week 52 (MMRM)		
n	160	144
LS mean (SE)	3.00 (1.27)	0.74 (1.33)
95% CI of LS mean	(0.51, 5.50)	(-1.88, 3.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.26 (-5.88, 1.35)
Absolute Change through Week 52 (MMRM)		
n	164	150
LS mean (SE)	0.95 (1.06)	-1.08 (1.11)
95% CI of LS mean	(-1.14, 3.04)	(-3.27, 1.11)
P-value within Treatment	0.3700	0.3331
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.03 (-5.07, 1.00)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1884
Hedges' G (SE)		-0.15 (0.11)
Hedges' 95% CI		(-0.37, 0.07)
Hedges' P-value		0.1880

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Baseline		
n	163	152
Mean (SD)	85.07 (16.65)	86.68 (17.27)
Week 8 (MMRM)		
n	161	151
LS mean (SE)	84.20 (1.34)	86.52 (1.38)
95% CI of LS mean	(81.56, 86.84)	(83.80, 89.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.32 (-1.47, 6.12)
Absolute Change at Week 8 (MMRM)		
n	158	149
LS mean (SE)	-1.02 (1.11)	-0.27 (1.14)
95% CI of LS mean	(-3.21, 1.16)	(-2.52, 1.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-2.38, 3.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Week 16 (MMRM)		
n	156	149
LS mean (SE)	84.88 (1.38)	85.91 (1.41)
95% CI of LS mean	(82.17, 87.59)	(83.14, 88.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-2.85, 4.92)
Absolute Change at Week 16 (MMRM)		
n	153	147
LS mean (SE)	-0.14 (1.16)	-0.67 (1.19)
95% CI of LS mean	(-2.43, 2.14)	(-3.00, 1.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.52 (-3.79, 2.75)
Week 24 (MMRM)		
n	156	147
LS mean (SE)	84.04 (1.49)	84.45 (1.53)
95% CI of LS mean	(81.11, 86.98)	(81.43, 87.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-3.80, 4.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 24 (MMRM)		
n	153	145
LS mean (SE)	-0.98 (1.32)	-2.13 (1.35)
95% CI of LS mean	(-3.56, 1.61)	(-4.79, 0.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.15 (-4.87, 2.56)
Week 52		
n	159	144
Mean (SD)	84.91 (18.54)	88.31 (15.05)
Absolute Change at Week 52		
n	156	142
Mean (SD)	0.27 (16.10)	1.00 (14.16)
Week 52 (MMRM)		
n	155	143
LS mean (SE)	85.09 (1.36)	87.95 (1.41)
95% CI of LS mean	(82.40, 87.77)	(85.17, 90.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.87 (-1.00, 6.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 52 (MMRM)		
n	152	141
LS mean (SE)	0.03 (1.25)	1.17 (1.29)
95% CI of LS mean	(-2.43, 2.50)	(-1.38, 3.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.14 (-2.41, 4.68)
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	-0.36 (0.99)	-0.54 (1.02)
95% CI of LS mean	(-2.31, 1.59)	(-2.54, 1.46)
P-value within Treatment	0.7148	0.5949
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-2.97, 2.62)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8999
Hedges' G (SE)		-0.01 (0.11)
Hedges' 95% CI		(-0.24, 0.21)
Hedges' P-value		0.8998

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Baseline		
n	103	109
Mean (SD)	88.92 (13.78)	86.77 (15.39)
Week 8 (MMRM)		
n	106	108
LS mean (SE)	89.82 (1.40)	88.62 (1.38)
95% CI of LS mean	(87.07, 92.57)	(85.90, 91.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.20 (-5.08, 2.68)
Absolute Change at Week 8 (MMRM)		
n	103	107
LS mean (SE)	1.04 (1.23)	1.83 (1.20)
95% CI of LS mean	(-1.38, 3.46)	(-0.54, 4.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.79 (-2.61, 4.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Week 16 (MMRM)		
n	105	106
LS mean (SE)	89.23 (1.45)	87.82 (1.44)
95% CI of LS mean	(86.38, 92.09)	(84.99, 90.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.41 (-5.45, 2.63)
Absolute Change at Week 16 (MMRM)		
n	102	105
LS mean (SE)	0.30 (1.27)	1.03 (1.24)
95% CI of LS mean	(-2.20, 2.80)	(-1.43, 3.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.73 (-2.78, 4.24)
Week 24 (MMRM)		
n	106	103
LS mean (SE)	88.95 (1.42)	88.96 (1.42)
95% CI of LS mean	(86.16, 91.75)	(86.16, 91.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.01 (-3.96, 3.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Absolute Change at Week 24 (MMRM)		
n	103	103
LS mean (SE)	0.07 (1.36)	2.09 (1.35)
95% CI of LS mean	(-2.62, 2.75)	(-0.57, 4.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.03 (-1.77, 5.82)
Week 52		
n	104	102
Mean (SD)	90.20 (14.24)	90.03 (12.41)
Absolute Change at Week 52		
n	101	101
Mean (SD)	1.05 (13.63)	2.89 (11.21)
Week 52 (MMRM)		
n	104	101
LS mean (SE)	90.24 (1.33)	89.78 (1.34)
95% CI of LS mean	(87.61, 92.87)	(87.14, 92.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.46 (-4.20, 3.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Absolute Change at Week 52 (MMRM)		
n	101	100
LS mean (SE)	1.07 (1.24)	2.97 (1.24)
95% CI of LS mean	(-1.38, 3.52)	(0.54, 5.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.90 (-1.56, 5.37)
Absolute Change through Week 52 (MMRM)		
n	103	106
LS mean (SE)	0.48 (1.07)	2.03 (1.06)
95% CI of LS mean	(-1.63, 2.59)	(-0.05, 4.11)
P-value within Treatment	0.6550	0.0557
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-1.42, 4.53)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3050
Hedges' G (SE)		0.14 (0.14)
Hedges' 95% CI		(-0.13, 0.41)
Hedges' P-value		0.3037

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Baseline		
n	24	26
Mean (SD)	91.32 (10.56)	83.97 (18.09)
Week 8 (MMRM)		
n	24	23
LS mean (SE)	93.21 (3.14)	89.78 (3.11)
95% CI of LS mean	(86.85, 99.57)	(83.51, 96.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.43 (-12.44, 5.59)
Absolute Change at Week 8 (MMRM)		
n	24	23
LS mean (SE)	2.64 (2.51)	3.84 (2.49)
95% CI of LS mean	(-2.52, 7.79)	(-1.26, 8.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.20 (-6.16, 8.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Week 16 (MMRM)		
n	22	23
LS mean (SE)	93.44 (3.12)	87.14 (3.05)
95% CI of LS mean	(87.11, 99.77)	(80.95, 93.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.30 (-15.22, 2.63)
Absolute Change at Week 16 (MMRM)		
n	22	23
LS mean (SE)	2.58 (3.08)	2.12 (3.01)
95% CI of LS mean	(-3.67, 8.83)	(-3.98, 8.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-9.28, 8.35)
Week 24 (MMRM)		
n	22	22
LS mean (SE)	90.76 (2.34)	90.03 (2.32)
95% CI of LS mean	(85.98, 95.55)	(85.30, 94.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-7.56, 6.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 24 (MMRM)		
n	22	22
LS mean (SE)	-0.70 (3.16)	3.34 (3.10)
95% CI of LS mean	(-7.08, 5.67)	(-2.92, 9.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.04 (-4.98, 13.05)
Week 52		
n	22	20
Mean (SD)	93.56 (7.24)	91.25 (9.92)
Absolute Change at Week 52		
n	22	20
Mean (SD)	1.52 (9.84)	1.67 (10.33)
Week 52 (MMRM)		
n	22	20
LS mean (SE)	93.31 (2.06)	90.02 (2.15)
95% CI of LS mean	(89.10, 97.53)	(85.64, 94.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.30 (-9.49, 2.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	22	20
LS mean (SE)	2.17 (2.23)	2.40 (2.31)
95% CI of LS mean	(-2.44, 6.77)	(-2.34, 7.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-6.49, 6.97)
Absolute Change through Week 52 (MMRM)		
n	22	24
LS mean (SE)	1.35 (2.46)	2.62 (2.41)
95% CI of LS mean	(-3.62, 6.32)	(-2.26, 7.49)
P-value within Treatment	0.5862	0.2840
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.27 (-5.81, 8.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7187
Hedges' G (SE)		0.11 (0.29)
Hedges' 95% CI		(-0.48, 0.69)
Hedges' P-value		0.7146

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	86.19 (15.98)	87.05 (16.22)
Week 8 (MMRM)		
n	243	236
LS mean (SE)	85.73 (1.03)	87.22 (1.05)
95% CI of LS mean	(83.70, 87.75)	(85.16, 89.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.49 (-1.40, 4.38)
Absolute Change at Week 8 (MMRM)		
n	237	233
LS mean (SE)	-0.41 (0.88)	0.22 (0.89)
95% CI of LS mean	(-2.15, 1.32)	(-1.53, 1.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-1.83, 3.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 16 (MMRM)		
n	239	232
LS mean (SE)	85.88 (1.07)	86.69 (1.08)
95% CI of LS mean	(83.78, 87.97)	(84.56, 88.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-2.17, 3.80)
Absolute Change at Week 16 (MMRM)		
n	233	229
LS mean (SE)	-0.21 (0.90)	-0.26 (0.91)
95% CI of LS mean	(-1.98, 1.56)	(-2.04, 1.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-2.56, 2.47)
Week 24 (MMRM)		
n	240	228
LS mean (SE)	85.55 (1.13)	86.06 (1.15)
95% CI of LS mean	(83.33, 87.76)	(83.80, 88.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.52 (-2.65, 3.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 24 (MMRM)		
n	234	226
LS mean (SE)	-0.50 (1.00)	-0.83 (1.02)
95% CI of LS mean	(-2.48, 1.47)	(-2.84, 1.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-3.14, 2.49)
Week 52		
n	244	230
Mean (SD)	86.57 (17.61)	88.77 (14.34)
Absolute Change at Week 52		
n	238	227
Mean (SD)	0.55 (15.49)	1.65 (13.56)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	86.53 (1.04)	88.65 (1.07)
95% CI of LS mean	(84.48, 88.58)	(86.55, 90.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-0.82, 5.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	0.33 (0.95)	1.78 (0.97)
95% CI of LS mean	(-1.54, 2.21)	(-0.13, 3.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.45 (-1.23, 4.12)
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	-0.13 (0.76)	0.23 (0.77)
95% CI of LS mean	(-1.63, 1.38)	(-1.29, 1.75)
P-value within Treatment	0.8680	0.7664
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-1.78, 2.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7432
Hedges' G (SE)		0.03 (0.09)
Hedges' 95% CI		(-0.15, 0.21)
Hedges' P-value		0.7429

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Baseline		
n	77	70
Mean (SD)	86.04 (15.08)	86.90 (17.70)
Week 8 (MMRM)		
n	78	67
LS mean (SE)	86.15 (1.92)	87.91 (2.06)
95% CI of LS mean	(82.36, 89.94)	(83.84, 91.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.75 (-3.82, 7.33)
Absolute Change at Week 8 (MMRM)		
n	76	66
LS mean (SE)	-0.05 (1.72)	1.30 (1.84)
95% CI of LS mean	(-3.45, 3.36)	(-2.34, 4.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-3.65, 6.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Week 16 (MMRM)		
n	76	66
LS mean (SE)	84.91 (2.06)	87.18 (2.21)
95% CI of LS mean	(80.84, 88.99)	(82.81, 91.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.27 (-3.72, 8.26)
Absolute Change at Week 16 (MMRM)		
n	74	65
LS mean (SE)	-0.87 (1.80)	0.84 (1.92)
95% CI of LS mean	(-4.44, 2.69)	(-2.97, 4.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-3.52, 6.93)
Week 24 (MMRM)		
n	78	62
LS mean (SE)	82.41 (2.16)	86.67 (2.39)
95% CI of LS mean	(78.14, 86.69)	(81.94, 91.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.26 (-2.13, 10.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Absolute Change at Week 24 (MMRM)		
n	76	62
LS mean (SE)	-3.67 (2.08)	0.36 (2.28)
95% CI of LS mean	(-7.78, 0.44)	(-4.15, 4.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.03 (-2.08, 10.14)
Week 52		
n	77	65
Mean (SD)	87.88 (15.62)	87.95 (16.27)
Absolute Change at Week 52		
n	75	64
Mean (SD)	1.78 (10.99)	0.13 (14.51)
Week 52 (MMRM)		
n	76	62
LS mean (SE)	88.01 (1.83)	88.09 (2.00)
95% CI of LS mean	(84.38, 91.64)	(84.13, 92.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.08 (-5.30, 5.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Absolute Change at Week 52 (MMRM)		
n	74	61
LS mean (SE)	1.76 (1.45)	1.48 (1.59)
95% CI of LS mean	(-1.11, 4.63)	(-1.66, 4.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.28 (-4.54, 3.99)
Absolute Change through Week 52 (MMRM)		
n	76	65
LS mean (SE)	-0.93 (1.40)	0.89 (1.52)
95% CI of LS mean	(-3.70, 1.85)	(-2.11, 3.89)
P-value within Treatment	0.5099	0.5570
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.82 (-2.28, 5.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3816
Hedges' G (SE)		0.15 (0.17)
Hedges' 95% CI		(-0.18, 0.48)
Hedges' P-value		0.3805

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Baseline		
n	187	194
Mean (SD)	87.03 (15.82)	86.60 (16.01)
Week 8 (MMRM)		
n	189	192
LS mean (SE)	86.53 (1.14)	87.23 (1.13)
95% CI of LS mean	(84.29, 88.77)	(85.01, 89.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.69 (-2.46, 3.85)
Absolute Change at Week 8 (MMRM)		
n	185	190
LS mean (SE)	-0.26 (0.94)	0.38 (0.93)
95% CI of LS mean	(-2.11, 1.60)	(-1.45, 2.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-1.98, 3.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Week 16 (MMRM)		
n	185	189
LS mean (SE)	87.28 (1.15)	86.55 (1.13)
95% CI of LS mean	(85.03, 89.54)	(84.32, 88.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-3.90, 2.44)
Absolute Change at Week 16 (MMRM)		
n	181	187
LS mean (SE)	0.37 (0.97)	-0.25 (0.96)
95% CI of LS mean	(-1.54, 2.29)	(-2.13, 1.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.62 (-3.31, 2.07)
Week 24 (MMRM)		
n	184	188
LS mean (SE)	87.49 (1.19)	86.21 (1.18)
95% CI of LS mean	(85.15, 89.83)	(83.89, 88.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.29 (-4.58, 2.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 24 (MMRM)		
n	180	186
LS mean (SE)	0.74 (1.03)	-0.61 (1.02)
95% CI of LS mean	(-1.29, 2.77)	(-2.61, 1.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.36 (-4.20, 1.49)
Week 52		
n	185	183
Mean (SD)	86.88 (17.62)	89.25 (13.24)
Absolute Change at Week 52		
n	181	181
Mean (SD)	0.08 (16.62)	2.21 (12.93)
Week 52 (MMRM)		
n	183	182
LS mean (SE)	86.73 (1.16)	88.92 (1.15)
95% CI of LS mean	(84.46, 89.01)	(86.66, 91.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-1.03, 5.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52 (MMRM)		
n	179	180
LS mean (SE)	-0.15 (1.10)	2.03 (1.09)
95% CI of LS mean	(-2.31, 2.02)	(-0.12, 4.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.18 (-0.87, 5.23)
Absolute Change through Week 52 (MMRM)		
n	183	189
LS mean (SE)	0.32 (0.85)	0.39 (0.83)
95% CI of LS mean	(-1.34, 1.99)	(-1.25, 2.03)
P-value within Treatment	0.7030	0.6399
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.07 (-2.27, 2.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9548
Hedges' G (SE)		0.01 (0.10)
Hedges' 95% CI		(-0.20, 0.21)
Hedges' P-value		0.9547

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Baseline		
n	133	141
Mean (SD)	88.16 (14.40)	89.07 (14.98)
Week 8 (MMRM)		
n	130	139
LS mean (SE)	86.69 (1.43)	89.09 (1.38)
95% CI of LS mean	(83.88, 89.50)	(86.37, 91.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.40 (-1.53, 6.32)
Absolute Change at Week 8 (MMRM)		
n	127	137
LS mean (SE)	-1.45 (1.19)	-0.03 (1.14)
95% CI of LS mean	(-3.79, 0.89)	(-2.29, 2.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-1.84, 4.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Week 16 (MMRM)		
n	125	135
LS mean (SE)	87.93 (1.31)	89.09 (1.26)
95% CI of LS mean	(85.35, 90.50)	(86.60, 91.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-2.45, 4.76)
Absolute Change at Week 16 (MMRM)		
n	122	133
LS mean (SE)	-0.04 (1.03)	0.08 (0.99)
95% CI of LS mean	(-2.08, 2.00)	(-1.87, 2.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-2.72, 2.96)
Week 24 (MMRM)		
n	127	134
LS mean (SE)	87.18 (1.45)	88.12 (1.41)
95% CI of LS mean	(84.33, 90.04)	(85.35, 90.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-3.07, 4.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Absolute Change at Week 24 (MMRM)		
n	124	132
LS mean (SE)	-0.82 (1.21)	-0.90 (1.17)
95% CI of LS mean	(-3.20, 1.56)	(-3.21, 1.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-3.41, 3.24)
Week 52		
n	132	137
Mean (SD)	87.67 (17.61)	90.45 (15.04)
Absolute Change at Week 52		
n	129	135
Mean (SD)	-0.34 (14.11)	1.54 (13.63)
Week 52 (MMRM)		
n	126	133
LS mean (SE)	87.27 (1.45)	90.47 (1.40)
95% CI of LS mean	(84.43, 90.12)	(87.71, 93.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.20 (-0.79, 7.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Male

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Absolute Change at Week 52 (MMRM)		
n	123	131
LS mean (SE)	-0.90 (1.25)	1.53 (1.21)
95% CI of LS mean	(-3.36, 1.55)	(-0.84, 3.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.43 (-0.99, 5.86)
Absolute Change through Week 52 (MMRM)		
n	125	134
LS mean (SE)	-0.59 (0.94)	0.24 (0.90)
95% CI of LS mean	(-2.43, 1.26)	(-1.54, 2.02)
P-value within Treatment	0.5314	0.7933
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.82 (-1.75, 3.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5298
Hedges' G (SE)		0.08 (0.12)
Hedges' 95% CI		(-0.17, 0.32)
Hedges' P-value		0.5275

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Baseline		
n	136	125
Mean (SD)	85.17 (16.66)	84.13 (17.56)
Week 8 (MMRM)		
n	137	120
LS mean (SE)	86.30 (1.36)	85.35 (1.45)
95% CI of LS mean	(83.61, 88.99)	(82.50, 88.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-4.89, 2.99)
Absolute Change at Week 8 (MMRM)		
n	134	119
LS mean (SE)	0.99 (1.16)	1.34 (1.23)
95% CI of LS mean	(-1.30, 3.28)	(-1.07, 3.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.35 (-2.99, 3.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Week 16 (MMRM)		
n	136	120
LS mean (SE)	85.54 (1.53)	83.87 (1.62)
95% CI of LS mean	(82.53, 88.55)	(80.68, 87.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.67 (-6.07, 2.74)
Absolute Change at Week 16 (MMRM)		
n	133	119
LS mean (SE)	0.10 (1.39)	-0.01 (1.46)
95% CI of LS mean	(-2.64, 2.83)	(-2.89, 2.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-4.10, 3.88)
Week 24 (MMRM)		
n	135	116
LS mean (SE)	84.99 (1.55)	84.14 (1.65)
95% CI of LS mean	(81.94, 88.03)	(80.89, 87.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.84 (-5.32, 3.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Absolute Change at Week 24 (MMRM)		
n	132	116
LS mean (SE)	-0.32 (1.50)	0.23 (1.59)
95% CI of LS mean	(-3.27, 2.63)	(-2.90, 3.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.55 (-3.76, 4.87)
Week 52		
n	134	113
Mean (SD)	86.63 (16.64)	87.17 (12.55)
Absolute Change at Week 52		
n	131	112
Mean (SD)	1.59 (15.98)	1.79 (12.97)
Week 52 (MMRM)		
n	133	111
LS mean (SE)	87.08 (1.32)	86.66 (1.42)
95% CI of LS mean	(84.48, 89.67)	(83.86, 89.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-4.25, 3.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Sex = Female

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Absolute Change at Week 52 (MMRM)		
n	130	110
LS mean (SE)	1.68 (1.29)	2.42 (1.38)
95% CI of LS mean	(-0.86, 4.22)	(-0.30, 5.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-3.00, 4.49)
Absolute Change through Week 52 (MMRM)		
n	134	120
LS mean (SE)	0.48 (1.13)	0.88 (1.20)
95% CI of LS mean	(-1.75, 2.72)	(-1.48, 3.24)
P-value within Treatment	0.6704	0.4633
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.40 (-2.87, 3.67)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8111
Hedges' G (SE)		0.03 (0.13)
Hedges' 95% CI		(-0.22, 0.28)
Hedges' P-value		0.8101

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Baseline		
n	99	108
Mean (SD)	87.63 (16.68)	90.43 (12.42)
Week 8 (MMRM)		
n	96	109
LS mean (SE)	85.68 (1.50)	89.97 (1.40)
95% CI of LS mean	(82.73, 88.63)	(87.21, 92.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.29 (0.25, 8.34)
Absolute Change at Week 8 (MMRM)		
n	95	106
LS mean (SE)	-1.54 (1.18)	-0.80 (1.12)
95% CI of LS mean	(-3.87, 0.80)	(-3.01, 1.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.74 (-2.48, 3.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Week 16 (MMRM)		
n	94	105
LS mean (SE)	86.77 (1.46)	90.36 (1.38)
95% CI of LS mean	(83.88, 89.65)	(87.65, 93.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (-0.37, 7.56)
Absolute Change at Week 16 (MMRM)		
n	93	102
LS mean (SE)	-0.52 (1.05)	-0.31 (1.00)
95% CI of LS mean	(-2.59, 1.55)	(-2.28, 1.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.21 (-2.65, 3.07)
Week 24 (MMRM)		
n	95	104
LS mean (SE)	87.53 (1.51)	89.31 (1.43)
95% CI of LS mean	(84.55, 90.51)	(86.50, 92.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.79 (-2.32, 5.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Absolute Change at Week 24 (MMRM)		
n	94	102
LS mean (SE)	0.34 (1.20)	-1.31 (1.14)
95% CI of LS mean	(-2.02, 2.70)	(-3.56, 0.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.65 (-4.91, 1.62)
Week 52		
n	98	101
Mean (SD)	87.22 (17.30)	90.43 (13.56)
Absolute Change at Week 52		
n	97	98
Mean (SD)	-0.03 (14.08)	0.09 (11.57)
Week 52 (MMRM)		
n	94	101
LS mean (SE)	86.94 (1.58)	90.69 (1.50)
95% CI of LS mean	(83.84, 90.05)	(87.74, 93.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.75 (-0.55, 8.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = North America

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Absolute Change at Week 52 (MMRM)		
n	93	98
LS mean (SE)	-0.23 (1.36)	0.22 (1.31)
95% CI of LS mean	(-2.90, 2.45)	(-2.37, 2.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-3.28, 4.17)
Absolute Change through Week 52 (MMRM)		
n	95	104
LS mean (SE)	-0.14 (0.99)	-0.47 (0.94)
95% CI of LS mean	(-2.09, 1.81)	(-2.33, 1.40)
P-value within Treatment	0.8907	0.6214
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-3.03, 2.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8093
Hedges' G (SE)		-0.03 (0.14)
Hedges' 95% CI		(-0.31, 0.24)
Hedges' P-value		0.8090

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Baseline		
n	170	158
Mean (SD)	86.08 (15.00)	84.23 (18.25)
Week 8 (MMRM)		
n	171	150
LS mean (SE)	86.80 (1.29)	85.59 (1.37)
95% CI of LS mean	(84.26, 89.33)	(82.89, 88.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.21 (-4.91, 2.50)
Absolute Change at Week 8 (MMRM)		
n	166	150
LS mean (SE)	0.55 (1.12)	1.58 (1.18)
95% CI of LS mean	(-1.66, 2.76)	(-0.73, 3.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.03 (-2.18, 4.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Week 16 (MMRM)		
n	167	150
LS mean (SE)	86.46 (1.35)	84.15 (1.43)
95% CI of LS mean	(83.80, 89.11)	(81.34, 86.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.31 (-6.18, 1.57)
Absolute Change at Week 16 (MMRM)		
n	162	150
LS mean (SE)	0.32 (1.23)	0.28 (1.28)
95% CI of LS mean	(-2.09, 2.74)	(-2.24, 2.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-3.54, 3.45)
Week 24 (MMRM)		
n	167	146
LS mean (SE)	85.05 (1.42)	84.25 (1.52)
95% CI of LS mean	(82.25, 87.86)	(81.26, 87.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.80 (-4.91, 3.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Absolute Change at Week 24 (MMRM)		
n	162	146
LS mean (SE)	-1.11 (1.36)	0.32 (1.43)
95% CI of LS mean	(-3.79, 1.56)	(-2.49, 3.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.43 (-2.45, 5.32)
Week 52		
n	168	149
Mean (SD)	87.10 (17.03)	87.98 (14.32)
Absolute Change at Week 52		
n	163	149
Mean (SD)	1.02 (15.68)	2.68 (14.28)
Week 52 (MMRM)		
n	165	143
LS mean (SE)	87.17 (1.24)	87.39 (1.32)
95% CI of LS mean	(84.73, 89.60)	(84.79, 90.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-3.34, 3.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Absolute Change at Week 52 (MMRM)		
n	160	143
LS mean (SE)	0.80 (1.18)	3.11 (1.25)
95% CI of LS mean	(-1.53, 3.12)	(0.66, 5.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.32 (-1.07, 5.70)
Absolute Change through Week 52 (MMRM)		
n	164	150
LS mean (SE)	0.00 (1.01)	1.24 (1.06)
95% CI of LS mean	(-1.99, 1.99)	(-0.85, 3.33)
P-value within Treatment	0.9975	0.2433
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-1.65, 4.13)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4003
Hedges' G (SE)		0.10 (0.11)
Hedges' 95% CI		(-0.13, 0.32)
Hedges' P-value		0.3996

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Baseline		
n	163	152
Mean (SD)	65.44 (19.43)	67.38 (19.28)
Week 8 (MMRM)		
n	161	153
LS mean (SE)	61.53 (1.69)	66.57 (1.73)
95% CI of LS mean	(58.21, 64.85)	(63.16, 69.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.03 (0.27, 9.79)
Absolute Change at Week 8 (MMRM)		
n	158	151
LS mean (SE)	-3.30 (1.35)	-0.75 (1.38)
95% CI of LS mean	(-5.95, -0.64)	(-3.46, 1.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.55 (-1.25, 6.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Week 16 (MMRM)		
n	158	149
LS mean (SE)	61.88 (1.65)	65.51 (1.70)
95% CI of LS mean	(58.63, 65.13)	(62.17, 68.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.63 (-1.03, 8.29)
Absolute Change at Week 16 (MMRM)		
n	155	147
LS mean (SE)	-2.77 (1.28)	-1.78 (1.31)
95% CI of LS mean	(-5.28, -0.25)	(-4.36, 0.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.99 (-2.62, 4.59)
Week 24 (MMRM)		
n	155	147
LS mean (SE)	59.96 (1.78)	65.23 (1.83)
95% CI of LS mean	(56.45, 63.46)	(61.63, 68.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.27 (0.24, 10.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 24 (MMRM)		
n	152	145
LS mean (SE)	-5.09 (1.41)	-1.94 (1.44)
95% CI of LS mean	(-7.86, -2.32)	(-4.78, 0.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.15 (-0.82, 7.12)
Week 52		
n	159	145
Mean (SD)	62.11 (21.33)	67.64 (19.46)
Absolute Change at Week 52		
n	156	143
Mean (SD)	-2.72 (16.40)	0.35 (14.76)
Week 52 (MMRM)		
n	155	144
LS mean (SE)	61.76 (1.60)	67.09 (1.65)
95% CI of LS mean	(58.60, 64.92)	(63.83, 70.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.32 (0.78, 9.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 52 (MMRM)		
n	152	142
LS mean (SE)	-3.09 (1.28)	0.05 (1.32)
95% CI of LS mean	(-5.60, -0.57)	(-2.55, 2.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.13 (-0.49, 6.75)
Absolute Change through Week 52 (MMRM)		
n	156	148
LS mean (SE)	-3.65 (1.05)	-1.22 (1.08)
95% CI of LS mean	(-5.72, -1.58)	(-3.35, 0.90)
P-value within Treatment	0.0006	0.2584
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.42 (-0.55, 5.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1095
Hedges' G (SE)		0.18 (0.11)
Hedges' 95% CI		(-0.04, 0.41)
Hedges' P-value		0.1099

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Baseline		
n	103	109
Mean (SD)	68.69 (18.54)	66.36 (18.56)
Week 8 (MMRM)		
n	105	108
LS mean (SE)	67.80 (1.85)	66.24 (1.83)
95% CI of LS mean	(64.14, 71.45)	(62.63, 69.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.56 (-6.71, 3.60)
Absolute Change at Week 8 (MMRM)		
n	103	107
LS mean (SE)	-0.87 (1.48)	-0.16 (1.45)
95% CI of LS mean	(-3.80, 2.05)	(-3.03, 2.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.71 (-3.40, 4.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Week 16 (MMRM)		
n	105	106
LS mean (SE)	66.89 (1.89)	65.70 (1.87)
95% CI of LS mean	(63.17, 70.61)	(62.02, 69.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.19 (-6.44, 4.07)
Absolute Change at Week 16 (MMRM)		
n	102	105
LS mean (SE)	-1.61 (1.48)	-0.66 (1.45)
95% CI of LS mean	(-4.52, 1.31)	(-3.53, 2.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.95 (-3.15, 5.05)
Week 24 (MMRM)		
n	106	104
LS mean (SE)	67.18 (1.77)	64.02 (1.77)
95% CI of LS mean	(63.69, 70.67)	(60.53, 67.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.17 (-8.12, 1.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Absolute Change at Week 24 (MMRM)		
n	103	104
LS mean (SE)	-1.60 (1.61)	-2.59 (1.60)
95% CI of LS mean	(-4.78, 1.58)	(-5.73, 0.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.99 (-5.48, 3.50)
Week 52		
n	104	102
Mean (SD)	68.99 (16.97)	67.32 (16.98)
Absolute Change at Week 52		
n	101	101
Mean (SD)	0.33 (15.76)	0.17 (15.41)
Week 52 (MMRM)		
n	104	101
LS mean (SE)	68.82 (1.68)	66.66 (1.69)
95% CI of LS mean	(65.50, 72.14)	(63.34, 69.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.16 (-6.88, 2.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Absolute Change at Week 52 (MMRM)		
n	101	100
LS mean (SE)	0.25 (1.57)	0.01 (1.56)
95% CI of LS mean	(-2.85, 3.34)	(-3.07, 3.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-4.61, 4.14)
Absolute Change through Week 52 (MMRM)		
n	103	106
LS mean (SE)	-0.99 (1.28)	-1.08 (1.26)
95% CI of LS mean	(-3.51, 1.54)	(-3.57, 1.41)
P-value within Treatment	0.4413	0.3927
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.09 (-3.65, 3.46)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9589
Hedges' G (SE)		-0.01 (0.14)
Hedges' 95% CI		(-0.28, 0.26)
Hedges' P-value		0.9588

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Baseline		
n	24	26
Mean (SD)	76.74 (18.87)	62.82 (22.01)
Week 8 (MMRM)		
n	24	24
LS mean (SE)	75.80 (4.08)	66.39 (4.02)
95% CI of LS mean	(67.54, 84.05)	(58.27, 74.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.41 (-21.19, 2.38)
Absolute Change at Week 8 (MMRM)		
n	24	24
LS mean (SE)	-1.44 (3.17)	3.97 (3.13)
95% CI of LS mean	(-7.83, 4.94)	(-2.34, 10.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.42 (-3.73, 14.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Week 16 (MMRM)		
n	22	23
LS mean (SE)	74.34 (4.11)	66.10 (4.03)
95% CI of LS mean	(66.05, 82.64)	(57.96, 74.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.24 (-20.07, 3.60)
Absolute Change at Week 16 (MMRM)		
n	22	23
LS mean (SE)	-2.13 (3.16)	3.60 (3.12)
95% CI of LS mean	(-8.52, 4.26)	(-2.70, 9.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.73 (-3.41, 14.88)
Week 24 (MMRM)		
n	22	22
LS mean (SE)	74.35 (3.70)	67.73 (3.66)
95% CI of LS mean	(66.85, 81.85)	(60.33, 75.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.62 (-17.37, 4.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 24 (MMRM)		
n	22	22
LS mean (SE)	-2.74 (3.40)	4.11 (3.37)
95% CI of LS mean	(-9.63, 4.15)	(-2.71, 10.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.85 (-2.99, 16.68)
Week 52		
n	22	21
Mean (SD)	75.38 (17.91)	71.83 (16.77)
Absolute Change at Week 52		
n	22	21
Mean (SD)	-0.38 (17.34)	3.57 (16.79)
Week 52 (MMRM)		
n	22	21
LS mean (SE)	74.40 (4.04)	67.73 (4.06)
95% CI of LS mean	(66.20, 82.61)	(59.52, 75.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.68 (-18.49, 5.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	22	21
LS mean (SE)	-2.62 (3.79)	4.37 (3.82)
95% CI of LS mean	(-10.33, 5.09)	(-3.36, 12.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.99 (-4.06, 18.04)
Absolute Change through Week 52 (MMRM)		
n	22	24
LS mean (SE)	-2.50 (2.91)	4.03 (2.88)
95% CI of LS mean	(-8.40, 3.40)	(-1.80, 9.86)
P-value within Treatment	0.3960	0.1699
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.52 (-1.95, 15.00)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1272
Hedges' G (SE)		0.46 (0.29)
Hedges' 95% CI		(-0.13, 1.05)
Hedges' P-value		0.1231

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	245	240
Mean (SD)	65.78 (18.81)	67.26 (18.53)
Week 8 (MMRM)		
n	242	237
LS mean (SE)	62.79 (1.31)	66.48 (1.33)
95% CI of LS mean	(60.21, 65.37)	(63.87, 69.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.69 (0.01, 7.36)
Absolute Change at Week 8 (MMRM)		
n	237	234
LS mean (SE)	-2.53 (1.06)	-0.90 (1.06)
95% CI of LS mean	(-4.61, -0.45)	(-2.99, 1.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-1.32, 4.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 16 (MMRM)		
n	241	232
LS mean (SE)	62.77 (1.30)	65.57 (1.32)
95% CI of LS mean	(60.21, 65.33)	(62.97, 68.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.80 (-0.85, 6.45)
Absolute Change at Week 16 (MMRM)		
n	235	229
LS mean (SE)	-2.46 (1.02)	-1.70 (1.03)
95% CI of LS mean	(-4.45, -0.46)	(-3.73, 0.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-2.09, 3.60)
Week 24 (MMRM)		
n	239	229
LS mean (SE)	61.65 (1.36)	64.45 (1.38)
95% CI of LS mean	(58.99, 64.31)	(61.74, 67.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.80 (-1.00, 6.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 24 (MMRM)		
n	233	227
LS mean (SE)	-3.96 (1.12)	-2.77 (1.13)
95% CI of LS mean	(-6.15, -1.76)	(-4.99, -0.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.19 (-1.94, 4.32)
Week 52		
n	244	230
Mean (SD)	64.00 (19.88)	67.28 (18.57)
Absolute Change at Week 52		
n	238	227
Mean (SD)	-1.58 (16.19)	0.26 (14.96)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	63.53 (1.23)	66.81 (1.26)
95% CI of LS mean	(61.11, 65.95)	(64.33, 69.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.27 (-0.19, 6.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 52 (MMRM)		
n	231	221
LS mean (SE)	-1.84 (1.03)	-0.31 (1.05)
95% CI of LS mean	(-3.86, 0.18)	(-2.37, 1.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-1.36, 4.41)
Absolute Change through Week 52 (MMRM)		
n	237	230
LS mean (SE)	-2.75 (0.85)	-1.59 (0.86)
95% CI of LS mean	(-4.41, -1.08)	(-3.28, 0.09)
P-value within Treatment	0.0013	0.0641
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.16 (-1.22, 3.53)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3388
Hedges' G (SE)		0.09 (0.09)
Hedges' 95% CI		(-0.09, 0.27)
Hedges' P-value		0.3384

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Baseline		
n	77	70
Mean (SD)	64.72 (19.21)	67.38 (20.94)
Week 8 (MMRM)		
n	78	68
LS mean (SE)	63.05 (2.17)	67.01 (2.33)
95% CI of LS mean	(58.76, 67.35)	(62.41, 71.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.96 (-2.35, 10.27)
Absolute Change at Week 8 (MMRM)		
n	76	67
LS mean (SE)	-1.76 (1.69)	-0.12 (1.80)
95% CI of LS mean	(-5.10, 1.58)	(-3.68, 3.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-3.26, 6.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Week 16 (MMRM)		
n	77	66
LS mean (SE)	62.78 (2.29)	63.86 (2.47)
95% CI of LS mean	(58.25, 67.32)	(58.98, 68.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.08 (-5.60, 7.76)
Absolute Change at Week 16 (MMRM)		
n	75	65
LS mean (SE)	-1.43 (1.72)	-3.21 (1.84)
95% CI of LS mean	(-4.83, 1.97)	(-6.85, 0.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.78 (-6.78, 3.22)
Week 24 (MMRM)		
n	77	62
LS mean (SE)	59.63 (2.43)	65.26 (2.66)
95% CI of LS mean	(54.82, 64.44)	(60.01, 70.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.63 (-1.50, 12.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Absolute Change at Week 24 (MMRM)		
n	75	62
LS mean (SE)	-5.31 (1.85)	-1.87 (2.02)
95% CI of LS mean	(-8.96, -1.66)	(-5.86, 2.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.44 (-1.98, 8.86)
Week 52		
n	77	66
Mean (SD)	64.29 (20.18)	69.44 (19.85)
Absolute Change at Week 52		
n	75	65
Mean (SD)	-0.33 (16.29)	1.41 (17.34)
Week 52 (MMRM)		
n	76	63
LS mean (SE)	64.18 (2.28)	67.95 (2.47)
95% CI of LS mean	(59.67, 68.68)	(63.05, 72.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.77 (-2.89, 10.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Absolute Change at Week 52 (MMRM)		
n	74	62
LS mean (SE)	-0.59 (1.93)	0.81 (2.10)
95% CI of LS mean	(-4.41, 3.23)	(-3.34, 4.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.40 (-4.25, 7.06)
Absolute Change through Week 52 (MMRM)		
n	76	65
LS mean (SE)	-2.44 (1.46)	-1.42 (1.58)
95% CI of LS mean	(-5.33, 0.44)	(-4.54, 1.70)
P-value within Treatment	0.0964	0.3693
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.02 (-3.24, 5.29)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6367
Hedges' G (SE)		0.08 (0.17)
Hedges' 95% CI		(-0.25, 0.41)
Hedges' P-value		0.6355

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Baseline		
n	187	194
Mean (SD)	67.38 (18.74)	66.45 (18.10)
Week 8 (MMRM)		
n	188	193
LS mean (SE)	64.49 (1.52)	66.16 (1.50)
95% CI of LS mean	(61.50, 67.47)	(63.21, 69.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.67 (-2.52, 5.86)
Absolute Change at Week 8 (MMRM)		
n	185	191
LS mean (SE)	-2.58 (1.23)	-0.64 (1.21)
95% CI of LS mean	(-5.00, -0.15)	(-3.03, 1.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.93 (-1.48, 5.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Week 16 (MMRM)		
n	186	189
LS mean (SE)	64.39 (1.48)	66.12 (1.46)
95% CI of LS mean	(61.48, 67.29)	(63.24, 68.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.73 (-2.36, 5.82)
Absolute Change at Week 16 (MMRM)		
n	182	187
LS mean (SE)	-2.68 (1.16)	-0.61 (1.14)
95% CI of LS mean	(-4.96, -0.40)	(-2.85, 1.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.07 (-1.13, 5.28)
Week 24 (MMRM)		
n	184	189
LS mean (SE)	64.25 (1.50)	64.43 (1.48)
95% CI of LS mean	(61.29, 67.20)	(61.52, 67.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.19 (-3.97, 4.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 24 (MMRM)		
n	180	187
LS mean (SE)	-3.04 (1.28)	-2.27 (1.25)
95% CI of LS mean	(-5.55, -0.53)	(-4.74, 0.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.77 (-2.75, 4.28)
Week 52		
n	185	183
Mean (SD)	64.82 (19.60)	66.89 (17.85)
Absolute Change at Week 52		
n	181	181
Mean (SD)	-2.12 (16.37)	0.28 (14.35)
Week 52 (MMRM)		
n	183	182
LS mean (SE)	64.79 (1.38)	66.45 (1.37)
95% CI of LS mean	(62.08, 67.50)	(63.75, 69.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.66 (-2.17, 5.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52 (MMRM)		
n	179	180
LS mean (SE)	-2.27 (1.15)	-0.18 (1.14)
95% CI of LS mean	(-4.52, -0.01)	(-2.42, 2.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.08 (-1.10, 5.26)
Absolute Change through Week 52 (MMRM)		
n	183	189
LS mean (SE)	-2.66 (0.97)	-1.02 (0.95)
95% CI of LS mean	(-4.56, -0.76)	(-2.89, 0.85)
P-value within Treatment	0.0062	0.2842
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-1.03, 4.31)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2273
Hedges' G (SE)		0.13 (0.10)
Hedges' 95% CI		(-0.08, 0.33)
Hedges' P-value		0.2273

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Baseline		
n	133	141
Mean (SD)	67.48 (18.23)	69.80 (19.30)
Week 8 (MMRM)		
n	130	139
LS mean (SE)	65.25 (1.76)	70.09 (1.70)
95% CI of LS mean	(61.79, 68.70)	(66.75, 73.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.85 (0.01, 9.68)
Absolute Change at Week 8 (MMRM)		
n	127	137
LS mean (SE)	-1.92 (1.48)	0.32 (1.43)
95% CI of LS mean	(-4.84, 0.99)	(-2.49, 3.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.25 (-1.82, 6.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Week 16 (MMRM)		
n	126	135
LS mean (SE)	65.65 (1.67)	70.18 (1.62)
95% CI of LS mean	(62.36, 68.94)	(67.00, 73.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.54 (-0.07, 9.14)
Absolute Change at Week 16 (MMRM)		
n	123	133
LS mean (SE)	-1.08 (1.36)	0.57 (1.31)
95% CI of LS mean	(-3.76, 1.61)	(-2.02, 3.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-2.10, 5.38)
Week 24 (MMRM)		
n	126	134
LS mean (SE)	64.85 (1.75)	68.02 (1.70)
95% CI of LS mean	(61.40, 68.29)	(64.68, 71.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.18 (-1.65, 8.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Absolute Change at Week 24 (MMRM)		
n	123	132
LS mean (SE)	-2.26 (1.54)	-1.50 (1.49)
95% CI of LS mean	(-5.30, 0.78)	(-4.43, 1.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.76 (-3.48, 5.00)
Week 52		
n	132	137
Mean (SD)	65.66 (18.96)	70.50 (17.30)
Absolute Change at Week 52		
n	129	135
Mean (SD)	-1.23 (16.96)	1.05 (14.45)
Week 52 (MMRM)		
n	126	133
LS mean (SE)	65.19 (1.59)	70.21 (1.54)
95% CI of LS mean	(62.07, 68.32)	(67.17, 73.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.02 (0.63, 9.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Absolute Change at Week 52 (MMRM)		
n	123	131
LS mean (SE)	-1.81 (1.41)	0.81 (1.37)
95% CI of LS mean	(-4.59, 0.97)	(-1.88, 3.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.63 (-1.26, 6.51)
Absolute Change through Week 52 (MMRM)		
n	125	134
LS mean (SE)	-1.72 (1.20)	-0.04 (1.16)
95% CI of LS mean	(-4.09, 0.65)	(-2.33, 2.25)
P-value within Treatment	0.1552	0.9726
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.68 (-1.64, 4.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3204
Hedges' G (SE)		0.12 (0.12)
Hedges' 95% CI		(-0.12, 0.37)
Hedges' P-value		0.3179

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Baseline		
n	136	125
Mean (SD)	66.05 (19.84)	63.47 (17.92)
Week 8 (MMRM)		
n	136	122
LS mean (SE)	63.01 (1.75)	62.11 (1.85)
95% CI of LS mean	(59.56, 66.46)	(58.47, 65.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.90 (-5.95, 4.15)
Absolute Change at Week 8 (MMRM)		
n	134	121
LS mean (SE)	-2.90 (1.34)	-1.24 (1.41)
95% CI of LS mean	(-5.55, -0.26)	(-4.02, 1.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.66 (-2.19, 5.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Week 16 (MMRM)		
n	137	120
LS mean (SE)	62.37 (1.79)	60.23 (1.90)
95% CI of LS mean	(58.84, 65.90)	(56.47, 63.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.15 (-7.33, 3.03)
Absolute Change at Week 16 (MMRM)		
n	134	119
LS mean (SE)	-3.63 (1.37)	-3.20 (1.44)
95% CI of LS mean	(-6.32, -0.94)	(-6.04, -0.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-3.50, 4.36)
Week 24 (MMRM)		
n	135	117
LS mean (SE)	61.12 (1.85)	60.71 (1.97)
95% CI of LS mean	(57.48, 64.76)	(56.84, 64.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.41 (-5.75, 4.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Absolute Change at Week 24 (MMRM)		
n	132	117
LS mean (SE)	-5.21 (1.47)	-2.79 (1.56)
95% CI of LS mean	(-8.11, -2.31)	(-5.85, 0.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.42 (-1.81, 6.65)
Week 52		
n	134	114
Mean (SD)	64.24 (20.91)	64.25 (19.26)
Absolute Change at Week 52		
n	131	113
Mean (SD)	-1.72 (15.60)	-0.07 (15.92)
Week 52 (MMRM)		
n	133	112
LS mean (SE)	64.15 (1.74)	62.88 (1.86)
95% CI of LS mean	(60.73, 67.57)	(59.22, 66.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.26 (-6.30, 3.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Absolute Change at Week 52 (MMRM)		
n	130	111
LS mean (SE)	-1.87 (1.38)	-0.65 (1.48)
95% CI of LS mean	(-4.59, 0.85)	(-3.56, 2.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-2.77, 5.23)
Absolute Change through Week 52 (MMRM)		
n	134	120
LS mean (SE)	-3.57 (1.09)	-2.21 (1.15)
95% CI of LS mean	(-5.72, -1.42)	(-4.48, 0.06)
P-value within Treatment	0.0012	0.0566
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.36 (-1.79, 4.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3955
Hedges' G (SE)		0.11 (0.13)
Hedges' 95% CI		(-0.14, 0.35)
Hedges' P-value		0.3928

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Baseline		
n	99	108
Mean (SD)	64.31 (19.64)	66.59 (18.25)
Week 8 (MMRM)		
n	96	109
LS mean (SE)	61.66 (2.04)	68.23 (1.91)
95% CI of LS mean	(57.65, 65.68)	(64.47, 71.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.57 (1.06, 12.07)
Absolute Change at Week 8 (MMRM)		
n	95	106
LS mean (SE)	-1.93 (1.51)	1.66 (1.43)
95% CI of LS mean	(-4.91, 1.04)	(-1.16, 4.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.59 (-0.51, 7.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Week 16 (MMRM)		
n	94	105
LS mean (SE)	61.03 (2.03)	66.58 (1.91)
95% CI of LS mean	(57.03, 65.02)	(62.82, 70.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.55 (0.06, 11.04)
Absolute Change at Week 16 (MMRM)		
n	93	102
LS mean (SE)	-2.72 (1.50)	0.12 (1.43)
95% CI of LS mean	(-5.68, 0.24)	(-2.70, 2.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.84 (-1.26, 6.94)
Week 24 (MMRM)		
n	94	105
LS mean (SE)	60.53 (1.98)	66.65 (1.86)
95% CI of LS mean	(56.64, 64.43)	(62.98, 70.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.11 (0.76, 11.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Absolute Change at Week 24 (MMRM)		
n	93	103
LS mean (SE)	-3.16 (1.46)	0.33 (1.38)
95% CI of LS mean	(-6.03, -0.28)	(-2.40, 3.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.48 (-0.49, 7.45)
Week 52		
n	98	101
Mean (SD)	62.59 (19.15)	67.99 (16.94)
Absolute Change at Week 52		
n	97	98
Mean (SD)	-1.37 (14.72)	1.36 (14.54)
Week 52 (MMRM)		
n	94	101
LS mean (SE)	61.79 (1.82)	67.21 (1.73)
95% CI of LS mean	(58.20, 65.37)	(63.80, 70.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.42 (0.46, 10.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Absolute Change at Week 52 (MMRM)		
n	93	98
LS mean (SE)	-1.76 (1.52)	0.95 (1.47)
95% CI of LS mean	(-4.75, 1.24)	(-1.94, 3.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.71 (-1.46, 6.88)
Absolute Change through Week 52 (MMRM)		
n	95	104
LS mean (SE)	-2.54 (1.22)	0.47 (1.16)
95% CI of LS mean	(-4.94, -0.15)	(-1.82, 2.75)
P-value within Treatment	0.0377	0.6878
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.01 (-0.31, 6.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0753
Hedges' G (SE)		0.25 (0.14)
Hedges' 95% CI		(-0.03, 0.53)
Hedges' P-value		0.0759

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Baseline		
n	170	158
Mean (SD)	68.19 (18.59)	66.98 (19.39)
Week 8 (MMRM)		
n	170	152
LS mean (SE)	65.29 (1.59)	65.18 (1.68)
95% CI of LS mean	(62.17, 68.41)	(61.87, 68.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.11 (-4.66, 4.44)
Absolute Change at Week 8 (MMRM)		
n	166	152
LS mean (SE)	-2.70 (1.33)	-1.88 (1.39)
95% CI of LS mean	(-5.31, -0.09)	(-4.60, 0.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.82 (-2.95, 4.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Week 16 (MMRM)		
n	169	150
LS mean (SE)	65.42 (1.57)	64.92 (1.67)
95% CI of LS mean	(62.33, 68.51)	(61.64, 68.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.50 (-5.01, 4.01)
Absolute Change at Week 16 (MMRM)		
n	164	150
LS mean (SE)	-2.18 (1.26)	-2.16 (1.32)
95% CI of LS mean	(-4.65, 0.30)	(-4.75, 0.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-3.57, 3.61)
Week 24 (MMRM)		
n	167	146
LS mean (SE)	64.08 (1.67)	63.34 (1.78)
95% CI of LS mean	(60.80, 67.36)	(59.84, 66.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.75 (-5.55, 4.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Absolute Change at Week 24 (MMRM)		
n	162	146
LS mean (SE)	-4.14 (1.45)	-3.82 (1.53)
95% CI of LS mean	(-7.00, -1.29)	(-6.83, -0.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-3.83, 4.47)
Week 52		
n	168	150
Mean (SD)	66.32 (20.32)	67.44 (19.44)
Absolute Change at Week 52		
n	163	150
Mean (SD)	-1.53 (17.15)	0.00 (15.51)
Week 52 (MMRM)		
n	165	144
LS mean (SE)	66.08 (1.54)	66.71 (1.64)
95% CI of LS mean	(63.06, 69.11)	(63.49, 69.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-3.80, 5.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Absolute Change at Week 52 (MMRM)		
n	160	144
LS mean (SE)	-1.88 (1.30)	-0.48 (1.36)
95% CI of LS mean	(-4.43, 0.67)	(-3.16, 2.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.40 (-2.31, 5.10)
Absolute Change through Week 52 (MMRM)		
n	164	150
LS mean (SE)	-2.73 (1.07)	-2.15 (1.12)
95% CI of LS mean	(-4.84, -0.62)	(-4.37, 0.06)
P-value within Treatment	0.0113	0.0563
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-2.48, 3.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7103
Hedges' G (SE)		0.04 (0.11)
Hedges' 95% CI		(-0.18, 0.26)
Hedges' P-value		0.7098

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Baseline		
n	160	152
Mean (SD)	90.00 (21.73)	85.31 (27.59)
Week 8 (MMRM)		
n	158	152
LS mean (SE)	86.32 (2.16)	85.54 (2.20)
95% CI of LS mean	(82.07, 90.56)	(81.21, 89.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.78 (-6.85, 5.29)
Absolute Change at Week 8 (MMRM)		
n	155	150
LS mean (SE)	-4.32 (1.65)	0.02 (1.68)
95% CI of LS mean	(-7.57, -1.06)	(-3.29, 3.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.33 (-0.31, 8.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Week 16 (MMRM)		
n	154	149
LS mean (SE)	83.91 (2.22)	86.18 (2.27)
95% CI of LS mean	(79.54, 88.28)	(81.72, 90.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.28 (-3.97, 8.53)
Absolute Change at Week 16 (MMRM)		
n	151	147
LS mean (SE)	-6.84 (1.79)	0.65 (1.81)
95% CI of LS mean	(-10.35, -3.32)	(-2.92, 4.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.48 (2.47, 12.50)
Week 24 (MMRM)		
n	153	147
LS mean (SE)	85.78 (2.16)	85.77 (2.20)
95% CI of LS mean	(81.54, 90.03)	(81.43, 90.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.01 (-6.09, 6.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 24 (MMRM)		
n	150	145
LS mean (SE)	-4.71 (1.73)	0.37 (1.76)
95% CI of LS mean	(-8.12, -1.30)	(-3.09, 3.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.08 (0.22, 9.94)
Week 52		
n	159	144
Mean (SD)	86.79 (26.79)	84.49 (27.29)
Absolute Change at Week 52		
n	153	142
Mean (SD)	-3.92 (23.55)	-0.94 (19.43)
Week 52 (MMRM)		
n	155	143
LS mean (SE)	86.29 (2.15)	84.31 (2.22)
95% CI of LS mean	(82.06, 90.53)	(79.93, 88.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.98 (-8.08, 4.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 166	VNZ/TEZ/D-IVA N = 154
Absolute Change at Week 52 (MMRM)		
n	149	141
LS mean (SE)	-4.37 (1.80)	-1.15 (1.85)
95% CI of LS mean	(-7.93, -0.82)	(-4.79, 2.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.22 (-1.86, 8.31)
Absolute Change through Week 52 (MMRM)		
n	153	148
LS mean (SE)	-5.31 (1.41)	-0.04 (1.44)
95% CI of LS mean	(-8.09, -2.52)	(-2.87, 2.78)
P-value within Treatment	0.0002	0.9753
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.26 (1.29, 9.24)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0096
Hedges' G (SE)		0.30 (0.12)
Hedges' 95% CI		(0.07, 0.53)
Hedges' P-value		0.0099

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Baseline		
n	103	109
Mean (SD)	86.08 (27.43)	82.87 (26.69)
Week 8 (MMRM)		
n	104	108
LS mean (SE)	88.84 (2.52)	83.86 (2.48)
95% CI of LS mean	(83.86, 93.82)	(78.97, 88.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.98 (-11.99, 2.03)
Absolute Change at Week 8 (MMRM)		
n	103	107
LS mean (SE)	2.58 (2.00)	0.77 (1.96)
95% CI of LS mean	(-1.37, 6.53)	(-3.09, 4.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.81 (-7.35, 3.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Week 16 (MMRM)		
n	103	106
LS mean (SE)	90.13 (2.59)	85.00 (2.56)
95% CI of LS mean	(85.03, 95.24)	(79.97, 90.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.13 (-12.33, 2.07)
Absolute Change at Week 16 (MMRM)		
n	102	105
LS mean (SE)	3.89 (2.21)	2.12 (2.17)
95% CI of LS mean	(-0.47, 8.25)	(-2.17, 6.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.77 (-7.90, 4.35)
Week 24 (MMRM)		
n	104	104
LS mean (SE)	86.95 (2.81)	84.46 (2.78)
95% CI of LS mean	(81.42, 92.48)	(78.98, 89.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.49 (-10.30, 5.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Absolute Change at Week 24 (MMRM)		
n	103	104
LS mean (SE)	0.64 (1.99)	1.58 (1.97)
95% CI of LS mean	(-3.29, 4.57)	(-2.30, 5.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.95 (-4.60, 6.49)
Week 52		
n	104	102
Mean (SD)	87.18 (25.99)	83.66 (29.57)
Absolute Change at Week 52		
n	101	101
Mean (SD)	0.99 (20.79)	0.99 (26.02)
Week 52 (MMRM)		
n	104	101
LS mean (SE)	87.39 (2.69)	84.08 (2.68)
95% CI of LS mean	(82.09, 92.69)	(78.79, 89.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.31 (-10.83, 4.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 106	VNZ/TEZ/D-IVA N = 110
Absolute Change at Week 52 (MMRM)		
n	101	100
LS mean (SE)	1.05 (2.30)	1.31 (2.28)
95% CI of LS mean	(-3.48, 5.58)	(-3.19, 5.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-6.14, 6.66)
Absolute Change through Week 52 (MMRM)		
n	103	106
LS mean (SE)	1.86 (1.86)	1.67 (1.83)
95% CI of LS mean	(-1.81, 5.53)	(-1.95, 5.29)
P-value within Treatment	0.3197	0.3641
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.19 (-5.36, 4.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9424
Hedges' G (SE)		-0.01 (0.14)
Hedges' 95% CI		(-0.28, 0.26)
Hedges' P-value		0.9422

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Baseline		
n	24	26
Mean (SD)	70.83 (35.86)	83.33 (25.39)
Week 8 (MMRM)		
n	24	24
LS mean (SE)	74.56 (6.01)	89.59 (5.93)
95% CI of LS mean	(62.44, 86.68)	(77.64, 101.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.02 (-2.30, 32.35)
Absolute Change at Week 8 (MMRM)		
n	24	24
LS mean (SE)	1.58 (4.08)	6.83 (4.05)
95% CI of LS mean	(-6.69, 9.84)	(-1.38, 15.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.26 (-6.66, 17.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Week 16 (MMRM)		
n	22	23
LS mean (SE)	75.21 (6.11)	90.79 (5.98)
95% CI of LS mean	(62.84, 87.58)	(78.70, 102.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.58 (-2.02, 33.18)
Absolute Change at Week 16 (MMRM)		
n	22	23
LS mean (SE)	1.95 (6.08)	9.44 (5.91)
95% CI of LS mean	(-10.33, 14.23)	(-2.49, 21.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.50 (-9.79, 24.78)
Week 24 (MMRM)		
n	22	22
LS mean (SE)	73.26 (6.43)	91.21 (6.31)
95% CI of LS mean	(60.27, 86.25)	(78.46, 103.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	17.95 (-0.52, 36.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 24 (MMRM)		
n	22	22
LS mean (SE)	0.48 (4.54)	9.68 (4.47)
95% CI of LS mean	(-8.70, 9.66)	(0.65, 18.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.20 (-3.89, 22.29)
Week 52		
n	22	20
Mean (SD)	78.79 (28.26)	91.67 (18.34)
Absolute Change at Week 52		
n	22	20
Mean (SD)	7.58 (25.05)	6.67 (25.59)
Week 52 (MMRM)		
n	22	20
LS mean (SE)	78.20 (5.40)	92.35 (5.48)
95% CI of LS mean	(67.25, 89.15)	(81.27, 103.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.15 (-1.75, 30.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

	ELX/TEZ/IVA N = 24	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	22	20
LS mean (SE)	4.95 (5.26)	11.30 (5.34)
95% CI of LS mean	(-5.66, 15.57)	(0.54, 22.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.35 (-8.95, 21.65)
Absolute Change through Week 52 (MMRM)		
n	22	24
LS mean (SE)	2.46 (4.66)	10.14 (4.56)
95% CI of LS mean	(-6.94, 11.86)	(0.95, 19.33)
P-value within Treatment	0.6001	0.0314
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.68 (-5.68, 21.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2527
Hedges' G (SE)		0.34 (0.29)
Hedges' 95% CI		(-0.25, 0.93)
Hedges' P-value		0.2487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Baseline		
n	242	240
Mean (SD)	90.22 (21.91)	84.44 (27.25)
Week 8 (MMRM)		
n	238	236
LS mean (SE)	88.59 (1.69)	84.33 (1.70)
95% CI of LS mean	(85.27, 91.91)	(80.99, 87.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.26 (-8.98, 0.46)
Absolute Change at Week 8 (MMRM)		
n	234	233
LS mean (SE)	-2.13 (1.34)	-0.14 (1.34)
95% CI of LS mean	(-4.77, 0.50)	(-2.78, 2.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.99 (-1.74, 5.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Week 16 (MMRM)		
n	235	232
LS mean (SE)	87.52 (1.75)	85.16 (1.77)
95% CI of LS mean	(84.07, 90.96)	(81.68, 88.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.36 (-7.26, 2.53)
Absolute Change at Week 16 (MMRM)		
n	231	229
LS mean (SE)	-3.22 (1.43)	0.69 (1.43)
95% CI of LS mean	(-6.02, -0.41)	(-2.13, 3.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.90 (-0.07, 7.88)
Week 24 (MMRM)		
n	235	229
LS mean (SE)	87.45 (1.77)	84.59 (1.79)
95% CI of LS mean	(83.97, 90.93)	(81.07, 88.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.86 (-7.82, 2.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 24 (MMRM)		
n	231	227
LS mean (SE)	-3.14 (1.36)	0.22 (1.37)
95% CI of LS mean	(-5.82, -0.46)	(-2.48, 2.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.35 (-0.45, 7.16)
Week 52		
n	244	230
Mean (SD)	87.84 (26.06)	83.62 (28.68)
Absolute Change at Week 52		
n	235	227
Mean (SD)	-2.70 (22.16)	-0.73 (21.83)
Week 52 (MMRM)		
n	237	224
LS mean (SE)	87.55 (1.76)	83.38 (1.80)
95% CI of LS mean	(84.09, 91.01)	(79.85, 86.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.17 (-9.12, 0.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

	ELX/TEZ/IVA N = 251	VNZ/TEZ/D-IVA N = 243
Absolute Change at Week 52 (MMRM)		
n	228	221
LS mean (SE)	-3.16 (1.48)	-1.00 (1.49)
95% CI of LS mean	(-6.05, -0.26)	(-3.93, 1.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.16 (-1.97, 6.29)
Absolute Change through Week 52 (MMRM)		
n	234	230
LS mean (SE)	-3.17 (1.16)	-0.03 (1.17)
95% CI of LS mean	(-5.45, -0.89)	(-2.33, 2.27)
P-value within Treatment	0.0066	0.9791
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.14 (-0.10, 6.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0577
Hedges' G (SE)		0.18 (0.09)
Hedges' 95% CI		(-0.01, 0.36)
Hedges' P-value		0.0578

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Baseline		
n	76	70
Mean (SD)	89.91 (24.36)	85.24 (26.40)
Week 8 (MMRM)		
n	77	68
LS mean (SE)	89.19 (3.01)	85.92 (3.21)
95% CI of LS mean	(83.24, 95.13)	(79.57, 92.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.26 (-11.98, 5.46)
Absolute Change at Week 8 (MMRM)		
n	75	67
LS mean (SE)	-0.97 (1.97)	0.59 (2.08)
95% CI of LS mean	(-4.87, 2.92)	(-3.53, 4.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.56 (-4.12, 7.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Week 16 (MMRM)		
n	75	66
LS mean (SE)	85.85 (3.04)	87.96 (3.25)
95% CI of LS mean	(79.84, 91.86)	(81.52, 94.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.11 (-6.71, 10.94)
Absolute Change at Week 16 (MMRM)		
n	73	65
LS mean (SE)	-4.40 (1.89)	2.51 (2.00)
95% CI of LS mean	(-8.13, -0.67)	(-1.46, 6.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.91 (1.45, 12.36)
Week 24 (MMRM)		
n	77	62
LS mean (SE)	87.44 (2.90)	86.24 (3.15)
95% CI of LS mean	(81.71, 93.18)	(80.01, 92.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.20 (-9.69, 7.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Absolute Change at Week 24 (MMRM)		
n	75	62
LS mean (SE)	-2.75 (1.69)	0.95 (1.84)
95% CI of LS mean	(-6.08, 0.59)	(-2.69, 4.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.70 (-1.25, 8.65)
Week 52		
n	77	65
Mean (SD)	87.45 (24.80)	85.64 (28.24)
Absolute Change at Week 52		
n	74	64
Mean (SD)	-3.15 (22.19)	0.52 (15.13)
Week 52 (MMRM)		
n	76	62
LS mean (SE)	86.74 (3.00)	85.75 (3.25)
95% CI of LS mean	(80.82, 92.67)	(79.33, 92.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.99 (-9.75, 7.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 79	VNZ/TEZ/D-IVA N = 71
Absolute Change at Week 52 (MMRM)		
n	73	61
LS mean (SE)	-3.53 (2.20)	0.44 (2.39)
95% CI of LS mean	(-7.88, 0.83)	(-4.28, 5.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.97 (-2.46, 10.41)
Absolute Change through Week 52 (MMRM)		
n	75	65
LS mean (SE)	-3.56 (1.55)	1.30 (1.66)
95% CI of LS mean	(-6.62, -0.49)	(-1.99, 4.59)
P-value within Treatment	0.0232	0.4358
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.86 (0.35, 9.37)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0350
Hedges' G (SE)		0.36 (0.17)
Hedges' 95% CI		(0.02, 0.70)
Hedges' P-value		0.0358

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Baseline		
n	185	194
Mean (SD)	88.29 (23.33)	83.85 (27.40)
Week 8 (MMRM)		
n	185	192
LS mean (SE)	86.57 (1.96)	84.44 (1.93)
95% CI of LS mean	(82.71, 90.42)	(80.65, 88.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.13 (-7.54, 3.28)
Absolute Change at Week 8 (MMRM)		
n	183	190
LS mean (SE)	-1.88 (1.62)	0.32 (1.59)
95% CI of LS mean	(-5.08, 1.31)	(-2.80, 3.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.21 (-2.27, 6.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Week 16 (MMRM)		
n	182	189
LS mean (SE)	86.66 (2.04)	84.89 (2.01)
95% CI of LS mean	(82.65, 90.67)	(80.95, 88.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.77 (-7.40, 3.87)
Absolute Change at Week 16 (MMRM)		
n	180	187
LS mean (SE)	-1.80 (1.83)	0.81 (1.79)
95% CI of LS mean	(-5.39, 1.79)	(-2.71, 4.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.61 (-2.42, 7.64)
Week 24 (MMRM)		
n	180	189
LS mean (SE)	85.73 (2.10)	84.77 (2.06)
95% CI of LS mean	(81.60, 89.87)	(80.71, 88.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.96 (-6.76, 4.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 24 (MMRM)		
n	178	187
LS mean (SE)	-2.53 (1.72)	0.83 (1.67)
95% CI of LS mean	(-5.91, 0.84)	(-2.46, 4.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.37 (-1.35, 8.08)
Week 52		
n	185	183
Mean (SD)	87.39 (26.41)	83.61 (28.14)
Absolute Change at Week 52		
n	179	181
Mean (SD)	-1.30 (23.00)	-0.37 (24.34)
Week 52 (MMRM)		
n	183	182
LS mean (SE)	86.70 (2.02)	83.60 (2.01)
95% CI of LS mean	(82.73, 90.67)	(79.65, 87.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.11 (-8.71, 2.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 191	VNZ/TEZ/D-IVA N = 196
Absolute Change at Week 52 (MMRM)		
n	177	180
LS mean (SE)	-1.69 (1.79)	-0.35 (1.77)
95% CI of LS mean	(-5.22, 1.83)	(-3.83, 3.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.34 (-3.61, 6.29)
Absolute Change through Week 52 (MMRM)		
n	181	189
LS mean (SE)	-2.01 (1.48)	0.43 (1.45)
95% CI of LS mean	(-4.91, 0.90)	(-2.41, 3.28)
P-value within Treatment	0.1749	0.7661
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.44 (-1.63, 6.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2394
Hedges' G (SE)		0.12 (0.10)
Hedges' 95% CI		(-0.08, 0.33)
Hedges' P-value		0.2395

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Baseline		
n	130	141
Mean (SD)	84.62 (27.27)	80.38 (29.83)
Week 8 (MMRM)		
n	127	139
LS mean (SE)	84.48 (2.61)	78.69 (2.50)
95% CI of LS mean	(79.34, 89.61)	(73.75, 83.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.79 (-12.96, 1.38)
Absolute Change at Week 8 (MMRM)		
n	124	137
LS mean (SE)	-1.54 (2.11)	-1.04 (2.01)
95% CI of LS mean	(-5.70, 2.62)	(-5.00, 2.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-5.27, 6.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Week 16 (MMRM)		
n	122	135
LS mean (SE)	86.09 (2.52)	81.30 (2.42)
95% CI of LS mean	(81.12, 91.05)	(76.53, 86.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.79 (-11.72, 2.14)
Absolute Change at Week 16 (MMRM)		
n	119	133
LS mean (SE)	0.17 (2.02)	1.59 (1.91)
95% CI of LS mean	(-3.80, 4.14)	(-2.18, 5.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-4.08, 6.92)
Week 24 (MMRM)		
n	124	134
LS mean (SE)	82.73 (2.70)	80.89 (2.60)
95% CI of LS mean	(77.41, 88.05)	(75.76, 86.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.84 (-9.27, 5.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Absolute Change at Week 24 (MMRM)		
n	121	132
LS mean (SE)	-3.02 (2.04)	1.30 (1.95)
95% CI of LS mean	(-7.04, 0.99)	(-2.53, 5.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.32 (-1.25, 9.90)
Week 52		
n	132	137
Mean (SD)	84.60 (28.06)	78.83 (31.28)
Absolute Change at Week 52		
n	126	135
Mean (SD)	-0.53 (23.85)	-1.73 (22.79)
Week 52 (MMRM)		
n	126	133
LS mean (SE)	84.40 (2.64)	78.53 (2.56)
95% CI of LS mean	(79.21, 89.59)	(73.49, 83.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.87 (-13.15, 1.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 136	VNZ/TEZ/D-IVA N = 143
Absolute Change at Week 52 (MMRM)		
n	120	131
LS mean (SE)	-1.42 (2.12)	-1.15 (2.03)
95% CI of LS mean	(-5.60, 2.76)	(-5.14, 2.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-5.53, 6.08)
Absolute Change through Week 52 (MMRM)		
n	122	134
LS mean (SE)	-1.42 (1.72)	0.58 (1.64)
95% CI of LS mean	(-4.82, 1.97)	(-2.65, 3.82)
P-value within Treatment	0.4092	0.7241
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.00 (-2.72, 6.73)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4038
Hedges' G (SE)		0.11 (0.12)
Hedges' 95% CI		(-0.14, 0.35)
Hedges' P-value		0.4008

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Baseline		
n	136	125
Mean (SD)	92.16 (19.97)	88.80 (22.78)
Week 8 (MMRM)		
n	135	121
LS mean (SE)	90.13 (1.95)	91.70 (2.06)
95% CI of LS mean	(86.28, 93.98)	(87.64, 95.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.57 (-4.06, 7.20)
Absolute Change at Week 8 (MMRM)		
n	134	120
LS mean (SE)	-1.76 (1.53)	2.04 (1.62)
95% CI of LS mean	(-4.78, 1.27)	(-1.14, 5.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.80 (-0.62, 8.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Week 16 (MMRM)		
n	135	120
LS mean (SE)	86.92 (2.26)	90.56 (2.39)
95% CI of LS mean	(82.47, 91.37)	(85.87, 95.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.64 (-2.86, 10.14)
Absolute Change at Week 16 (MMRM)		
n	134	119
LS mean (SE)	-4.99 (1.99)	1.07 (2.10)
95% CI of LS mean	(-8.90, -1.08)	(-3.07, 5.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.05 (0.34, 11.77)
Week 24 (MMRM)		
n	133	117
LS mean (SE)	89.67 (2.11)	89.89 (2.24)
95% CI of LS mean	(85.50, 93.83)	(85.48, 94.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-5.87, 6.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Absolute Change at Week 24 (MMRM)		
n	132	117
LS mean (SE)	-2.25 (1.71)	0.48 (1.81)
95% CI of LS mean	(-5.62, 1.12)	(-3.08, 4.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.73 (-2.19, 7.66)
Week 52		
n	134	113
Mean (SD)	89.55 (24.33)	90.86 (21.93)
Absolute Change at Week 52		
n	131	112
Mean (SD)	-3.05 (21.26)	1.79 (21.38)
Week 52 (MMRM)		
n	133	111
LS mean (SE)	89.18 (2.03)	90.55 (2.18)
95% CI of LS mean	(85.18, 93.17)	(86.25, 94.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.37 (-4.52, 7.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 139	VNZ/TEZ/D-IVA N = 126
Absolute Change at Week 52 (MMRM)		
n	130	110
LS mean (SE)	-2.88 (1.92)	1.12 (2.06)
95% CI of LS mean	(-6.67, 0.91)	(-2.94, 5.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.00 (-1.58, 9.58)
Absolute Change through Week 52 (MMRM)		
n	134	120
LS mean (SE)	-3.37 (1.53)	0.89 (1.62)
95% CI of LS mean	(-6.40, -0.35)	(-2.30, 4.09)
P-value within Treatment	0.0289	0.5836
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.26 (-0.16, 8.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0589
Hedges' G (SE)		0.24 (0.13)
Hedges' 95% CI		(-0.01, 0.49)
Hedges' P-value		0.0583

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Baseline		
n	99	108
Mean (SD)	89.56 (22.16)	84.26 (28.99)
Week 8 (MMRM)		
n	96	109
LS mean (SE)	89.81 (2.67)	84.95 (2.50)
95% CI of LS mean	(84.54, 95.08)	(80.02, 89.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.86 (-12.08, 2.35)
Absolute Change at Week 8 (MMRM)		
n	95	106
LS mean (SE)	0.76 (1.96)	-0.16 (1.85)
95% CI of LS mean	(-3.11, 4.63)	(-3.81, 3.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.92 (-6.25, 4.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Week 16 (MMRM)		
n	94	105
LS mean (SE)	89.07 (2.72)	86.07 (2.56)
95% CI of LS mean	(83.70, 94.44)	(81.03, 91.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.00 (-10.38, 4.38)
Absolute Change at Week 16 (MMRM)		
n	93	102
LS mean (SE)	0.02 (2.07)	0.91 (1.97)
95% CI of LS mean	(-4.07, 4.10)	(-2.97, 4.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.89 (-4.75, 6.53)
Week 24 (MMRM)		
n	95	105
LS mean (SE)	89.54 (2.71)	84.59 (2.55)
95% CI of LS mean	(84.20, 94.88)	(79.57, 89.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.95 (-12.29, 2.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Absolute Change at Week 24 (MMRM)		
n	94	103
LS mean (SE)	0.87 (1.92)	-0.44 (1.82)
95% CI of LS mean	(-2.91, 4.66)	(-4.04, 3.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.31 (-6.55, 3.92)
Week 52		
n	98	101
Mean (SD)	92.52 (20.60)	82.84 (31.13)
Absolute Change at Week 52		
n	97	98
Mean (SD)	3.44 (20.12)	-2.72 (23.29)
Week 52 (MMRM)		
n	94	101
LS mean (SE)	91.83 (2.71)	83.39 (2.56)
95% CI of LS mean	(86.49, 97.17)	(78.33, 88.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.44 (-15.80, -1.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 100	VNZ/TEZ/D-IVA N = 111
Absolute Change at Week 52 (MMRM)		
n	93	98
LS mean (SE)	3.12 (2.26)	-1.70 (2.18)
95% CI of LS mean	(-1.34, 7.59)	(-6.00, 2.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.83 (-11.03, 1.38)
Absolute Change through Week 52 (MMRM)		
n	95	104
LS mean (SE)	1.34 (1.76)	-0.41 (1.68)
95% CI of LS mean	(-2.14, 4.82)	(-3.72, 2.90)
P-value within Treatment	0.4496	0.8061
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.75 (-6.56, 3.06)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4742
Hedges' G (SE)		-0.10 (0.14)
Hedges' 95% CI		(-0.38, 0.18)
Hedges' P-value		0.4736

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Baseline		
n	167	158
Mean (SD)	87.82 (25.18)	84.39 (25.70)
Week 8 (MMRM)		
n	166	151
LS mean (SE)	85.61 (2.04)	85.13 (2.15)
95% CI of LS mean	(81.59, 89.62)	(80.90, 89.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-6.31, 5.37)
Absolute Change at Week 8 (MMRM)		
n	163	151
LS mean (SE)	-3.05 (1.67)	0.85 (1.74)
95% CI of LS mean	(-6.34, 0.24)	(-2.56, 4.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.91 (-0.84, 8.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Week 16 (MMRM)		
n	163	150
LS mean (SE)	84.57 (2.13)	85.83 (2.24)
95% CI of LS mean	(80.39, 88.76)	(81.43, 90.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.26 (-4.82, 7.34)
Absolute Change at Week 16 (MMRM)		
n	160	150
LS mean (SE)	-4.13 (1.86)	1.63 (1.92)
95% CI of LS mean	(-7.79, -0.47)	(-2.16, 5.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.76 (0.49, 11.03)
Week 24 (MMRM)		
n	162	146
LS mean (SE)	84.00 (2.19)	85.98 (2.31)
95% CI of LS mean	(79.71, 88.30)	(81.44, 90.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.98 (-4.28, 8.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Absolute Change at Week 24 (MMRM)		
n	159	146
LS mean (SE)	-4.70 (1.76)	1.92 (1.83)
95% CI of LS mean	(-8.15, -1.24)	(-1.68, 5.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.62 (1.62, 11.61)
Week 52		
n	168	149
Mean (SD)	83.93 (28.72)	85.23 (25.81)
Absolute Change at Week 52		
n	160	149
Mean (SD)	-5.00 (23.41)	1.57 (21.34)
Week 52 (MMRM)		
n	165	143
LS mean (SE)	83.46 (2.10)	85.09 (2.24)
95% CI of LS mean	(79.32, 87.59)	(80.67, 89.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.63 (-4.43, 7.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

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Table 2.2.2.9.3.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 175	VNZ/TEZ/D-IVA N = 158
Absolute Change at Week 52 (MMRM)		
n	157	143
LS mean (SE)	-5.48 (1.81)	1.11 (1.89)
95% CI of LS mean	(-9.04, -1.91)	(-2.62, 4.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.58 (1.42, 11.74)
Absolute Change through Week 52 (MMRM)		
n	161	150
LS mean (SE)	-4.77 (1.47)	1.55 (1.52)
95% CI of LS mean	(-7.66, -1.88)	(-1.45, 4.55)
P-value within Treatment	0.0013	0.3096
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.32 (2.15, 10.49)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0031
Hedges' G (SE)		0.34 (0.11)
Hedges' 95% CI		(0.11, 0.56)
Hedges' P-value		0.0032

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Baseline		
n	243	237
Mean (SD)	76.22 (23.64)	79.32 (21.12)
Week 8 (MMRM)		
n	240	234
LS mean (SE)	79.16 (1.44)	79.37 (1.46)
95% CI of LS mean	(76.33, 81.99)	(76.51, 82.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.21 (-3.81, 4.23)
Absolute Change at Week 8 (MMRM)		
n	233	231
LS mean (SE)	2.54 (0.95)	0.03 (0.95)
95% CI of LS mean	(0.68, 4.41)	(-1.84, 1.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.51 (-5.16, 0.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Week 16 (MMRM)		
n	236	229
LS mean (SE)	78.98 (1.36)	79.66 (1.38)
95% CI of LS mean	(76.31, 81.66)	(76.95, 82.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.68 (-3.13, 4.49)
Absolute Change at Week 16 (MMRM)		
n	229	226
LS mean (SE)	2.14 (0.92)	0.13 (0.93)
95% CI of LS mean	(0.32, 3.96)	(-1.70, 1.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.01 (-4.58, 0.57)
Week 24 (MMRM)		
n	238	226
LS mean (SE)	79.98 (1.40)	79.70 (1.42)
95% CI of LS mean	(77.23, 82.74)	(76.90, 82.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-4.22, 3.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 24 (MMRM)		
n	231	223
LS mean (SE)	3.35 (0.97)	0.30 (0.98)
95% CI of LS mean	(1.45, 5.26)	(-1.63, 2.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.05 (-5.76, -0.33)
Week 52		
n	241	224
Mean (SD)	78.47 (21.01)	79.51 (21.97)
Absolute Change at Week 52		
n	234	220
Mean (SD)	1.99 (17.32)	0.40 (16.13)
Week 52 (MMRM)		
n	235	221
LS mean (SE)	78.57 (1.39)	79.93 (1.41)
95% CI of LS mean	(75.84, 81.29)	(77.15, 82.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.36 (-2.54, 5.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 52 (MMRM)		
n	228	217
LS mean (SE)	1.76 (1.11)	0.57 (1.13)
95% CI of LS mean	(-0.41, 3.93)	(-1.64, 2.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.19 (-4.29, 1.91)
Absolute Change through Week 52 (MMRM)		
n	233	229
LS mean (SE)	2.42 (0.84)	0.34 (0.85)
95% CI of LS mean	(0.77, 4.07)	(-1.33, 2.00)
P-value within Treatment	0.0041	0.6924
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.08 (-4.43, 0.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0815
Hedges' G (SE)		-0.16 (0.09)
Hedges' 95% CI		(-0.35, 0.02)
Hedges' P-value		0.0818

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Baseline		
n	39	43
Mean (SD)	73.22 (23.87)	74.68 (22.79)
Week 8 (MMRM)		
n	37	39
LS mean (SE)	73.95 (3.51)	79.11 (3.38)
95% CI of LS mean	(66.96, 80.94)	(72.37, 85.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.16 (-4.69, 15.01)
Absolute Change at Week 8 (MMRM)		
n	37	39
LS mean (SE)	1.43 (2.51)	3.91 (2.42)
95% CI of LS mean	(-3.57, 6.44)	(-0.92, 8.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.48 (-4.57, 9.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Week 16 (MMRM)		
n	37	38
LS mean (SE)	74.25 (3.20)	79.40 (3.09)
95% CI of LS mean	(67.87, 80.63)	(73.23, 85.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.16 (-3.87, 14.18)
Absolute Change at Week 16 (MMRM)		
n	37	38
LS mean (SE)	1.73 (2.34)	4.19 (2.27)
95% CI of LS mean	(-2.93, 6.39)	(-0.33, 8.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.46 (-4.13, 9.06)
Week 24 (MMRM)		
n	36	39
LS mean (SE)	74.15 (3.55)	80.19 (3.41)
95% CI of LS mean	(67.07, 81.23)	(73.39, 86.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.04 (-3.92, 16.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 24 (MMRM)		
n	36	39
LS mean (SE)	1.47 (2.99)	5.09 (2.88)
95% CI of LS mean	(-4.49, 7.43)	(-0.64, 10.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.62 (-4.74, 11.99)
Week 52		
n	36	41
Mean (SD)	79.63 (21.82)	79.95 (21.40)
Absolute Change at Week 52		
n	36	41
Mean (SD)	5.86 (15.14)	6.23 (17.58)
Week 52 (MMRM)		
n	34	38
LS mean (SE)	77.67 (3.43)	81.36 (3.28)
95% CI of LS mean	(70.83, 84.51)	(74.82, 87.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.69 (-5.93, 13.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 52 (MMRM)		
n	34	38
LS mean (SE)	5.08 (2.88)	6.36 (2.75)
95% CI of LS mean	(-0.66, 10.82)	(0.88, 11.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.28 (-6.76, 9.32)
Absolute Change through Week 52 (MMRM)		
n	37	39
LS mean (SE)	2.76 (2.36)	5.22 (2.27)
95% CI of LS mean	(-1.95, 7.47)	(0.69, 9.75)
P-value within Treatment	0.2467	0.0246
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.46 (-4.20, 9.11)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4641
Hedges' G (SE)		0.17 (0.23)
Hedges' 95% CI		(-0.28, 0.62)
Hedges' P-value		0.4568

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Baseline		
n	219	219
Mean (SD)	75.04 (24.07)	77.02 (22.02)
Week 8 (MMRM)		
n	215	215
LS mean (SE)	77.69 (1.55)	78.29 (1.55)
95% CI of LS mean	(74.64, 80.73)	(75.25, 81.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.61 (-3.70, 4.92)
Absolute Change at Week 8 (MMRM)		
n	210	213
LS mean (SE)	2.48 (1.04)	1.04 (1.03)
95% CI of LS mean	(0.43, 4.52)	(-0.99, 3.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.43 (-4.32, 1.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Week 16 (MMRM)		
n	211	211
LS mean (SE)	77.54 (1.47)	78.15 (1.46)
95% CI of LS mean	(74.65, 80.42)	(75.27, 81.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.61 (-3.46, 4.69)
Absolute Change at Week 16 (MMRM)		
n	206	209
LS mean (SE)	2.01 (0.99)	0.69 (0.98)
95% CI of LS mean	(0.07, 3.94)	(-1.23, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.31 (-4.04, 1.42)
Week 24 (MMRM)		
n	212	211
LS mean (SE)	78.67 (1.52)	78.37 (1.52)
95% CI of LS mean	(75.68, 81.66)	(75.39, 81.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.30 (-4.52, 3.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 24 (MMRM)		
n	207	208
LS mean (SE)	3.30 (1.07)	1.08 (1.07)
95% CI of LS mean	(1.19, 5.40)	(-1.01, 3.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.22 (-5.18, 0.75)
Week 52		
n	212	209
Mean (SD)	77.41 (21.62)	78.47 (22.38)
Absolute Change at Week 52		
n	207	206
Mean (SD)	1.99 (17.46)	1.56 (17.19)
Week 52 (MMRM)		
n	207	206
LS mean (SE)	77.23 (1.51)	78.82 (1.51)
95% CI of LS mean	(74.26, 80.21)	(75.85, 81.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.59 (-2.62, 5.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 52 (MMRM)		
n	202	203
LS mean (SE)	1.74 (1.21)	1.52 (1.20)
95% CI of LS mean	(-0.64, 4.11)	(-0.84, 3.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.21 (-3.56, 3.14)
Absolute Change through Week 52 (MMRM)		
n	210	212
LS mean (SE)	2.35 (0.92)	1.10 (0.91)
95% CI of LS mean	(0.54, 4.15)	(-0.70, 2.90)
P-value within Treatment	0.0111	0.2301
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.25 (-3.80, 1.30)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3371
Hedges' G (SE)		-0.09 (0.10)
Hedges' 95% CI		(-0.28, 0.10)
Hedges' P-value		0.3370

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	18	19
Mean (SD)	75.93 (25.06)	85.96 (17.70)
Week 8 (MMRM)		
n	19	18
LS mean (SE)	78.05 (5.65)	87.36 (5.80)
95% CI of LS mean	(66.47, 89.64)	(75.46, 99.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.31 (-7.34, 25.97)
Absolute Change at Week 8 (MMRM)		
n	17	18
LS mean (SE)	-0.87 (2.87)	2.05 (2.79)
95% CI of LS mean	(-6.76, 5.02)	(-3.67, 7.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.92 (-5.33, 11.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Week 16 (MMRM)		
n	19	16
LS mean (SE)	75.13 (5.43)	88.82 (5.66)
95% CI of LS mean	(64.05, 86.20)	(77.29, 100.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	13.69 (-2.34, 29.72)
Absolute Change at Week 16 (MMRM)		
n	17	16
LS mean (SE)	-3.48 (2.74)	3.73 (2.83)
95% CI of LS mean	(-9.08, 2.12)	(-2.04, 9.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.21 (-0.88, 15.30)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	74.54 (5.61)	85.20 (5.89)
95% CI of LS mean	(63.06, 86.03)	(73.16, 97.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.65 (-6.02, 27.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 24 (MMRM)		
n	17	16
LS mean (SE)	-3.48 (4.28)	0.03 (4.35)
95% CI of LS mean	(-12.22, 5.25)	(-8.83, 8.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.51 (-8.96, 15.98)
Week 52		
n	20	16
Mean (SD)	75.00 (23.60)	88.89 (16.73)
Absolute Change at Week 52		
n	18	16
Mean (SD)	-1.23 (17.42)	4.17 (13.38)
Week 52 (MMRM)		
n	19	15
LS mean (SE)	75.71 (4.79)	90.06 (5.14)
95% CI of LS mean	(65.93, 85.50)	(79.61, 100.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.35 (-0.02, 28.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 52 (MMRM)		
n	17	15
LS mean (SE)	-2.83 (3.91)	5.15 (4.13)
95% CI of LS mean	(-10.90, 5.25)	(-3.34, 13.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.97 (-3.77, 19.72)
Absolute Change through Week 52 (MMRM)		
n	17	17
LS mean (SE)	-3.26 (3.12)	2.97 (3.19)
95% CI of LS mean	(-9.64, 3.11)	(-3.53, 9.47)
P-value within Treatment	0.3035	0.3595
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.23 (-2.91, 15.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1745
Hedges' G (SE)		0.47 (0.34)
Hedges' 95% CI		(-0.22, 1.16)
Hedges' P-value		0.1780

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Baseline		
n	23	22
Mean (SD)	77.78 (20.38)	85.86 (16.51)
Week 8 (MMRM)		
n	23	23
LS mean (SE)	80.86 (3.56)	80.98 (3.56)
95% CI of LS mean	(73.66, 88.05)	(73.79, 88.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.12 (-10.07, 10.32)
Absolute Change at Week 8 (MMRM)		
n	23	22
LS mean (SE)	2.84 (2.30)	-4.48 (2.36)
95% CI of LS mean	(-1.82, 7.50)	(-9.25, 0.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.32 (-14.00, -0.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Week 16 (MMRM)		
n	23	23
LS mean (SE)	85.20 (3.14)	83.40 (3.14)
95% CI of LS mean	(78.86, 91.55)	(77.05, 89.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.81 (-10.80, 7.19)
Absolute Change at Week 16 (MMRM)		
n	23	22
LS mean (SE)	7.19 (3.16)	-1.96 (3.23)
95% CI of LS mean	(0.82, 13.55)	(-8.47, 4.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.14 (-18.26, -0.03)
Week 24 (MMRM)		
n	23	22
LS mean (SE)	84.24 (3.57)	84.69 (3.60)
95% CI of LS mean	(77.03, 91.44)	(77.42, 91.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-9.80, 10.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 24 (MMRM)		
n	23	22
LS mean (SE)	6.22 (2.39)	-0.44 (2.44)
95% CI of LS mean	(1.39, 11.05)	(-5.38, 4.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.66 (-13.59, 0.26)
Week 52		
n	23	23
Mean (SD)	85.02 (14.06)	85.02 (18.23)
Absolute Change at Week 52		
n	23	22
Mean (SD)	7.25 (13.65)	0.00 (14.95)
Week 52 (MMRM)		
n	23	23
LS mean (SE)	85.20 (3.51)	84.84 (3.51)
95% CI of LS mean	(78.13, 92.28)	(77.77, 91.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-10.39, 9.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 52 (MMRM)		
n	23	22
LS mean (SE)	7.19 (2.93)	0.06 (2.99)
95% CI of LS mean	(1.27, 13.10)	(-5.98, 6.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.12 (-15.59, 1.34)
Absolute Change through Week 52 (MMRM)		
n	23	22
LS mean (SE)	6.86 (2.20)	-0.78 (2.25)
95% CI of LS mean	(2.41, 11.32)	(-5.33, 3.77)
P-value within Treatment	0.0034	0.7312
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.64 (-14.02, -1.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0201
Hedges' G (SE)		-0.71 (0.30)
Hedges' 95% CI		(-1.32, -0.10)
Hedges' P-value		0.0234

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	20
Mean (SD)	81.31 (22.06)	81.11 (20.42)
Week 8 (MMRM)		
n	20	17
LS mean (SE)	85.79 (4.37)	80.54 (4.66)
95% CI of LS mean	(76.90, 94.68)	(71.05, 90.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.25 (-18.45, 7.95)
Absolute Change at Week 8 (MMRM)		
n	20	17
LS mean (SE)	4.70 (3.38)	-0.94 (3.63)
95% CI of LS mean	(-2.18, 11.58)	(-8.32, 6.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.65 (-15.87, 4.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Week 16 (MMRM)		
n	20	17
LS mean (SE)	83.57 (3.76)	82.28 (4.03)
95% CI of LS mean	(75.91, 91.23)	(74.08, 90.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.29 (-12.74, 10.17)
Absolute Change at Week 16 (MMRM)		
n	20	17
LS mean (SE)	2.48 (3.00)	1.11 (3.24)
95% CI of LS mean	(-3.62, 8.58)	(-5.47, 7.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.37 (-10.52, 7.79)
Week 24 (MMRM)		
n	20	16
LS mean (SE)	84.68 (4.27)	83.53 (4.63)
95% CI of LS mean	(75.99, 93.37)	(74.12, 92.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.15 (-14.16, 11.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 24 (MMRM)		
n	20	16
LS mean (SE)	3.59 (3.23)	2.27 (3.55)
95% CI of LS mean	(-2.97, 10.15)	(-4.93, 9.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.32 (-11.21, 8.58)
Week 52		
n	22	17
Mean (SD)	86.87 (17.02)	77.12 (22.04)
Absolute Change at Week 52		
n	22	17
Mean (SD)	5.56 (15.99)	-2.61 (11.47)
Week 52 (MMRM)		
n	20	15
LS mean (SE)	86.90 (3.64)	78.38 (4.04)
95% CI of LS mean	(79.47, 94.33)	(70.16, 86.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.52 (-19.81, 2.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	5.81 (3.33)	-2.74 (3.76)
95% CI of LS mean	(-1.01, 12.63)	(-10.42, 4.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.55 (-18.96, 1.86)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	3.96 (2.71)	0.21 (2.95)
95% CI of LS mean	(-1.56, 9.48)	(-5.78, 6.21)
P-value within Treatment	0.1535	0.9426
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.75 (-12.09, 4.59)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3675
Hedges' G (SE)		-0.30 (0.32)
Hedges' 95% CI		(-0.96, 0.36)
Hedges' P-value		0.3587

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Baseline		
n	243	237
Mean (SD)	80.61 (17.44)	82.37 (18.74)
Week 8 (MMRM)		
n	240	234
LS mean (SE)	80.56 (1.21)	81.16 (1.22)
95% CI of LS mean	(78.18, 82.93)	(78.75, 83.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.60 (-2.79, 3.98)
Absolute Change at Week 8 (MMRM)		
n	233	231
LS mean (SE)	-0.13 (0.95)	-1.24 (0.95)
95% CI of LS mean	(-1.98, 1.73)	(-3.11, 0.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.12 (-3.75, 1.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Week 16 (MMRM)		
n	236	230
LS mean (SE)	80.14 (1.21)	81.94 (1.23)
95% CI of LS mean	(77.75, 82.52)	(79.52, 84.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.80 (-1.60, 5.20)
Absolute Change at Week 16 (MMRM)		
n	229	227
LS mean (SE)	-0.52 (0.98)	-0.54 (0.98)
95% CI of LS mean	(-2.44, 1.41)	(-2.47, 1.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.02 (-2.75, 2.70)
Week 24 (MMRM)		
n	237	226
LS mean (SE)	80.13 (1.29)	80.05 (1.31)
95% CI of LS mean	(77.60, 82.66)	(77.49, 82.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-3.68, 3.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 24 (MMRM)		
n	230	223
LS mean (SE)	-0.40 (0.98)	-2.42 (0.99)
95% CI of LS mean	(-2.33, 1.52)	(-4.37, -0.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.02 (-4.76, 0.72)
Week 52		
n	241	224
Mean (SD)	78.61 (20.80)	79.61 (19.27)
Absolute Change at Week 52		
n	234	220
Mean (SD)	-1.85 (15.62)	-2.73 (16.63)
Week 52 (MMRM)		
n	235	221
LS mean (SE)	78.41 (1.30)	79.79 (1.33)
95% CI of LS mean	(75.85, 80.97)	(77.18, 82.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.38 (-2.28, 5.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 52 (MMRM)		
n	228	217
LS mean (SE)	-2.22 (1.07)	-2.65 (1.09)
95% CI of LS mean	(-4.33, -0.12)	(-4.80, -0.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-3.43, 2.58)
Absolute Change through Week 52 (MMRM)		
n	233	229
LS mean (SE)	-1.05 (0.84)	-1.87 (0.85)
95% CI of LS mean	(-2.70, 0.60)	(-3.54, -0.21)
P-value within Treatment	0.2122	0.0276
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.82 (-3.17, 1.52)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4899
Hedges' G (SE)		-0.06 (0.09)
Hedges' 95% CI		(-0.25, 0.12)
Hedges' P-value		0.4898

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Baseline		
n	39	43
Mean (SD)	84.05 (15.04)	80.36 (16.42)
Week 8 (MMRM)		
n	37	39
LS mean (SE)	86.22 (2.86)	81.38 (2.76)
95% CI of LS mean	(80.52, 91.93)	(75.87, 86.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.85 (-12.87, 3.18)
Absolute Change at Week 8 (MMRM)		
n	37	39
LS mean (SE)	1.89 (2.49)	2.55 (2.41)
95% CI of LS mean	(-3.08, 6.87)	(-2.25, 7.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.66 (-6.34, 7.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Week 16 (MMRM)		
n	36	38
LS mean (SE)	86.24 (2.73)	76.55 (2.64)
95% CI of LS mean	(80.79, 91.68)	(71.28, 81.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.69 (-17.38, -2.00)
Absolute Change at Week 16 (MMRM)		
n	36	38
LS mean (SE)	1.89 (2.60)	-2.41 (2.52)
95% CI of LS mean	(-3.31, 7.08)	(-7.44, 2.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.30 (-11.62, 3.02)
Week 24 (MMRM)		
n	36	39
LS mean (SE)	87.38 (2.52)	79.70 (2.44)
95% CI of LS mean	(82.35, 92.41)	(74.84, 84.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.69 (-14.81, -0.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 24 (MMRM)		
n	36	39
LS mean (SE)	2.94 (2.45)	0.67 (2.36)
95% CI of LS mean	(-1.94, 7.81)	(-4.04, 5.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.27 (-9.15, 4.62)
Week 52		
n	36	40
Mean (SD)	86.11 (15.34)	80.83 (18.14)
Absolute Change at Week 52		
n	36	40
Mean (SD)	0.93 (16.45)	-0.83 (13.17)
Week 52 (MMRM)		
n	34	37
LS mean (SE)	84.45 (2.88)	80.49 (2.77)
95% CI of LS mean	(78.70, 90.20)	(74.96, 86.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.96 (-12.05, 4.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 52 (MMRM)		
n	34	37
LS mean (SE)	0.13 (2.53)	1.33 (2.43)
95% CI of LS mean	(-4.91, 5.17)	(-3.52, 6.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.20 (-5.89, 8.29)
Absolute Change through Week 52 (MMRM)		
n	37	39
LS mean (SE)	1.65 (2.26)	-0.14 (2.18)
95% CI of LS mean	(-2.85, 6.15)	(-4.49, 4.22)
P-value within Treatment	0.4668	0.9504
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.79 (-8.16, 4.58)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5776
Hedges' G (SE)		-0.13 (0.23)
Hedges' 95% CI		(-0.58, 0.32)
Hedges' P-value		0.5712

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Baseline		
n	219	219
Mean (SD)	80.72 (17.85)	82.19 (18.53)
Week 8 (MMRM)		
n	215	214
LS mean (SE)	81.01 (1.27)	81.82 (1.26)
95% CI of LS mean	(78.53, 83.50)	(79.34, 84.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-2.71, 4.33)
Absolute Change at Week 8 (MMRM)		
n	210	212
LS mean (SE)	0.22 (1.01)	-0.46 (1.01)
95% CI of LS mean	(-1.77, 2.22)	(-2.44, 1.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.68 (-3.49, 2.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Week 16 (MMRM)		
n	210	212
LS mean (SE)	80.36 (1.27)	81.80 (1.26)
95% CI of LS mean	(77.87, 82.85)	(79.31, 84.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.44 (-2.08, 4.96)
Absolute Change at Week 16 (MMRM)		
n	205	210
LS mean (SE)	-0.34 (1.07)	-0.48 (1.06)
95% CI of LS mean	(-2.45, 1.76)	(-2.57, 1.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.14 (-3.10, 2.82)
Week 24 (MMRM)		
n	212	211
LS mean (SE)	79.83 (1.35)	80.59 (1.35)
95% CI of LS mean	(77.18, 82.49)	(77.93, 83.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.76 (-3.00, 4.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 24 (MMRM)		
n	207	208
LS mean (SE)	-0.74 (1.06)	-1.72 (1.06)
95% CI of LS mean	(-2.82, 1.35)	(-3.80, 0.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.98 (-3.93, 1.96)
Week 52		
n	212	208
Mean (SD)	78.83 (21.23)	79.75 (18.99)
Absolute Change at Week 52		
n	207	205
Mean (SD)	-1.72 (16.22)	-2.38 (16.95)
Week 52 (MMRM)		
n	207	205
LS mean (SE)	78.44 (1.38)	79.99 (1.38)
95% CI of LS mean	(75.72, 81.16)	(77.27, 82.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-2.30, 5.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
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Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 52 (MMRM)		
n	202	202
LS mean (SE)	-2.25 (1.16)	-2.28 (1.16)
95% CI of LS mean	(-4.53, 0.04)	(-4.56, 0.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.03 (-3.26, 3.20)
Absolute Change through Week 52 (MMRM)		
n	210	212
LS mean (SE)	-1.11 (0.92)	-1.49 (0.91)
95% CI of LS mean	(-2.92, 0.70)	(-3.29, 0.30)
P-value within Treatment	0.2276	0.1027
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-2.93, 2.16)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7672
Hedges' G (SE)		-0.03 (0.10)
Hedges' 95% CI		(-0.22, 0.16)
Hedges' P-value		0.7670

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	18	19
Mean (SD)	81.48 (14.76)	81.87 (19.32)
Week 8 (MMRM)		
n	19	18
LS mean (SE)	86.51 (3.71)	77.82 (3.81)
95% CI of LS mean	(78.97, 94.06)	(70.07, 85.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.69 (-19.55, 2.17)
Absolute Change at Week 8 (MMRM)		
n	17	18
LS mean (SE)	4.26 (3.44)	-2.79 (3.34)
95% CI of LS mean	(-2.76, 11.29)	(-9.62, 4.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.06 (-16.89, 2.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Week 16 (MMRM)		
n	19	16
LS mean (SE)	83.00 (4.37)	80.57 (4.64)
95% CI of LS mean	(74.08, 91.92)	(71.13, 90.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.43 (-15.45, 10.58)
Absolute Change at Week 16 (MMRM)		
n	17	16
LS mean (SE)	-0.31 (3.15)	-0.67 (3.27)
95% CI of LS mean	(-6.75, 6.13)	(-7.32, 5.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-9.68, 8.96)
Week 24 (MMRM)		
n	18	16
LS mean (SE)	87.50 (4.70)	77.76 (4.89)
95% CI of LS mean	(77.93, 97.06)	(67.84, 87.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.74 (-23.55, 4.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 24 (MMRM)		
n	16	16
LS mean (SE)	4.85 (3.84)	-2.99 (3.79)
95% CI of LS mean	(-2.99, 12.69)	(-10.72, 4.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.84 (-18.89, 3.20)
Week 52		
n	20	16
Mean (SD)	80.00 (19.61)	79.17 (21.80)
Absolute Change at Week 52		
n	18	16
Mean (SD)	-3.09 (17.80)	-5.56 (11.48)
Week 52 (MMRM)		
n	19	15
LS mean (SE)	80.08 (4.94)	78.60 (5.34)
95% CI of LS mean	(69.99, 90.17)	(67.75, 89.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.48 (-16.32, 13.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 52 (MMRM)		
n	17	15
LS mean (SE)	-3.58 (3.75)	-2.46 (3.97)
95% CI of LS mean	(-11.25, 4.10)	(-10.56, 5.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.12 (-10.09, 12.32)
Absolute Change through Week 52 (MMRM)		
n	17	17
LS mean (SE)	0.32 (2.74)	-2.04 (2.78)
95% CI of LS mean	(-5.29, 5.93)	(-7.70, 3.62)
P-value within Treatment	0.9077	0.4681
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.36 (-10.40, 5.67)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5532
Hedges' G (SE)		-0.20 (0.34)
Hedges' 95% CI		(-0.89, 0.48)
Hedges' P-value		0.5507

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Baseline		
n	23	22
Mean (SD)	78.26 (12.30)	82.32 (14.81)
Week 8 (MMRM)		
n	23	23
LS mean (SE)	77.56 (3.56)	77.52 (3.56)
95% CI of LS mean	(70.36, 84.75)	(70.32, 84.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-10.25, 10.16)
Absolute Change at Week 8 (MMRM)		
n	23	22
LS mean (SE)	-0.57 (2.26)	-4.46 (2.31)
95% CI of LS mean	(-5.14, 4.01)	(-9.13, 0.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.89 (-10.44, 2.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Week 16 (MMRM)		
n	23	23
LS mean (SE)	78.04 (3.52)	76.55 (3.52)
95% CI of LS mean	(70.93, 85.15)	(69.44, 83.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.49 (-11.57, 8.59)
Absolute Change at Week 16 (MMRM)		
n	23	22
LS mean (SE)	-0.08 (2.22)	-5.47 (2.27)
95% CI of LS mean	(-4.57, 4.40)	(-10.06, -0.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.39 (-11.82, 1.04)
Week 24 (MMRM)		
n	23	22
LS mean (SE)	79.97 (3.36)	75.60 (3.38)
95% CI of LS mean	(73.18, 86.76)	(68.77, 82.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.38 (-14.03, 5.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 24 (MMRM)		
n	23	22
LS mean (SE)	1.85 (2.33)	-6.48 (2.39)
95% CI of LS mean	(-2.86, 6.56)	(-11.30, -1.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.33 (-15.08, -1.57)
Week 52		
n	23	23
Mean (SD)	77.29 (15.16)	77.29 (19.67)
Absolute Change at Week 52		
n	23	22
Mean (SD)	-0.97 (9.42)	-4.55 (11.71)
Week 52 (MMRM)		
n	23	23
LS mean (SE)	77.07 (3.75)	77.52 (3.75)
95% CI of LS mean	(69.52, 84.63)	(69.96, 85.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.44 (-10.27, 11.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 52 (MMRM)		
n	23	22
LS mean (SE)	-1.05 (2.24)	-4.46 (2.29)
95% CI of LS mean	(-5.57, 3.47)	(-9.08, 0.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.41 (-9.88, 3.06)
Absolute Change through Week 52 (MMRM)		
n	23	22
LS mean (SE)	0.24 (1.95)	-5.47 (1.99)
95% CI of LS mean	(-3.70, 4.18)	(-9.49, -1.44)
P-value within Treatment	0.9027	0.0090
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.71 (-11.35, -0.06)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0475
Hedges' G (SE)		-0.60 (0.30)
Hedges' 95% CI		(-1.20, 0.00)
Hedges' P-value		0.0515

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	20
Mean (SD)	87.37 (15.45)	80.56 (20.67)
Week 8 (MMRM)		
n	20	18
LS mean (SE)	83.42 (4.88)	82.00 (5.15)
95% CI of LS mean	(73.53, 93.31)	(71.57, 92.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.41 (-15.93, 13.10)
Absolute Change at Week 8 (MMRM)		
n	20	18
LS mean (SE)	-4.73 (3.91)	4.64 (4.13)
95% CI of LS mean	(-12.66, 3.21)	(-3.74, 13.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.36 (-2.33, 21.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Week 16 (MMRM)		
n	20	17
LS mean (SE)	88.42 (4.54)	80.30 (4.86)
95% CI of LS mean	(79.20, 97.64)	(70.44, 90.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.12 (-21.76, 5.52)
Absolute Change at Week 16 (MMRM)		
n	20	17
LS mean (SE)	0.27 (4.00)	2.79 (4.31)
95% CI of LS mean	(-7.87, 8.41)	(-5.96, 11.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.52 (-9.59, 14.62)
Week 24 (MMRM)		
n	20	16
LS mean (SE)	89.53 (3.50)	82.36 (3.78)
95% CI of LS mean	(82.38, 96.68)	(74.66, 90.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.17 (-17.85, 3.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 24 (MMRM)		
n	20	16
LS mean (SE)	1.38 (3.27)	3.92 (3.56)
95% CI of LS mean	(-5.27, 8.04)	(-3.31, 11.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.54 (-7.46, 12.54)
Week 52		
n	22	17
Mean (SD)	88.89 (14.14)	84.31 (17.59)
Absolute Change at Week 52		
n	22	17
Mean (SD)	1.52 (15.06)	2.61 (14.45)
Week 52 (MMRM)		
n	20	15
LS mean (SE)	88.97 (3.45)	83.72 (3.83)
95% CI of LS mean	(81.92, 96.03)	(75.93, 91.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.25 (-15.93, 5.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	0.83 (3.48)	5.45 (3.89)
95% CI of LS mean	(-6.24, 7.90)	(-2.45, 13.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.62 (-6.13, 15.38)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	0.83 (3.23)	4.05 (3.50)
95% CI of LS mean	(-5.76, 7.41)	(-3.06, 11.17)
P-value within Treatment	0.7995	0.2548
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.23 (-6.64, 13.09)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5110
Hedges' G (SE)		0.22 (0.32)
Hedges' 95% CI		(-0.44, 0.88)
Hedges' P-value		0.5044

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Baseline		
n	243	237
Mean (SD)	93.03 (14.22)	94.37 (11.82)
Week 8 (MMRM)		
n	240	235
LS mean (SE)	92.43 (0.85)	94.29 (0.86)
95% CI of LS mean	(90.75, 94.10)	(92.60, 95.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.86 (-0.52, 4.24)
Absolute Change at Week 8 (MMRM)		
n	233	232
LS mean (SE)	-0.22 (0.70)	-0.11 (0.70)
95% CI of LS mean	(-1.60, 1.16)	(-1.49, 1.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-1.85, 2.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Week 16 (MMRM)		
n	236	230
LS mean (SE)	92.67 (0.88)	93.64 (0.89)
95% CI of LS mean	(90.95, 94.40)	(91.90, 95.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-1.48, 3.42)
Absolute Change at Week 16 (MMRM)		
n	229	227
LS mean (SE)	0.05 (0.71)	-0.78 (0.72)
95% CI of LS mean	(-1.36, 1.45)	(-2.19, 0.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.83 (-2.82, 1.16)
Week 24 (MMRM)		
n	238	226
LS mean (SE)	92.66 (0.96)	92.90 (0.98)
95% CI of LS mean	(90.77, 94.55)	(90.97, 94.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-2.46, 2.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 24 (MMRM)		
n	231	223
LS mean (SE)	-0.06 (0.80)	-1.52 (0.82)
95% CI of LS mean	(-1.64, 1.52)	(-3.12, 0.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.47 (-3.71, 0.78)
Week 52		
n	241	224
Mean (SD)	92.81 (15.16)	94.05 (12.04)
Absolute Change at Week 52		
n	234	220
Mean (SD)	0.02 (13.11)	-0.56 (10.58)
Week 52 (MMRM)		
n	235	221
LS mean (SE)	92.85 (0.89)	93.93 (0.91)
95% CI of LS mean	(91.09, 94.60)	(92.14, 95.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.08 (-1.42, 3.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 52 (MMRM)		
n	228	217
LS mean (SE)	0.04 (0.79)	-0.49 (0.81)
95% CI of LS mean	(-1.52, 1.60)	(-2.08, 1.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-2.76, 1.70)
Absolute Change through Week 52 (MMRM)		
n	233	229
LS mean (SE)	0.01 (0.59)	-0.93 (0.60)
95% CI of LS mean	(-1.16, 1.18)	(-2.11, 0.25)
P-value within Treatment	0.9867	0.1215
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.94 (-2.60, 0.72)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2657
Hedges' G (SE)		-0.10 (0.09)
Hedges' 95% CI		(-0.29, 0.08)
Hedges' P-value		0.2658

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Baseline		
n	39	43
Mean (SD)	91.17 (15.96)	93.41 (12.73)
Week 8 (MMRM)		
n	37	39
LS mean (SE)	93.84 (2.86)	92.17 (2.75)
95% CI of LS mean	(88.15, 99.54)	(86.69, 97.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.67 (-9.70, 6.35)
Absolute Change at Week 8 (MMRM)		
n	37	39
LS mean (SE)	2.92 (2.01)	-0.76 (1.93)
95% CI of LS mean	(-1.08, 6.93)	(-4.62, 3.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.68 (-9.33, 1.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Week 16 (MMRM)		
n	37	38
LS mean (SE)	92.94 (3.28)	89.80 (3.20)
95% CI of LS mean	(86.40, 99.48)	(83.43, 96.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.15 (-12.38, 6.09)
Absolute Change at Week 16 (MMRM)		
n	37	38
LS mean (SE)	2.02 (2.83)	-3.11 (2.77)
95% CI of LS mean	(-3.62, 7.66)	(-8.63, 2.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.14 (-13.09, 2.82)
Week 24 (MMRM)		
n	36	39
LS mean (SE)	91.93 (3.10)	90.08 (2.98)
95% CI of LS mean	(85.76, 98.10)	(84.14, 96.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.85 (-10.53, 6.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 24 (MMRM)		
n	36	39
LS mean (SE)	1.03 (2.09)	-2.89 (2.01)
95% CI of LS mean	(-3.13, 5.19)	(-6.89, 1.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.92 (-9.79, 1.94)
Week 52		
n	36	41
Mean (SD)	93.83 (13.40)	89.70 (19.47)
Absolute Change at Week 52		
n	36	41
Mean (SD)	3.40 (14.26)	-3.66 (15.19)
Week 52 (MMRM)		
n	34	38
LS mean (SE)	93.56 (2.89)	89.82 (2.76)
95% CI of LS mean	(87.80, 99.32)	(84.31, 95.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.75 (-11.85, 4.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 52 (MMRM)		
n	34	38
LS mean (SE)	2.71 (2.53)	-3.06 (2.42)
95% CI of LS mean	(-2.35, 7.76)	(-7.89, 1.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.77 (-12.84, 1.29)
Absolute Change through Week 52 (MMRM)		
n	37	39
LS mean (SE)	1.92 (2.11)	-3.02 (2.04)
95% CI of LS mean	(-2.29, 6.12)	(-7.08, 1.03)
P-value within Treatment	0.3659	0.1419
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.94 (-10.88, 0.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1014
Hedges' G (SE)		-0.38 (0.23)
Hedges' 95% CI		(-0.84, 0.07)
Hedges' P-value		0.0990

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Baseline		
n	219	219
Mean (SD)	93.71 (13.37)	94.29 (11.60)
Week 8 (MMRM)		
n	215	215
LS mean (SE)	92.81 (0.89)	94.15 (0.89)
95% CI of LS mean	(91.06, 94.55)	(92.41, 95.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-1.12, 3.81)
Absolute Change at Week 8 (MMRM)		
n	210	213
LS mean (SE)	-0.45 (0.74)	-0.08 (0.73)
95% CI of LS mean	(-1.90, 1.01)	(-1.53, 1.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-1.69, 2.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Week 16 (MMRM)		
n	211	212
LS mean (SE)	93.47 (0.89)	93.36 (0.89)
95% CI of LS mean	(91.72, 95.21)	(91.62, 95.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.10 (-2.57, 2.36)
Absolute Change at Week 16 (MMRM)		
n	206	210
LS mean (SE)	0.11 (0.78)	-0.87 (0.77)
95% CI of LS mean	(-1.42, 1.65)	(-2.39, 0.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.98 (-3.14, 1.18)
Week 24 (MMRM)		
n	212	211
LS mean (SE)	92.95 (1.04)	92.18 (1.04)
95% CI of LS mean	(90.91, 94.98)	(90.14, 94.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.77 (-3.65, 2.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 24 (MMRM)		
n	207	208
LS mean (SE)	-0.40 (0.89)	-2.08 (0.89)
95% CI of LS mean	(-2.15, 1.36)	(-3.83, -0.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.68 (-4.16, 0.80)
Week 52		
n	212	209
Mean (SD)	92.82 (15.23)	93.57 (12.87)
Absolute Change at Week 52		
n	207	206
Mean (SD)	-0.48 (14.08)	-0.89 (11.53)
Week 52 (MMRM)		
n	207	206
LS mean (SE)	92.81 (0.96)	93.59 (0.96)
95% CI of LS mean	(90.93, 94.70)	(91.70, 95.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.77 (-1.89, 3.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 52 (MMRM)		
n	202	203
LS mean (SE)	-0.64 (0.90)	-0.68 (0.90)
95% CI of LS mean	(-2.41, 1.13)	(-2.45, 1.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-2.55, 2.45)
Absolute Change through Week 52 (MMRM)		
n	210	212
LS mean (SE)	-0.31 (0.67)	-1.21 (0.66)
95% CI of LS mean	(-1.62, 1.01)	(-2.52, 0.10)
P-value within Treatment	0.6452	0.0692
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.90 (-2.76, 0.95)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3388
Hedges' G (SE)		-0.09 (0.10)
Hedges' 95% CI		(-0.28, 0.10)
Hedges' P-value		0.3386

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	18	19
Mean (SD)	87.04 (17.98)	90.06 (14.77)
Week 8 (MMRM)		
n	19	18
LS mean (SE)	89.95 (3.86)	91.47 (3.96)
95% CI of LS mean	(82.10, 97.81)	(83.40, 99.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-9.77, 12.80)
Absolute Change at Week 8 (MMRM)		
n	17	18
LS mean (SE)	1.77 (1.87)	2.03 (1.82)
95% CI of LS mean	(-2.04, 5.59)	(-1.68, 5.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-5.08, 5.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Week 16 (MMRM)		
n	19	16
LS mean (SE)	88.20 (3.86)	93.58 (4.01)
95% CI of LS mean	(80.33, 96.07)	(85.41, 101.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.38 (-6.00, 16.75)
Absolute Change at Week 16 (MMRM)		
n	17	16
LS mean (SE)	1.12 (1.64)	3.81 (1.67)
95% CI of LS mean	(-2.23, 4.47)	(0.42, 7.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.69 (-2.10, 7.48)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	89.37 (3.77)	92.14 (3.91)
95% CI of LS mean	(81.68, 97.06)	(84.17, 100.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.77 (-8.33, 13.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 24 (MMRM)		
n	17	16
LS mean (SE)	1.12 (1.67)	2.36 (1.69)
95% CI of LS mean	(-2.30, 4.54)	(-1.10, 5.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-3.64, 6.12)
Week 52		
n	20	16
Mean (SD)	91.67 (13.90)	91.67 (13.76)
Absolute Change at Week 52		
n	18	16
Mean (SD)	3.70 (8.52)	0.00 (8.11)
Week 52 (MMRM)		
n	19	15
LS mean (SE)	91.71 (3.31)	91.27 (3.49)
95% CI of LS mean	(84.96, 98.46)	(84.16, 98.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-10.27, 9.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 52 (MMRM)		
n	17	15
LS mean (SE)	3.73 (1.76)	1.72 (1.90)
95% CI of LS mean	(0.13, 7.34)	(-2.15, 5.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.02 (-7.33, 3.30)
Absolute Change through Week 52 (MMRM)		
n	17	17
LS mean (SE)	1.99 (1.25)	2.63 (1.28)
95% CI of LS mean	(-0.57, 4.55)	(0.02, 5.24)
P-value within Treatment	0.1222	0.0485
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-3.05, 4.32)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7266
Hedges' G (SE)		0.12 (0.34)
Hedges' 95% CI		(-0.56, 0.80)
Hedges' P-value		0.7245

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Baseline		
n	23	22
Mean (SD)	91.55 (15.34)	96.97 (8.53)
Week 8 (MMRM)		
n	23	23
LS mean (SE)	90.97 (2.92)	95.50 (2.92)
95% CI of LS mean	(85.07, 96.86)	(89.61, 101.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.53 (-3.82, 12.89)
Absolute Change at Week 8 (MMRM)		
n	23	22
LS mean (SE)	-0.71 (2.17)	-1.53 (2.22)
95% CI of LS mean	(-5.09, 3.67)	(-6.01, 2.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.82 (-7.10, 5.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Week 16 (MMRM)		
n	23	23
LS mean (SE)	89.04 (4.11)	91.16 (4.11)
95% CI of LS mean	(80.75, 97.33)	(82.87, 99.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-9.62, 13.86)
Absolute Change at Week 16 (MMRM)		
n	23	22
LS mean (SE)	-2.64 (3.60)	-5.57 (3.68)
95% CI of LS mean	(-9.90, 4.62)	(-12.99, 1.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.93 (-13.32, 7.46)
Week 24 (MMRM)		
n	23	22
LS mean (SE)	89.52 (2.82)	96.21 (2.84)
95% CI of LS mean	(83.83, 95.21)	(90.47, 101.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.69 (-1.42, 14.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 24 (MMRM)		
n	23	22
LS mean (SE)	-2.16 (1.49)	-0.52 (1.52)
95% CI of LS mean	(-5.16, 0.84)	(-3.59, 2.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-2.67, 5.95)
Week 52		
n	23	23
Mean (SD)	91.79 (16.82)	95.65 (10.45)
Absolute Change at Week 52		
n	23	22
Mean (SD)	0.24 (5.92)	-1.01 (11.83)
Week 52 (MMRM)		
n	23	23
LS mean (SE)	91.94 (2.94)	95.50 (2.94)
95% CI of LS mean	(85.99, 97.88)	(89.56, 101.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.57 (-4.86, 12.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 52 (MMRM)		
n	23	22
LS mean (SE)	0.26 (1.97)	-1.03 (2.01)
95% CI of LS mean	(-3.71, 4.22)	(-5.08, 3.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.28 (-6.96, 4.40)
Absolute Change through Week 52 (MMRM)		
n	23	22
LS mean (SE)	-1.52 (1.85)	-2.37 (1.89)
95% CI of LS mean	(-5.24, 2.21)	(-6.19, 1.44)
P-value within Treatment	0.4170	0.2163
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.86 (-6.20, 4.49)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7477
Hedges' G (SE)		-0.10 (0.29)
Hedges' 95% CI		(-0.69, 0.50)
Hedges' P-value		0.7474

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	20
Mean (SD)	89.39 (19.54)	94.44 (15.51)
Week 8 (MMRM)		
n	20	18
LS mean (SE)	94.72 (4.46)	92.90 (4.71)
95% CI of LS mean	(85.66, 103.78)	(83.33, 102.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.82 (-15.27, 11.63)
Absolute Change at Week 8 (MMRM)		
n	20	18
LS mean (SE)	5.97 (3.14)	-1.07 (3.31)
95% CI of LS mean	(-0.42, 12.35)	(-7.81, 5.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.04 (-16.50, 2.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Week 16 (MMRM)		
n	20	17
LS mean (SE)	93.05 (4.79)	92.23 (5.10)
95% CI of LS mean	(83.31, 102.79)	(81.86, 102.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.82 (-15.30, 13.65)
Absolute Change at Week 16 (MMRM)		
n	20	17
LS mean (SE)	4.30 (3.12)	-1.74 (3.36)
95% CI of LS mean	(-2.05, 10.65)	(-8.57, 5.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.04 (-15.55, 3.48)
Week 24 (MMRM)		
n	20	16
LS mean (SE)	94.72 (4.42)	92.21 (4.68)
95% CI of LS mean	(85.73, 103.71)	(82.69, 101.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.51 (-15.87, 10.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 24 (MMRM)		
n	20	16
LS mean (SE)	5.97 (3.04)	-1.76 (3.23)
95% CI of LS mean	(-0.22, 12.15)	(-8.32, 4.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.73 (-16.93, 1.48)
Week 52		
n	22	17
Mean (SD)	96.46 (10.51)	89.54 (22.39)
Absolute Change at Week 52		
n	22	17
Mean (SD)	7.07 (12.62)	-3.92 (12.99)
Week 52 (MMRM)		
n	20	15
LS mean (SE)	96.39 (4.03)	89.72 (4.32)
95% CI of LS mean	(88.18, 104.59)	(80.95, 98.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.66 (-18.96, 5.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	7.63 (3.08)	-4.08 (3.34)
95% CI of LS mean	(1.37, 13.89)	(-10.86, 2.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-11.71 (-21.12, -2.31)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	5.97 (2.80)	-2.53 (2.99)
95% CI of LS mean	(0.27, 11.66)	(-8.59, 3.54)
P-value within Treatment	0.0407	0.4034
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.49 (-17.02, 0.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0510
Hedges' G (SE)		-0.67 (0.33)
Hedges' 95% CI		(-1.34, 0.01)
Hedges' P-value		0.0517

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Baseline		
n	243	237
Mean (SD)	81.49 (16.49)	82.62 (17.43)
Week 8 (MMRM)		
n	239	235
LS mean (SE)	82.28 (1.11)	83.03 (1.12)
95% CI of LS mean	(80.11, 84.45)	(80.83, 85.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-2.34, 3.83)
Absolute Change at Week 8 (MMRM)		
n	233	232
LS mean (SE)	0.80 (0.69)	0.44 (0.69)
95% CI of LS mean	(-0.55, 2.15)	(-0.92, 1.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.37 (-2.28, 1.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Week 16 (MMRM)		
n	236	230
LS mean (SE)	82.63 (1.11)	81.91 (1.12)
95% CI of LS mean	(80.46, 84.81)	(79.71, 84.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.72 (-3.81, 2.37)
Absolute Change at Week 16 (MMRM)		
n	229	227
LS mean (SE)	1.39 (0.73)	-0.65 (0.74)
95% CI of LS mean	(-0.05, 2.83)	(-2.10, 0.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.04 (-4.08, 0.01)
Week 24 (MMRM)		
n	237	226
LS mean (SE)	82.07 (1.13)	81.72 (1.14)
95% CI of LS mean	(79.85, 84.28)	(79.47, 83.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.35 (-3.51, 2.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 24 (MMRM)		
n	230	223
LS mean (SE)	0.64 (0.78)	-0.91 (0.79)
95% CI of LS mean	(-0.89, 2.17)	(-2.46, 0.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.56 (-3.73, 0.62)
Week 52		
n	241	224
Mean (SD)	81.58 (17.17)	82.47 (17.73)
Absolute Change at Week 52		
n	234	220
Mean (SD)	-0.06 (14.41)	-0.08 (13.73)
Week 52 (MMRM)		
n	235	221
LS mean (SE)	81.39 (1.13)	82.31 (1.16)
95% CI of LS mean	(79.16, 83.62)	(80.04, 84.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-2.27, 4.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 52 (MMRM)		
n	228	217
LS mean (SE)	-0.17 (0.93)	-0.22 (0.95)
95% CI of LS mean	(-2.00, 1.65)	(-2.08, 1.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.05 (-2.65, 2.56)
Absolute Change through Week 52 (MMRM)		
n	233	229
LS mean (SE)	0.62 (0.67)	-0.59 (0.68)
95% CI of LS mean	(-0.70, 1.94)	(-1.93, 0.74)
P-value within Treatment	0.3581	0.3825
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.21 (-3.09, 0.67)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2055
Hedges' G (SE)		-0.12 (0.09)
Hedges' 95% CI		(-0.30, 0.06)
Hedges' P-value		0.2057

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Baseline		
n	39	43
Mean (SD)	83.82 (15.33)	76.96 (18.99)
Week 8 (MMRM)		
n	37	39
LS mean (SE)	82.58 (2.72)	81.77 (2.62)
95% CI of LS mean	(77.16, 88.00)	(76.56, 86.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.81 (-8.45, 6.84)
Absolute Change at Week 8 (MMRM)		
n	37	39
LS mean (SE)	-0.01 (2.45)	4.57 (2.36)
95% CI of LS mean	(-4.89, 4.87)	(-0.14, 9.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.58 (-2.30, 11.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Week 16 (MMRM)		
n	37	38
LS mean (SE)	81.68 (2.84)	76.71 (2.75)
95% CI of LS mean	(76.01, 87.35)	(71.23, 82.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.97 (-12.98, 3.04)
Absolute Change at Week 16 (MMRM)		
n	37	38
LS mean (SE)	-0.91 (2.53)	-0.43 (2.46)
95% CI of LS mean	(-5.96, 4.14)	(-5.32, 4.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-6.66, 7.62)
Week 24 (MMRM)		
n	36	39
LS mean (SE)	79.52 (2.84)	77.69 (2.74)
95% CI of LS mean	(73.85, 85.19)	(72.23, 83.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.83 (-9.83, 6.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 24 (MMRM)		
n	36	39
LS mean (SE)	-3.08 (2.73)	0.60 (2.63)
95% CI of LS mean	(-8.52, 2.36)	(-4.64, 5.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.68 (-3.98, 11.33)
Week 52		
n	36	41
Mean (SD)	82.38 (15.87)	78.76 (20.91)
Absolute Change at Week 52		
n	36	41
Mean (SD)	-2.31 (10.92)	2.60 (18.69)
Week 52 (MMRM)		
n	34	38
LS mean (SE)	81.85 (3.20)	78.78 (3.06)
95% CI of LS mean	(75.48, 88.22)	(72.68, 84.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.07 (-12.00, 5.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 52 (MMRM)		
n	34	38
LS mean (SE)	-0.83 (2.68)	1.74 (2.57)
95% CI of LS mean	(-6.18, 4.52)	(-3.38, 6.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.57 (-4.93, 10.08)
Absolute Change through Week 52 (MMRM)		
n	37	39
LS mean (SE)	-1.61 (2.33)	0.64 (2.25)
95% CI of LS mean	(-6.26, 3.05)	(-3.85, 5.12)
P-value within Treatment	0.4937	0.7778
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.24 (-4.34, 8.83)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4992
Hedges' G (SE)		0.16 (0.23)
Hedges' 95% CI		(-0.30, 0.61)
Hedges' P-value		0.4917

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Baseline		
n	219	219
Mean (SD)	82.39 (15.37)	81.69 (18.48)
Week 8 (MMRM)		
n	214	215
LS mean (SE)	82.91 (1.16)	82.55 (1.16)
95% CI of LS mean	(80.62, 85.19)	(80.27, 84.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-3.59, 2.87)
Absolute Change at Week 8 (MMRM)		
n	210	213
LS mean (SE)	0.49 (0.79)	0.62 (0.78)
95% CI of LS mean	(-1.06, 2.03)	(-0.91, 2.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-2.04, 2.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Week 16 (MMRM)		
n	211	212
LS mean (SE)	83.19 (1.16)	80.99 (1.16)
95% CI of LS mean	(80.91, 85.48)	(78.71, 83.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.20 (-5.43, 1.03)
Absolute Change at Week 16 (MMRM)		
n	206	210
LS mean (SE)	0.88 (0.82)	-0.87 (0.81)
95% CI of LS mean	(-0.73, 2.49)	(-2.47, 0.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.76 (-4.03, 0.52)
Week 24 (MMRM)		
n	211	211
LS mean (SE)	82.28 (1.20)	81.06 (1.20)
95% CI of LS mean	(79.92, 84.65)	(78.70, 83.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.22 (-4.56, 2.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 24 (MMRM)		
n	206	208
LS mean (SE)	-0.08 (0.90)	-0.85 (0.89)
95% CI of LS mean	(-1.84, 1.68)	(-2.60, 0.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.77 (-3.26, 1.71)
Week 52		
n	212	209
Mean (SD)	81.72 (17.03)	81.70 (18.99)
Absolute Change at Week 52		
n	207	206
Mean (SD)	-1.03 (14.14)	0.21 (14.43)
Week 52 (MMRM)		
n	207	206
LS mean (SE)	81.30 (1.23)	81.71 (1.23)
95% CI of LS mean	(78.88, 83.73)	(79.29, 84.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.41 (-3.02, 3.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 52 (MMRM)		
n	202	203
LS mean (SE)	-1.14 (1.00)	-0.10 (0.99)
95% CI of LS mean	(-3.10, 0.82)	(-2.05, 1.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-1.72, 3.81)
Absolute Change through Week 52 (MMRM)		
n	210	212
LS mean (SE)	-0.11 (0.76)	-0.61 (0.75)
95% CI of LS mean	(-1.60, 1.37)	(-2.08, 0.87)
P-value within Treatment	0.8817	0.4199
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.49 (-2.59, 1.60)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6434
Hedges' G (SE)		-0.05 (0.10)
Hedges' 95% CI		(-0.24, 0.15)
Hedges' P-value		0.6432

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	18	19
Mean (SD)	77.59 (16.40)	82.11 (18.06)
Week 8 (MMRM)		
n	19	18
LS mean (SE)	76.91 (3.47)	85.11 (3.57)
95% CI of LS mean	(69.84, 83.98)	(77.84, 92.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.20 (-1.98, 18.38)
Absolute Change at Week 8 (MMRM)		
n	17	18
LS mean (SE)	-0.01 (2.08)	3.53 (2.02)
95% CI of LS mean	(-4.26, 4.24)	(-0.60, 7.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.53 (-2.43, 9.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Week 16 (MMRM)		
n	19	16
LS mean (SE)	77.61 (4.15)	85.50 (4.34)
95% CI of LS mean	(69.14, 86.09)	(76.66, 94.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.89 (-4.39, 20.16)
Absolute Change at Week 16 (MMRM)		
n	17	16
LS mean (SE)	2.34 (2.50)	4.04 (2.52)
95% CI of LS mean	(-2.76, 7.45)	(-1.10, 9.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.69 (-5.59, 8.97)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	78.32 (3.94)	82.34 (4.13)
95% CI of LS mean	(70.24, 86.39)	(73.89, 90.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.02 (-7.70, 15.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 24 (MMRM)		
n	17	16
LS mean (SE)	1.17 (3.39)	0.28 (3.39)
95% CI of LS mean	(-5.81, 8.14)	(-6.67, 7.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.89 (-10.76, 8.99)
Week 52		
n	20	16
Mean (SD)	79.33 (18.72)	86.67 (14.19)
Absolute Change at Week 52		
n	18	16
Mean (SD)	1.67 (16.89)	3.33 (15.40)
Week 52 (MMRM)		
n	19	15
LS mean (SE)	79.72 (4.19)	84.85 (4.46)
95% CI of LS mean	(71.17, 88.27)	(75.79, 93.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.13 (-7.36, 17.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 52 (MMRM)		
n	17	15
LS mean (SE)	1.95 (4.08)	2.50 (4.12)
95% CI of LS mean	(-6.39, 10.29)	(-5.91, 10.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.54 (-11.31, 12.39)
Absolute Change through Week 52 (MMRM)		
n	17	17
LS mean (SE)	1.82 (2.91)	2.27 (2.89)
95% CI of LS mean	(-4.15, 7.79)	(-3.65, 8.19)
P-value within Treatment	0.5370	0.4389
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.45 (-7.98, 8.88)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9139
Hedges' G (SE)		0.04 (0.33)
Hedges' 95% CI		(-0.65, 0.72)
Hedges' P-value		0.9135

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Baseline		
n	23	22
Mean (SD)	73.41 (22.30)	81.82 (12.71)
Week 8 (MMRM)		
n	23	23
LS mean (SE)	76.37 (3.93)	83.23 (3.93)
95% CI of LS mean	(68.42, 84.31)	(75.29, 91.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.86 (-4.40, 18.12)
Absolute Change at Week 8 (MMRM)		
n	23	22
LS mean (SE)	2.26 (2.14)	2.90 (2.19)
95% CI of LS mean	(-2.07, 6.59)	(-1.52, 7.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-5.57, 6.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Week 16 (MMRM)		
n	23	23
LS mean (SE)	76.55 (3.78)	80.62 (3.78)
95% CI of LS mean	(68.91, 84.19)	(72.98, 88.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.07 (-6.76, 14.90)
Absolute Change at Week 16 (MMRM)		
n	23	22
LS mean (SE)	2.44 (2.88)	0.48 (2.94)
95% CI of LS mean	(-3.38, 8.26)	(-5.48, 6.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.97 (-10.31, 6.37)
Week 24 (MMRM)		
n	23	22
LS mean (SE)	76.55 (3.55)	82.33 (3.56)
95% CI of LS mean	(69.38, 83.72)	(75.14, 89.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.78 (-4.40, 15.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 24 (MMRM)		
n	23	22
LS mean (SE)	2.44 (2.31)	1.99 (2.36)
95% CI of LS mean	(-2.23, 7.11)	(-2.78, 6.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-7.14, 6.24)
Week 52		
n	23	23
Mean (SD)	78.44 (16.97)	80.87 (16.97)
Absolute Change at Week 52		
n	23	22
Mean (SD)	5.04 (12.81)	0.00 (16.46)
Week 52 (MMRM)		
n	23	23
LS mean (SE)	78.98 (3.52)	80.33 (3.52)
95% CI of LS mean	(71.87, 86.09)	(73.22, 87.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-8.73, 11.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 52 (MMRM)		
n	23	22
LS mean (SE)	4.87 (3.18)	0.17 (3.25)
95% CI of LS mean	(-1.55, 11.29)	(-6.39, 6.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.70 (-13.89, 4.50)
Absolute Change through Week 52 (MMRM)		
n	23	22
LS mean (SE)	3.25 (2.47)	0.88 (2.53)
95% CI of LS mean	(-1.75, 8.25)	(-4.23, 6.00)
P-value within Treatment	0.1962	0.7293
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.37 (-9.54, 4.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5076
Hedges' G (SE)		-0.20 (0.29)
Hedges' 95% CI		(-0.79, 0.40)
Hedges' P-value		0.5073

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	20
Mean (SD)	88.30 (15.30)	82.00 (15.00)
Week 8 (MMRM)		
n	20	18
LS mean (SE)	88.62 (3.47)	83.02 (3.66)
95% CI of LS mean	(81.58, 95.66)	(75.58, 90.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.60 (-16.02, 4.82)
Absolute Change at Week 8 (MMRM)		
n	20	18
LS mean (SE)	0.88 (2.62)	1.99 (2.76)
95% CI of LS mean	(-4.43, 6.19)	(-3.62, 7.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.11 (-6.74, 8.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Week 16 (MMRM)		
n	20	17
LS mean (SE)	87.29 (3.05)	78.55 (3.26)
95% CI of LS mean	(81.07, 93.50)	(71.92, 85.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.73 (-18.04, 0.57)
Absolute Change at Week 16 (MMRM)		
n	20	17
LS mean (SE)	-0.45 (2.32)	-2.20 (2.49)
95% CI of LS mean	(-5.17, 4.26)	(-7.27, 2.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.75 (-8.82, 5.32)
Week 24 (MMRM)		
n	20	16
LS mean (SE)	85.62 (3.44)	77.86 (3.72)
95% CI of LS mean	(78.61, 92.62)	(70.29, 85.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.75 (-18.24, 2.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 24 (MMRM)		
n	20	16
LS mean (SE)	-2.12 (2.69)	-3.13 (2.95)
95% CI of LS mean	(-7.60, 3.36)	(-9.13, 2.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.00 (-9.24, 7.23)
Week 52		
n	22	17
Mean (SD)	86.93 (14.49)	81.18 (14.38)
Absolute Change at Week 52		
n	22	17
Mean (SD)	-1.36 (10.22)	-0.39 (14.62)
Week 52 (MMRM)		
n	20	15
LS mean (SE)	87.62 (3.43)	79.91 (3.80)
95% CI of LS mean	(80.63, 94.61)	(72.20, 87.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.71 (-18.29, 2.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	-0.12 (2.90)	-0.96 (3.27)
95% CI of LS mean	(-6.04, 5.79)	(-7.61, 5.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.84 (-9.84, 8.17)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	-0.90 (2.16)	-2.10 (2.34)
95% CI of LS mean	(-5.29, 3.50)	(-6.85, 2.66)
P-value within Treatment	0.6800	0.3768
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.20 (-7.82, 5.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7155
Hedges' G (SE)		-0.12 (0.32)
Hedges' 95% CI		(-0.78, 0.53)
Hedges' P-value		0.7093

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Baseline		
n	243	237
Mean (SD)	80.71 (20.03)	83.05 (19.10)
Week 8 (MMRM)		
n	239	235
LS mean (SE)	79.82 (1.31)	82.12 (1.33)
95% CI of LS mean	(77.24, 82.40)	(79.51, 84.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.30 (-1.38, 5.97)
Absolute Change at Week 8 (MMRM)		
n	233	232
LS mean (SE)	-1.05 (1.04)	-1.25 (1.05)
95% CI of LS mean	(-3.10, 1.00)	(-3.30, 0.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-3.10, 2.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Week 16 (MMRM)		
n	236	230
LS mean (SE)	81.27 (1.25)	83.34 (1.27)
95% CI of LS mean	(78.81, 83.74)	(80.85, 85.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.07 (-1.44, 5.57)
Absolute Change at Week 16 (MMRM)		
n	229	227
LS mean (SE)	0.71 (0.96)	0.05 (0.97)
95% CI of LS mean	(-1.19, 2.60)	(-1.85, 1.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.65 (-3.34, 2.04)
Week 24 (MMRM)		
n	237	226
LS mean (SE)	80.20 (1.32)	82.37 (1.34)
95% CI of LS mean	(77.60, 82.79)	(79.73, 85.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.18 (-1.53, 5.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 24 (MMRM)		
n	230	223
LS mean (SE)	-0.65 (0.99)	-0.80 (1.01)
95% CI of LS mean	(-2.60, 1.30)	(-2.78, 1.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-2.93, 2.62)
Week 52		
n	241	224
Mean (SD)	81.82 (20.25)	84.36 (18.68)
Absolute Change at Week 52		
n	234	220
Mean (SD)	1.31 (16.61)	1.06 (12.61)
Week 52 (MMRM)		
n	235	221
LS mean (SE)	81.81 (1.22)	83.99 (1.24)
95% CI of LS mean	(79.42, 84.21)	(81.54, 86.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.17 (-1.25, 5.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 52 (MMRM)		
n	228	217
LS mean (SE)	1.12 (0.98)	0.68 (1.00)
95% CI of LS mean	(-0.80, 3.04)	(-1.28, 2.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-3.19, 2.30)
Absolute Change through Week 52 (MMRM)		
n	233	229
LS mean (SE)	0.39 (0.79)	-0.02 (0.80)
95% CI of LS mean	(-1.16, 1.94)	(-1.59, 1.54)
P-value within Treatment	0.6188	0.9767
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.42 (-2.62, 1.79)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7109
Hedges' G (SE)		-0.03 (0.09)
Hedges' 95% CI		(-0.22, 0.15)
Hedges' P-value		0.7108

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Baseline		
n	39	43
Mean (SD)	80.34 (22.19)	81.58 (15.67)
Week 8 (MMRM)		
n	37	39
LS mean (SE)	83.32 (2.87)	81.96 (2.77)
95% CI of LS mean	(77.59, 89.04)	(76.43, 87.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.36 (-9.42, 6.71)
Absolute Change at Week 8 (MMRM)		
n	37	39
LS mean (SE)	2.33 (2.32)	1.38 (2.24)
95% CI of LS mean	(-2.29, 6.95)	(-3.09, 5.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-7.44, 5.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Week 16 (MMRM)		
n	37	38
LS mean (SE)	82.53 (3.61)	77.72 (3.51)
95% CI of LS mean	(75.33, 89.72)	(70.73, 84.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.81 (-14.93, 5.31)
Absolute Change at Week 16 (MMRM)		
n	37	38
LS mean (SE)	1.54 (2.79)	-2.66 (2.72)
95% CI of LS mean	(-4.01, 7.10)	(-8.09, 2.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.21 (-12.03, 3.61)
Week 24 (MMRM)		
n	36	39
LS mean (SE)	82.59 (3.01)	79.90 (2.90)
95% CI of LS mean	(76.60, 88.58)	(74.12, 85.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.69 (-11.13, 5.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 24 (MMRM)		
n	36	39
LS mean (SE)	1.63 (2.28)	-0.09 (2.20)
95% CI of LS mean	(-2.91, 6.18)	(-4.47, 4.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.72 (-8.12, 4.68)
Week 52		
n	36	41
Mean (SD)	78.82 (21.35)	84.45 (15.87)
Absolute Change at Week 52		
n	36	41
Mean (SD)	-0.81 (15.33)	3.36 (11.35)
Week 52 (MMRM)		
n	34	38
LS mean (SE)	80.84 (2.81)	82.99 (2.68)
95% CI of LS mean	(75.25, 86.44)	(77.65, 88.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.14 (-5.72, 10.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 52 (MMRM)		
n	34	38
LS mean (SE)	0.02 (2.34)	3.07 (2.22)
95% CI of LS mean	(-4.64, 4.68)	(-1.37, 7.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.04 (-3.47, 9.56)
Absolute Change through Week 52 (MMRM)		
n	37	39
LS mean (SE)	1.07 (1.93)	0.11 (1.86)
95% CI of LS mean	(-2.77, 4.91)	(-3.60, 3.81)
P-value within Treatment	0.5817	0.9550
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.96 (-6.39, 4.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7254
Hedges' G (SE)		-0.08 (0.23)
Hedges' 95% CI		(-0.53, 0.37)
Hedges' P-value		0.7207

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Baseline		
n	219	219
Mean (SD)	82.67 (18.44)	83.82 (17.56)
Week 8 (MMRM)		
n	214	215
LS mean (SE)	81.83 (1.29)	83.17 (1.29)
95% CI of LS mean	(79.29, 84.37)	(80.64, 85.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.34 (-2.25, 4.92)
Absolute Change at Week 8 (MMRM)		
n	210	213
LS mean (SE)	-0.87 (1.09)	-1.07 (1.09)
95% CI of LS mean	(-3.02, 1.28)	(-3.20, 1.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-3.23, 2.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Week 16 (MMRM)		
n	211	212
LS mean (SE)	83.34 (1.26)	84.50 (1.25)
95% CI of LS mean	(80.87, 85.80)	(82.04, 86.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-2.32, 4.65)
Absolute Change at Week 16 (MMRM)		
n	206	210
LS mean (SE)	0.79 (1.03)	0.41 (1.02)
95% CI of LS mean	(-1.23, 2.81)	(-1.59, 2.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.38 (-3.22, 2.46)
Week 24 (MMRM)		
n	211	211
LS mean (SE)	82.04 (1.34)	83.11 (1.33)
95% CI of LS mean	(79.42, 84.67)	(80.48, 85.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.07 (-2.65, 4.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 24 (MMRM)		
n	206	208
LS mean (SE)	-0.66 (1.07)	-0.91 (1.06)
95% CI of LS mean	(-2.76, 1.44)	(-3.00, 1.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.25 (-3.21, 2.71)
Week 52		
n	212	209
Mean (SD)	83.54 (18.45)	84.91 (17.88)
Absolute Change at Week 52		
n	207	206
Mean (SD)	1.04 (16.52)	0.86 (12.77)
Week 52 (MMRM)		
n	207	206
LS mean (SE)	83.54 (1.20)	84.77 (1.20)
95% CI of LS mean	(81.18, 85.89)	(82.41, 87.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-2.11, 4.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 52 (MMRM)		
n	202	203
LS mean (SE)	0.86 (1.03)	0.62 (1.03)
95% CI of LS mean	(-1.17, 2.89)	(-1.40, 2.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-3.11, 2.62)
Absolute Change through Week 52 (MMRM)		
n	210	212
LS mean (SE)	0.33 (0.84)	0.04 (0.84)
95% CI of LS mean	(-1.33, 1.99)	(-1.61, 1.69)
P-value within Treatment	0.6954	0.9639
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-2.63, 2.05)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8061
Hedges' G (SE)		-0.02 (0.10)
Hedges' 95% CI		(-0.21, 0.17)
Hedges' P-value		0.8059

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	18	19
Mean (SD)	72.45 (24.64)	82.77 (20.37)
Week 8 (MMRM)		
n	19	18
LS mean (SE)	72.81 (5.07)	86.47 (5.21)
95% CI of LS mean	(62.45, 83.18)	(75.82, 97.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	13.66 (-1.24, 28.56)
Absolute Change at Week 8 (MMRM)		
n	17	18
LS mean (SE)	-1.50 (4.08)	4.16 (3.96)
95% CI of LS mean	(-9.84, 6.84)	(-3.94, 12.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.67 (-6.00, 17.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Week 16 (MMRM)		
n	19	16
LS mean (SE)	76.76 (4.62)	87.17 (4.89)
95% CI of LS mean	(67.35, 86.17)	(77.24, 97.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.42 (-3.31, 24.14)
Absolute Change at Week 16 (MMRM)		
n	17	16
LS mean (SE)	4.87 (3.32)	5.54 (3.39)
95% CI of LS mean	(-1.91, 11.64)	(-1.36, 12.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.67 (-9.06, 10.40)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	75.44 (5.01)	83.75 (5.29)
95% CI of LS mean	(65.23, 85.66)	(72.98, 94.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.31 (-6.57, 23.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 24 (MMRM)		
n	17	16
LS mean (SE)	1.68 (3.63)	2.17 (3.71)
95% CI of LS mean	(-5.74, 9.11)	(-5.40, 9.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.48 (-10.16, 11.13)
Week 52		
n	20	16
Mean (SD)	75.63 (25.05)	86.98 (16.66)
Absolute Change at Week 52		
n	18	16
Mean (SD)	3.70 (20.64)	5.10 (10.68)
Week 52 (MMRM)		
n	19	15
LS mean (SE)	75.66 (4.94)	86.59 (5.20)
95% CI of LS mean	(65.61, 85.72)	(76.03, 97.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.93 (-3.69, 25.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 52 (MMRM)		
n	17	15
LS mean (SE)	3.40 (3.54)	4.79 (3.59)
95% CI of LS mean	(-3.84, 10.64)	(-2.51, 12.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.40 (-8.94, 11.73)
Absolute Change through Week 52 (MMRM)		
n	17	17
LS mean (SE)	3.32 (2.76)	4.17 (2.78)
95% CI of LS mean	(-2.32, 8.96)	(-1.48, 9.82)
P-value within Treatment	0.2389	0.1430
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.85 (-7.20, 8.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8309
Hedges' G (SE)		0.07 (0.34)
Hedges' 95% CI		(-0.61, 0.76)
Hedges' P-value		0.8295

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Baseline		
n	23	22
Mean (SD)	70.82 (25.20)	74.05 (26.29)
Week 8 (MMRM)		
n	23	23
LS mean (SE)	71.43 (4.95)	71.67 (4.95)
95% CI of LS mean	(61.42, 81.43)	(61.67, 81.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.24 (-13.94, 14.43)
Absolute Change at Week 8 (MMRM)		
n	23	22
LS mean (SE)	-0.90 (2.55)	-1.90 (2.60)
95% CI of LS mean	(-6.05, 4.25)	(-7.16, 3.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.00 (-8.37, 6.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Week 16 (MMRM)		
n	23	23
LS mean (SE)	70.40 (5.30)	67.32 (5.30)
95% CI of LS mean	(59.70, 81.10)	(56.62, 78.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.08 (-18.25, 12.09)
Absolute Change at Week 16 (MMRM)		
n	23	22
LS mean (SE)	-1.93 (3.79)	-6.63 (3.87)
95% CI of LS mean	(-9.57, 5.72)	(-14.45, 1.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.71 (-15.65, 6.24)
Week 24 (MMRM)		
n	23	22
LS mean (SE)	71.57 (4.52)	73.93 (4.54)
95% CI of LS mean	(62.43, 80.70)	(64.76, 83.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.37 (-10.61, 15.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 24 (MMRM)		
n	23	22
LS mean (SE)	-0.76 (2.44)	0.75 (2.50)
95% CI of LS mean	(-5.69, 4.16)	(-4.29, 5.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.51 (-5.55, 8.58)
Week 52		
n	23	23
Mean (SD)	71.38 (26.45)	78.80 (24.20)
Absolute Change at Week 52		
n	23	22
Mean (SD)	0.56 (15.95)	4.36 (10.33)
Week 52 (MMRM)		
n	23	23
LS mean (SE)	72.71 (4.62)	77.47 (4.62)
95% CI of LS mean	(63.38, 82.04)	(68.14, 86.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.76 (-8.47, 17.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 52 (MMRM)		
n	23	22
LS mean (SE)	0.38 (2.78)	4.54 (2.85)
95% CI of LS mean	(-5.24, 6.01)	(-1.22, 10.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.15 (-3.91, 12.22)
Absolute Change through Week 52 (MMRM)		
n	23	22
LS mean (SE)	-0.77 (2.11)	-0.45 (2.15)
95% CI of LS mean	(-5.03, 3.49)	(-4.81, 3.91)
P-value within Treatment	0.7174	0.8365
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-5.79, 6.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9161
Hedges' G (SE)		0.03 (0.29)
Hedges' 95% CI		(-0.56, 0.62)
Hedges' P-value		0.9158

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	20
Mean (SD)	77.73 (24.76)	81.64 (16.89)
Week 8 (MMRM)		
n	20	18
LS mean (SE)	80.68 (5.11)	78.18 (5.40)
95% CI of LS mean	(70.27, 91.09)	(67.19, 89.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.50 (-17.98, 12.98)
Absolute Change at Week 8 (MMRM)		
n	20	18
LS mean (SE)	2.74 (3.39)	-1.49 (3.58)
95% CI of LS mean	(-4.15, 9.63)	(-8.77, 5.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.24 (-14.39, 5.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Week 16 (MMRM)		
n	20	17
LS mean (SE)	78.09 (5.38)	73.77 (5.74)
95% CI of LS mean	(67.15, 89.04)	(62.11, 85.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.32 (-20.63, 12.00)
Absolute Change at Week 16 (MMRM)		
n	20	17
LS mean (SE)	0.15 (3.09)	-5.54 (3.34)
95% CI of LS mean	(-6.14, 6.45)	(-12.33, 1.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.69 (-15.12, 3.74)
Week 24 (MMRM)		
n	20	16
LS mean (SE)	78.98 (5.33)	77.18 (5.70)
95% CI of LS mean	(68.12, 89.84)	(65.58, 88.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.80 (-18.01, 14.41)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 24 (MMRM)		
n	20	16
LS mean (SE)	1.05 (2.82)	-1.85 (3.07)
95% CI of LS mean	(-4.71, 6.80)	(-8.10, 4.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.90 (-11.56, 5.76)
Week 52		
n	22	17
Mean (SD)	76.89 (22.99)	82.84 (14.57)
Absolute Change at Week 52		
n	22	17
Mean (SD)	-0.84 (12.68)	0.98 (12.02)
Week 52 (MMRM)		
n	20	15
LS mean (SE)	78.15 (4.98)	78.52 (5.39)
95% CI of LS mean	(67.98, 88.32)	(67.55, 89.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.37 (-14.92, 15.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	0.21 (3.04)	-0.74 (3.37)
95% CI of LS mean	(-5.98, 6.41)	(-7.60, 6.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.95 (-10.32, 8.42)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	0.47 (2.50)	-2.71 (2.70)
95% CI of LS mean	(-4.63, 5.57)	(-8.20, 2.79)
P-value within Treatment	0.8517	0.3233
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.18 (-10.86, 4.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4055
Hedges' G (SE)		-0.28 (0.32)
Hedges' 95% CI		(-0.94, 0.38)
Hedges' P-value		0.3961

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Baseline		
n	243	237
Mean (SD)	73.01 (18.26)	75.49 (17.99)
Week 8 (MMRM)		
n	240	234
LS mean (SE)	74.22 (1.15)	76.17 (1.16)
95% CI of LS mean	(71.96, 76.48)	(73.88, 78.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.95 (-1.26, 5.17)
Absolute Change at Week 8 (MMRM)		
n	233	231
LS mean (SE)	0.84 (0.87)	0.48 (0.88)
95% CI of LS mean	(-0.88, 2.55)	(-1.24, 2.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.36 (-2.79, 2.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Week 16 (MMRM)		
n	236	229
LS mean (SE)	75.12 (1.14)	77.12 (1.16)
95% CI of LS mean	(72.88, 77.37)	(74.84, 79.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.00 (-1.20, 5.20)
Absolute Change at Week 16 (MMRM)		
n	229	226
LS mean (SE)	2.01 (0.89)	1.48 (0.89)
95% CI of LS mean	(0.27, 3.75)	(-0.27, 3.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.53 (-3.00, 1.94)
Week 24 (MMRM)		
n	238	226
LS mean (SE)	74.30 (1.14)	77.18 (1.16)
95% CI of LS mean	(72.06, 76.54)	(74.90, 79.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.88 (-0.32, 6.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 24 (MMRM)		
n	231	223
LS mean (SE)	1.10 (0.90)	1.55 (0.91)
95% CI of LS mean	(-0.67, 2.87)	(-0.25, 3.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.44 (-2.08, 2.97)
Week 52		
n	241	224
Mean (SD)	77.05 (18.54)	79.84 (17.88)
Absolute Change at Week 52		
n	234	220
Mean (SD)	4.16 (14.54)	3.94 (14.02)
Week 52 (MMRM)		
n	235	221
LS mean (SE)	77.01 (1.16)	79.61 (1.18)
95% CI of LS mean	(74.73, 79.29)	(77.28, 81.93)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.60 (-0.66, 5.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 52 (MMRM)		
n	228	217
LS mean (SE)	3.78 (0.95)	3.92 (0.96)
95% CI of LS mean	(1.91, 5.64)	(2.03, 5.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.15 (-2.51, 2.80)
Absolute Change through Week 52 (MMRM)		
n	233	229
LS mean (SE)	2.30 (0.76)	2.32 (0.77)
95% CI of LS mean	(0.81, 3.79)	(0.81, 3.82)
P-value within Treatment	0.0026	0.0026
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.02 (-2.10, 2.14)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9861
Hedges' G (SE)		0.00 (0.09)
Hedges' 95% CI		(-0.18, 0.18)
Hedges' P-value		0.9861

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Baseline		
n	39	43
Mean (SD)	69.37 (14.52)	72.52 (17.03)
Week 8 (MMRM)		
n	37	39
LS mean (SE)	70.98 (2.61)	72.86 (2.52)
95% CI of LS mean	(65.78, 76.17)	(67.83, 77.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.88 (-5.42, 9.18)
Absolute Change at Week 8 (MMRM)		
n	37	39
LS mean (SE)	1.48 (2.62)	0.00 (2.53)
95% CI of LS mean	(-3.74, 6.69)	(-5.04, 5.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.48 (-8.80, 5.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Week 16 (MMRM)		
n	37	38
LS mean (SE)	71.58 (2.71)	70.14 (2.65)
95% CI of LS mean	(66.17, 76.98)	(64.87, 75.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-9.07, 6.20)
Absolute Change at Week 16 (MMRM)		
n	37	38
LS mean (SE)	2.08 (2.73)	-2.45 (2.66)
95% CI of LS mean	(-3.36, 7.52)	(-7.75, 2.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.53 (-12.20, 3.15)
Week 24 (MMRM)		
n	36	39
LS mean (SE)	68.02 (2.68)	77.38 (2.59)
95% CI of LS mean	(62.66, 73.37)	(72.22, 82.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.37 (1.85, 16.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 24 (MMRM)		
n	36	39
LS mean (SE)	-1.34 (2.61)	4.90 (2.51)
95% CI of LS mean	(-6.54, 3.86)	(-0.11, 9.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.24 (-1.07, 13.54)
Week 52		
n	36	41
Mean (SD)	72.69 (13.95)	78.17 (15.64)
Absolute Change at Week 52		
n	36	41
Mean (SD)	3.56 (15.32)	6.18 (13.09)
Week 52 (MMRM)		
n	34	38
LS mean (SE)	72.28 (2.52)	77.72 (2.40)
95% CI of LS mean	(67.26, 77.30)	(72.92, 82.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.44 (-1.61, 12.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 52 (MMRM)		
n	34	38
LS mean (SE)	2.97 (2.34)	5.41 (2.24)
95% CI of LS mean	(-1.71, 7.64)	(0.95, 9.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.44 (-4.12, 9.00)
Absolute Change through Week 52 (MMRM)		
n	37	39
LS mean (SE)	1.24 (2.19)	2.62 (2.11)
95% CI of LS mean	(-3.12, 5.59)	(-1.60, 6.83)
P-value within Treatment	0.5735	0.2195
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.38 (-4.78, 7.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6559
Hedges' G (SE)		0.10 (0.23)
Hedges' 95% CI		(-0.35, 0.56)
Hedges' P-value		0.6506

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Baseline		
n	219	219
Mean (SD)	73.73 (17.36)	75.01 (18.22)
Week 8 (MMRM)		
n	215	215
LS mean (SE)	74.40 (1.19)	76.07 (1.19)
95% CI of LS mean	(72.05, 76.75)	(73.73, 78.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.67 (-1.65, 4.99)
Absolute Change at Week 8 (MMRM)		
n	210	213
LS mean (SE)	0.47 (0.91)	0.74 (0.91)
95% CI of LS mean	(-1.33, 2.27)	(-1.04, 2.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-2.26, 2.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Week 16 (MMRM)		
n	211	211
LS mean (SE)	75.68 (1.19)	76.73 (1.19)
95% CI of LS mean	(73.34, 78.02)	(74.39, 79.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.05 (-2.26, 4.36)
Absolute Change at Week 16 (MMRM)		
n	206	209
LS mean (SE)	1.91 (0.94)	1.48 (0.93)
95% CI of LS mean	(0.07, 3.75)	(-0.35, 3.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.43 (-3.02, 2.17)
Week 24 (MMRM)		
n	212	211
LS mean (SE)	74.84 (1.20)	77.31 (1.20)
95% CI of LS mean	(72.48, 77.21)	(74.95, 79.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.47 (-0.88, 5.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 24 (MMRM)		
n	207	208
LS mean (SE)	1.05 (1.00)	2.11 (1.00)
95% CI of LS mean	(-0.92, 3.02)	(0.15, 4.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.06 (-1.72, 3.84)
Week 52		
n	212	209
Mean (SD)	77.48 (17.86)	79.56 (17.86)
Absolute Change at Week 52		
n	207	206
Mean (SD)	3.88 (15.47)	4.23 (13.78)
Week 52 (MMRM)		
n	207	206
LS mean (SE)	77.20 (1.21)	79.52 (1.21)
95% CI of LS mean	(74.83, 79.57)	(77.15, 81.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.32 (-1.03, 5.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 52 (MMRM)		
n	202	203
LS mean (SE)	3.36 (1.02)	4.26 (1.02)
95% CI of LS mean	(1.35, 5.37)	(2.26, 6.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.90 (-1.93, 3.74)
Absolute Change through Week 52 (MMRM)		
n	210	212
LS mean (SE)	2.10 (0.83)	2.62 (0.82)
95% CI of LS mean	(0.48, 3.73)	(1.00, 4.23)
P-value within Treatment	0.0111	0.0015
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.51 (-1.78, 2.80)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6602
Hedges' G (SE)		0.04 (0.10)
Hedges' 95% CI		(-0.15, 0.23)
Hedges' P-value		0.6600

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	18	19
Mean (SD)	66.36 (16.11)	76.32 (17.65)
Week 8 (MMRM)		
n	19	18
LS mean (SE)	74.17 (4.31)	73.87 (4.43)
95% CI of LS mean	(65.40, 82.93)	(64.87, 82.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.29 (-12.89, 12.31)
Absolute Change at Week 8 (MMRM)		
n	17	18
LS mean (SE)	5.55 (4.12)	-2.46 (4.00)
95% CI of LS mean	(-2.84, 13.93)	(-10.61, 5.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.01 (-19.73, 3.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Week 16 (MMRM)		
n	19	16
LS mean (SE)	71.83 (4.31)	76.81 (4.59)
95% CI of LS mean	(63.05, 80.60)	(67.49, 86.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.98 (-7.85, 17.81)
Absolute Change at Week 16 (MMRM)		
n	17	16
LS mean (SE)	4.57 (3.25)	-0.26 (3.36)
95% CI of LS mean	(-2.09, 11.22)	(-7.11, 6.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.82 (-14.42, 4.77)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	70.07 (3.91)	76.76 (4.14)
95% CI of LS mean	(62.11, 78.04)	(68.34, 85.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.69 (-4.94, 18.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 24 (MMRM)		
n	17	16
LS mean (SE)	1.95 (2.73)	0.02 (2.79)
95% CI of LS mean	(-3.63, 7.53)	(-5.67, 5.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.93 (-9.94, 6.08)
Week 52		
n	20	16
Mean (SD)	73.89 (19.75)	78.47 (15.96)
Absolute Change at Week 52		
n	18	16
Mean (SD)	6.79 (13.68)	0.35 (11.01)
Week 52 (MMRM)		
n	19	15
LS mean (SE)	75.04 (4.22)	78.13 (4.52)
95% CI of LS mean	(66.42, 83.66)	(68.94, 87.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.08 (-9.55, 15.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 52 (MMRM)		
n	17	15
LS mean (SE)	7.18 (2.91)	1.50 (3.04)
95% CI of LS mean	(1.22, 13.14)	(-4.70, 7.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.68 (-14.32, 2.95)
Absolute Change through Week 52 (MMRM)		
n	17	17
LS mean (SE)	4.57 (2.32)	0.42 (2.37)
95% CI of LS mean	(-0.19, 9.32)	(-4.42, 5.26)
P-value within Treatment	0.0592	0.8609
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.15 (-10.99, 2.69)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2254
Hedges' G (SE)		-0.42 (0.34)
Hedges' 95% CI		(-1.11, 0.27)
Hedges' P-value		0.2260

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Baseline		
n	23	22
Mean (SD)	64.98 (22.56)	74.24 (17.19)
Week 8 (MMRM)		
n	23	23
LS mean (SE)	66.80 (4.04)	69.61 (4.04)
95% CI of LS mean	(58.65, 74.95)	(61.46, 77.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.81 (-8.74, 14.37)
Absolute Change at Week 8 (MMRM)		
n	23	22
LS mean (SE)	1.23 (2.71)	-4.14 (2.78)
95% CI of LS mean	(-4.25, 6.71)	(-9.74, 1.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.37 (-13.22, 2.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Week 16 (MMRM)		
n	23	23
LS mean (SE)	66.87 (4.01)	70.33 (4.01)
95% CI of LS mean	(58.77, 74.97)	(62.23, 78.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.47 (-8.02, 14.95)
Absolute Change at Week 16 (MMRM)		
n	23	22
LS mean (SE)	1.30 (3.18)	-3.13 (3.25)
95% CI of LS mean	(-5.12, 7.72)	(-9.70, 3.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.43 (-13.62, 4.76)
Week 24 (MMRM)		
n	23	22
LS mean (SE)	63.48 (3.59)	77.13 (3.61)
95% CI of LS mean	(56.23, 70.74)	(69.84, 84.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	13.64 (3.33, 23.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 24 (MMRM)		
n	23	22
LS mean (SE)	-2.08 (2.30)	3.69 (2.35)
95% CI of LS mean	(-6.73, 2.57)	(-1.06, 8.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.77 (-0.89, 12.43)
Week 52		
n	23	23
Mean (SD)	67.63 (21.62)	79.23 (18.82)
Absolute Change at Week 52		
n	23	22
Mean (SD)	2.66 (9.75)	5.56 (11.11)
Week 52 (MMRM)		
n	23	23
LS mean (SE)	68.31 (4.13)	78.55 (4.13)
95% CI of LS mean	(59.97, 76.66)	(70.20, 86.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.23 (-1.60, 22.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 52 (MMRM)		
n	23	22
LS mean (SE)	2.75 (2.06)	5.46 (2.10)
95% CI of LS mean	(-1.40, 6.91)	(1.21, 9.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.71 (-3.25, 8.66)
Absolute Change through Week 52 (MMRM)		
n	23	22
LS mean (SE)	0.66 (2.06)	2.01 (2.11)
95% CI of LS mean	(-3.51, 4.82)	(-2.26, 6.27)
P-value within Treatment	0.7513	0.3470
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.35 (-4.63, 7.32)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6507
Hedges' G (SE)		0.13 (0.29)
Hedges' 95% CI		(-0.46, 0.73)
Hedges' P-value		0.6501

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	20
Mean (SD)	73.23 (16.23)	75.00 (15.56)
Week 8 (MMRM)		
n	20	17
LS mean (SE)	74.52 (3.01)	82.09 (3.21)
95% CI of LS mean	(68.35, 80.68)	(75.53, 88.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.58 (-1.54, 16.70)
Absolute Change at Week 8 (MMRM)		
n	20	17
LS mean (SE)	0.23 (3.43)	7.43 (3.65)
95% CI of LS mean	(-6.78, 7.23)	(-0.01, 14.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.20 (-3.17, 17.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Week 16 (MMRM)		
n	20	17
LS mean (SE)	75.07 (3.84)	75.90 (4.12)
95% CI of LS mean	(67.23, 82.91)	(67.50, 84.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.83 (-10.78, 12.43)
Absolute Change at Week 16 (MMRM)		
n	20	17
LS mean (SE)	0.78 (4.47)	0.89 (4.77)
95% CI of LS mean	(-8.35, 9.91)	(-8.85, 10.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.11 (-13.38, 13.59)
Week 24 (MMRM)		
n	20	16
LS mean (SE)	73.35 (3.50)	76.59 (3.82)
95% CI of LS mean	(66.22, 80.48)	(68.81, 84.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.24 (-7.43, 13.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 24 (MMRM)		
n	20	16
LS mean (SE)	-0.94 (3.65)	1.95 (3.97)
95% CI of LS mean	(-8.42, 6.54)	(-6.15, 10.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.89 (-8.29, 14.08)
Week 52		
n	22	17
Mean (SD)	78.55 (11.28)	81.37 (14.16)
Absolute Change at Week 52		
n	22	17
Mean (SD)	5.32 (11.29)	7.19 (19.81)
Week 52 (MMRM)		
n	20	15
LS mean (SE)	78.18 (2.94)	79.64 (3.36)
95% CI of LS mean	(72.18, 84.18)	(72.80, 86.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.46 (-7.75, 10.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	3.89 (3.58)	5.35 (4.03)
95% CI of LS mean	(-3.41, 11.19)	(-2.86, 13.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.46 (-9.67, 12.59)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	1.24 (3.42)	2.73 (3.68)
95% CI of LS mean	(-5.74, 8.23)	(-4.77, 10.23)
P-value within Treatment	0.7183	0.4633
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.49 (-8.93, 11.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7729
Hedges' G (SE)		0.10 (0.32)
Hedges' 95% CI		(-0.56, 0.75)
Hedges' P-value		0.7692

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Baseline		
n	243	237
Mean (SD)	70.74 (19.82)	71.64 (19.17)
Week 8 (MMRM)		
n	240	234
LS mean (SE)	71.10 (1.28)	73.66 (1.30)
95% CI of LS mean	(68.57, 73.62)	(71.11, 76.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.56 (-1.03, 6.16)
Absolute Change at Week 8 (MMRM)		
n	233	231
LS mean (SE)	0.65 (0.89)	1.82 (0.90)
95% CI of LS mean	(-1.11, 2.41)	(0.06, 3.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.17 (-1.32, 3.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Week 16 (MMRM)		
n	236	230
LS mean (SE)	71.63 (1.28)	73.45 (1.30)
95% CI of LS mean	(69.12, 74.15)	(70.91, 76.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.82 (-1.76, 5.40)
Absolute Change at Week 16 (MMRM)		
n	229	227
LS mean (SE)	1.24 (0.92)	1.64 (0.92)
95% CI of LS mean	(-0.56, 3.04)	(-0.16, 3.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.40 (-2.15, 2.95)
Week 24 (MMRM)		
n	238	226
LS mean (SE)	70.31 (1.32)	73.91 (1.34)
95% CI of LS mean	(67.73, 72.90)	(71.29, 76.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.60 (-0.09, 7.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 24 (MMRM)		
n	231	223
LS mean (SE)	0.01 (0.96)	2.13 (0.97)
95% CI of LS mean	(-1.87, 1.89)	(0.22, 4.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.12 (-0.56, 4.80)
Week 52		
n	241	224
Mean (SD)	73.08 (20.04)	75.10 (19.73)
Absolute Change at Week 52		
n	234	220
Mean (SD)	2.52 (16.16)	3.59 (14.60)
Week 52 (MMRM)		
n	235	221
LS mean (SE)	72.97 (1.28)	74.88 (1.30)
95% CI of LS mean	(70.46, 75.48)	(72.32, 77.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.91 (-1.67, 5.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250	VNZ/TEZ/D-IVA N = 241
Absolute Change at Week 52 (MMRM)		
n	228	217
LS mean (SE)	2.57 (1.02)	3.08 (1.04)
95% CI of LS mean	(0.57, 4.58)	(1.04, 5.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-2.35, 3.36)
Absolute Change through Week 52 (MMRM)		
n	233	229
LS mean (SE)	1.27 (0.81)	2.28 (0.82)
95% CI of LS mean	(-0.32, 2.87)	(0.67, 3.90)
P-value within Treatment	0.1174	0.0056
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.01 (-1.26, 3.28)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3826
Hedges' G (SE)		0.08 (0.09)
Hedges' 95% CI		(-0.10, 0.26)
Hedges' P-value		0.3825

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Baseline		
n	39	43
Mean (SD)	67.81 (19.21)	71.83 (18.68)
Week 8 (MMRM)		
n	37	39
LS mean (SE)	67.84 (3.49)	72.80 (3.37)
95% CI of LS mean	(60.90, 74.79)	(66.09, 79.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.96 (-4.79, 14.70)
Absolute Change at Week 8 (MMRM)		
n	37	39
LS mean (SE)	1.23 (2.49)	2.20 (2.40)
95% CI of LS mean	(-3.72, 6.18)	(-2.59, 6.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.97 (-5.99, 7.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Week 16 (MMRM)		
n	37	38
LS mean (SE)	72.35 (3.27)	73.27 (3.17)
95% CI of LS mean	(65.84, 78.86)	(66.95, 79.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-8.26, 10.11)
Absolute Change at Week 16 (MMRM)		
n	37	38
LS mean (SE)	5.73 (2.80)	2.51 (2.73)
95% CI of LS mean	(0.15, 11.31)	(-2.93, 7.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.22 (-11.09, 4.65)
Week 24 (MMRM)		
n	36	39
LS mean (SE)	72.47 (3.17)	72.72 (3.05)
95% CI of LS mean	(66.15, 78.78)	(66.64, 78.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.25 (-8.63, 9.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 24 (MMRM)		
n	36	39
LS mean (SE)	5.82 (2.40)	1.86 (2.32)
95% CI of LS mean	(1.04, 10.60)	(-2.75, 6.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.95 (-10.69, 2.79)
Week 52		
n	36	41
Mean (SD)	76.23 (19.18)	80.49 (16.44)
Absolute Change at Week 52		
n	36	41
Mean (SD)	8.95 (18.37)	8.67 (18.00)
Week 52 (MMRM)		
n	34	38
LS mean (SE)	74.99 (2.93)	80.97 (2.81)
95% CI of LS mean	(69.14, 80.83)	(75.36, 86.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.98 (-2.25, 14.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39	VNZ/TEZ/D-IVA N = 43
Absolute Change at Week 52 (MMRM)		
n	34	38
LS mean (SE)	8.54 (3.17)	10.23 (3.03)
95% CI of LS mean	(2.23, 14.85)	(4.18, 16.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.68 (-7.13, 10.50)
Absolute Change through Week 52 (MMRM)		
n	37	39
LS mean (SE)	6.70 (2.40)	4.87 (2.32)
95% CI of LS mean	(1.92, 11.48)	(0.24, 9.49)
P-value within Treatment	0.0067	0.0395
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.83 (-8.57, 4.91)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5902
Hedges' G (SE)		-0.12 (0.23)
Hedges' 95% CI		(-0.58, 0.33)
Hedges' P-value		0.5851

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Baseline		
n	219	219
Mean (SD)	71.08 (18.77)	71.69 (18.16)
Week 8 (MMRM)		
n	215	215
LS mean (SE)	71.10 (1.31)	73.97 (1.31)
95% CI of LS mean	(68.53, 73.68)	(71.39, 76.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.86 (-0.78, 6.50)
Absolute Change at Week 8 (MMRM)		
n	210	213
LS mean (SE)	0.22 (0.93)	1.98 (0.92)
95% CI of LS mean	(-1.61, 2.05)	(0.16, 3.80)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.76 (-0.82, 4.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Week 16 (MMRM)		
n	211	212
LS mean (SE)	72.37 (1.30)	73.91 (1.29)
95% CI of LS mean	(69.82, 74.92)	(71.36, 76.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.53 (-2.07, 5.14)
Absolute Change at Week 16 (MMRM)		
n	206	210
LS mean (SE)	1.74 (0.96)	1.97 (0.96)
95% CI of LS mean	(-0.15, 3.64)	(0.09, 3.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.23 (-2.44, 2.90)
Week 24 (MMRM)		
n	212	211
LS mean (SE)	71.77 (1.36)	73.95 (1.36)
95% CI of LS mean	(69.09, 74.45)	(71.28, 76.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-1.61, 5.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 24 (MMRM)		
n	207	208
LS mean (SE)	0.98 (1.02)	1.96 (1.02)
95% CI of LS mean	(-1.03, 2.99)	(-0.04, 3.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.98 (-1.86, 3.82)
Week 52		
n	212	209
Mean (SD)	74.21 (19.38)	75.81 (18.88)
Absolute Change at Week 52		
n	207	206
Mean (SD)	3.38 (17.06)	4.15 (15.45)
Week 52 (MMRM)		
n	207	206
LS mean (SE)	74.14 (1.31)	75.70 (1.31)
95% CI of LS mean	(71.57, 76.71)	(73.13, 78.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.56 (-2.08, 5.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: F/F

	ELX/TEZ/IVA N = 224	VNZ/TEZ/D-IVA N = 222
Absolute Change at Week 52 (MMRM)		
n	202	203
LS mean (SE)	3.45 (1.14)	3.72 (1.13)
95% CI of LS mean	(1.22, 5.69)	(1.49, 5.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.27 (-2.89, 3.43)
Absolute Change through Week 52 (MMRM)		
n	210	212
LS mean (SE)	2.06 (0.88)	2.55 (0.87)
95% CI of LS mean	(0.33, 3.79)	(0.83, 4.27)
P-value within Treatment	0.0196	0.0037
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-1.95, 2.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6922
Hedges' G (SE)		0.04 (0.10)
Hedges' 95% CI		(-0.15, 0.23)
Hedges' P-value		0.6921

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	18	19
Mean (SD)	69.14 (26.00)	77.19 (18.69)
Week 8 (MMRM)		
n	19	18
LS mean (SE)	69.10 (4.73)	79.53 (4.86)
95% CI of LS mean	(59.48, 78.73)	(69.63, 89.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.42 (-3.42, 24.27)
Absolute Change at Week 8 (MMRM)		
n	17	18
LS mean (SE)	0.31 (3.51)	3.41 (3.41)
95% CI of LS mean	(-6.84, 7.46)	(-3.54, 10.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.10 (-6.92, 13.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Week 16 (MMRM)		
n	19	16
LS mean (SE)	72.03 (4.41)	78.45 (4.63)
95% CI of LS mean	(63.03, 81.02)	(69.03, 87.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.42 (-6.65, 19.49)
Absolute Change at Week 16 (MMRM)		
n	17	16
LS mean (SE)	1.62 (3.38)	2.77 (3.41)
95% CI of LS mean	(-5.28, 8.52)	(-4.17, 9.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.15 (-8.69, 11.00)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	65.01 (4.75)	74.04 (5.02)
95% CI of LS mean	(55.32, 74.69)	(63.83, 84.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.03 (-5.08, 23.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 24 (MMRM)		
n	17	16
LS mean (SE)	-2.96 (3.81)	-2.03 (3.88)
95% CI of LS mean	(-10.74, 4.83)	(-9.94, 5.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.92 (-10.22, 12.06)
Week 52		
n	20	16
Mean (SD)	71.11 (25.08)	80.56 (16.48)
Absolute Change at Week 52		
n	18	16
Mean (SD)	1.85 (15.83)	2.78 (8.61)
Week 52 (MMRM)		
n	19	15
LS mean (SE)	70.86 (4.93)	78.09 (5.17)
95% CI of LS mean	(60.82, 80.89)	(67.58, 88.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.23 (-7.34, 21.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 52 (MMRM)		
n	17	15
LS mean (SE)	0.97 (3.06)	2.61 (3.13)
95% CI of LS mean	(-5.30, 7.23)	(-3.77, 8.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-7.36, 10.64)
Absolute Change through Week 52 (MMRM)		
n	17	17
LS mean (SE)	-0.12 (2.83)	1.12 (2.83)
95% CI of LS mean	(-5.91, 5.66)	(-4.66, 6.89)
P-value within Treatment	0.9655	0.6963
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.24 (-7.00, 9.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7609
Hedges' G (SE)		0.10 (0.34)
Hedges' 95% CI		(-0.58, 0.79)
Hedges' P-value		0.7590

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Baseline		
n	23	22
Mean (SD)	63.29 (23.55)	63.64 (25.70)
Week 8 (MMRM)		
n	23	23
LS mean (SE)	65.33 (5.38)	60.76 (5.38)
95% CI of LS mean	(54.47, 76.18)	(49.90, 71.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.57 (-19.96, 10.82)
Absolute Change at Week 8 (MMRM)		
n	23	22
LS mean (SE)	1.55 (2.91)	-2.63 (2.98)
95% CI of LS mean	(-4.33, 7.42)	(-8.64, 3.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.17 (-12.59, 4.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Week 16 (MMRM)		
n	23	23
LS mean (SE)	61.95 (5.53)	62.69 (5.53)
95% CI of LS mean	(50.78, 73.11)	(51.53, 73.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.75 (-15.08, 16.57)
Absolute Change at Week 16 (MMRM)		
n	23	22
LS mean (SE)	-1.84 (3.44)	-0.61 (3.52)
95% CI of LS mean	(-8.78, 5.10)	(-7.70, 6.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-8.71, 11.17)
Week 24 (MMRM)		
n	23	22
LS mean (SE)	60.50 (4.90)	70.62 (4.93)
95% CI of LS mean	(50.60, 70.40)	(60.67, 80.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.12 (-3.95, 24.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 24 (MMRM)		
n	23	22
LS mean (SE)	-3.28 (2.85)	7.47 (2.91)
95% CI of LS mean	(-9.04, 2.47)	(1.59, 13.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.76 (2.51, 19.01)
Week 52		
n	23	23
Mean (SD)	65.22 (21.79)	72.46 (25.70)
Absolute Change at Week 52		
n	23	22
Mean (SD)	1.93 (12.82)	9.09 (15.95)
Week 52 (MMRM)		
n	23	23
LS mean (SE)	65.81 (5.08)	71.87 (5.08)
95% CI of LS mean	(55.55, 76.07)	(61.61, 82.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.06 (-8.49, 20.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: F/RF

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 52 (MMRM)		
n	23	22
LS mean (SE)	2.03 (3.09)	8.99 (3.16)
95% CI of LS mean	(-4.21, 8.27)	(2.61, 15.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.96 (-1.98, 15.90)
Absolute Change through Week 52 (MMRM)		
n	23	22
LS mean (SE)	-1.03 (2.57)	5.29 (2.63)
95% CI of LS mean	(-6.23, 4.17)	(-0.03, 10.60)
P-value within Treatment	0.6909	0.0511
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.32 (-1.14, 13.77)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0945
Hedges' G (SE)		0.50 (0.30)
Hedges' 95% CI		(-0.10, 1.10)
Hedges' P-value		0.0984

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Baseline		
n	22	20
Mean (SD)	71.21 (18.99)	75.00 (19.37)
Week 8 (MMRM)		
n	20	17
LS mean (SE)	75.82 (4.50)	76.45 (4.79)
95% CI of LS mean	(66.67, 84.96)	(66.71, 86.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.63 (-12.93, 14.19)
Absolute Change at Week 8 (MMRM)		
n	20	17
LS mean (SE)	5.37 (3.23)	4.72 (3.47)
95% CI of LS mean	(-1.20, 11.93)	(-2.33, 11.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.65 (-10.39, 9.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Week 16 (MMRM)		
n	20	17
LS mean (SE)	78.04 (4.25)	73.71 (4.55)
95% CI of LS mean	(69.38, 86.70)	(64.45, 82.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.32 (-17.23, 8.58)
Absolute Change at Week 16 (MMRM)		
n	20	17
LS mean (SE)	7.59 (3.33)	1.74 (3.59)
95% CI of LS mean	(0.81, 14.37)	(-5.56, 9.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.85 (-15.93, 4.23)
Week 24 (MMRM)		
n	20	16
LS mean (SE)	77.48 (3.69)	71.98 (3.98)
95% CI of LS mean	(69.97, 84.99)	(63.90, 80.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.50 (-16.77, 5.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 24 (MMRM)		
n	20	16
LS mean (SE)	7.03 (2.26)	0.04 (2.48)
95% CI of LS mean	(2.42, 11.64)	(-5.00, 5.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.99 (-13.96, -0.02)
Week 52		
n	22	17
Mean (SD)	77.27 (16.61)	77.78 (18.00)
Absolute Change at Week 52		
n	22	17
Mean (SD)	6.06 (16.70)	2.61 (16.91)
Week 52 (MMRM)		
n	20	15
LS mean (SE)	76.93 (3.87)	76.11 (4.27)
95% CI of LS mean	(69.05, 84.80)	(67.44, 84.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.82 (-12.75, 11.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Pooled Domains)
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	6.48 (3.76)	4.21 (4.21)
95% CI of LS mean	(-1.17, 14.13)	(-4.31, 12.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.26 (-13.81, 9.28)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	7.03 (2.77)	2.00 (3.02)
95% CI of LS mean	(1.39, 12.68)	(-4.13, 8.13)
P-value within Treatment	0.0161	0.5125
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.04 (-13.49, 3.42)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2349
Hedges' G (SE)		-0.40 (0.33)
Hedges' 95% CI		(-1.06, 0.27)
Hedges' P-value		0.2321

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Baseline		
n	231	225
Mean (SD)	71.14 (19.84)	73.09 (20.37)
Week 8 (MMRM)		
n	230	222
LS mean (SE)	71.28 (1.28)	72.05 (1.30)
95% CI of LS mean	(68.75, 73.80)	(69.49, 74.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.78 (-2.82, 4.38)
Absolute Change at Week 8 (MMRM)		
n	224	219
LS mean (SE)	0.24 (0.95)	-1.20 (0.96)
95% CI of LS mean	(-1.63, 2.11)	(-3.09, 0.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.44 (-4.10, 1.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Week 16 (MMRM)		
n	226	217
LS mean (SE)	71.77 (1.29)	72.59 (1.31)
95% CI of LS mean	(69.25, 74.30)	(70.02, 75.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-2.79, 4.42)
Absolute Change at Week 16 (MMRM)		
n	220	214
LS mean (SE)	1.09 (0.99)	-0.75 (1.00)
95% CI of LS mean	(-0.86, 3.04)	(-2.72, 1.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.83 (-4.61, 0.94)
Week 24 (MMRM)		
n	226	214
LS mean (SE)	69.81 (1.37)	72.40 (1.40)
95% CI of LS mean	(67.12, 72.51)	(69.65, 75.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.58 (-1.27, 6.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Absolute Change at Week 24 (MMRM)		
n	220	212
LS mean (SE)	-0.91 (1.04)	-0.91 (1.06)
95% CI of LS mean	(-2.95, 1.13)	(-2.99, 1.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.00 (-2.91, 2.91)
Week 52		
n	231	212
Mean (SD)	73.79 (19.57)	73.74 (19.70)
Absolute Change at Week 52		
n	225	209
Mean (SD)	2.57 (15.89)	0.32 (15.13)
Week 52 (MMRM)		
n	225	209
LS mean (SE)	73.51 (1.29)	73.27 (1.33)
95% CI of LS mean	(70.97, 76.06)	(70.67, 75.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.24 (-3.88, 3.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Absolute Change at Week 52 (MMRM)		
n	219	206
LS mean (SE)	2.54 (1.06)	0.01 (1.08)
95% CI of LS mean	(0.46, 4.61)	(-2.12, 2.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.53 (-5.50, 0.44)
Absolute Change through Week 52 (MMRM)		
n	222	217
LS mean (SE)	0.90 (0.83)	-0.55 (0.84)
95% CI of LS mean	(-0.72, 2.53)	(-2.20, 1.10)
P-value within Treatment	0.2754	0.5132
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.45 (-3.77, 0.87)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2186
Hedges' G (SE)		-0.12 (0.10)
Hedges' 95% CI		(-0.30, 0.07)
Hedges' P-value		0.2187

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	38	41
Mean (SD)	73.39 (18.36)	71.14 (18.39)
Week 8 (MMRM)		
n	37	38
LS mean (SE)	71.78 (3.31)	71.05 (3.26)
95% CI of LS mean	(65.19, 78.37)	(64.54, 77.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-10.08, 8.62)
Absolute Change at Week 8 (MMRM)		
n	37	38
LS mean (SE)	-1.36 (2.77)	-0.29 (2.74)
95% CI of LS mean	(-6.89, 4.17)	(-5.74, 5.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.07 (-6.77, 8.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 16 (MMRM)		
n	37	37
LS mean (SE)	66.97 (3.17)	68.29 (3.15)
95% CI of LS mean	(60.65, 73.30)	(62.00, 74.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.31 (-7.71, 10.33)
Absolute Change at Week 16 (MMRM)		
n	37	37
LS mean (SE)	-6.16 (2.81)	-2.83 (2.80)
95% CI of LS mean	(-11.76, -0.56)	(-8.40, 2.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.33 (-4.64, 11.31)
Week 24 (MMRM)		
n	36	37
LS mean (SE)	68.57 (3.53)	70.21 (3.49)
95% CI of LS mean	(61.53, 75.61)	(63.25, 77.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-8.35, 11.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 24 (MMRM)		
n	36	37
LS mean (SE)	-4.58 (3.41)	-0.88 (3.37)
95% CI of LS mean	(-11.38, 2.22)	(-7.60, 5.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.71 (-5.91, 13.32)
Week 52		
n	35	39
Mean (SD)	75.24 (18.88)	71.51 (19.55)
Absolute Change at Week 52		
n	35	39
Mean (SD)	1.27 (15.66)	1.28 (13.21)
Week 52 (MMRM)		
n	34	36
LS mean (SE)	74.24 (3.19)	72.34 (3.13)
95% CI of LS mean	(67.88, 80.61)	(66.10, 78.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.90 (-10.92, 7.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 52 (MMRM)		
n	34	36
LS mean (SE)	0.94 (2.58)	1.28 (2.52)
95% CI of LS mean	(-4.20, 6.08)	(-3.75, 6.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.34 (-6.93, 7.61)
Absolute Change through Week 52 (MMRM)		
n	37	37
LS mean (SE)	-3.27 (2.44)	-0.81 (2.42)
95% CI of LS mean	(-8.14, 1.60)	(-5.63, 4.02)
P-value within Treatment	0.1854	0.7397
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.46 (-4.48, 9.40)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4819
Hedges' G (SE)		0.16 (0.23)
Hedges' 95% CI		(-0.29, 0.62)
Hedges' P-value		0.4774

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Baseline		
n	208	205
Mean (SD)	72.70 (19.10)	72.66 (19.90)
Week 8 (MMRM)		
n	206	202
LS mean (SE)	71.79 (1.34)	72.46 (1.35)
95% CI of LS mean	(69.16, 74.43)	(69.81, 75.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.67 (-3.08, 4.41)
Absolute Change at Week 8 (MMRM)		
n	202	200
LS mean (SE)	-0.52 (1.04)	-0.60 (1.04)
95% CI of LS mean	(-2.56, 1.53)	(-2.66, 1.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.08 (-2.98, 2.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Week 16 (MMRM)		
n	202	198
LS mean (SE)	72.37 (1.31)	73.14 (1.32)
95% CI of LS mean	(69.79, 74.94)	(70.55, 75.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.78 (-2.88, 4.43)
Absolute Change at Week 16 (MMRM)		
n	198	196
LS mean (SE)	0.25 (1.05)	0.07 (1.05)
95% CI of LS mean	(-1.81, 2.31)	(-2.00, 2.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.18 (-3.11, 2.74)
Week 24 (MMRM)		
n	201	197
LS mean (SE)	69.96 (1.43)	71.83 (1.44)
95% CI of LS mean	(67.15, 72.77)	(69.00, 74.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.87 (-2.12, 5.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Absolute Change at Week 24 (MMRM)		
n	197	195
LS mean (SE)	-2.16 (1.19)	-1.23 (1.19)
95% CI of LS mean	(-4.49, 0.18)	(-3.57, 1.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-2.38, 4.24)
Week 52		
n	203	195
Mean (SD)	74.82 (18.49)	73.56 (19.44)
Absolute Change at Week 52		
n	199	193
Mean (SD)	2.01 (16.48)	0.72 (14.82)
Week 52 (MMRM)		
n	198	192
LS mean (SE)	74.31 (1.32)	73.36 (1.34)
95% CI of LS mean	(71.71, 76.92)	(70.73, 75.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.96 (-4.66, 2.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Absolute Change at Week 52 (MMRM)		
n	194	190
LS mean (SE)	2.01 (1.13)	0.33 (1.14)
95% CI of LS mean	(-0.20, 4.22)	(-1.90, 2.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.68 (-4.83, 1.46)
Absolute Change through Week 52 (MMRM)		
n	200	198
LS mean (SE)	0.03 (0.92)	-0.28 (0.92)
95% CI of LS mean	(-1.78, 1.84)	(-2.10, 1.54)
P-value within Treatment	0.9705	0.7647
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-2.88, 2.26)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8119
Hedges' G (SE)		-0.02 (0.10)
Hedges' 95% CI		(-0.22, 0.17)
Hedges' P-value		0.8117

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	18	19
Mean (SD)	66.67 (15.24)	79.53 (16.67)
Week 8 (MMRM)		
n	19	18
LS mean (SE)	70.80 (3.72)	76.50 (3.82)
95% CI of LS mean	(63.22, 78.38)	(68.71, 84.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.70 (-5.20, 16.60)
Absolute Change at Week 8 (MMRM)		
n	17	18
LS mean (SE)	1.45 (3.22)	-2.61 (3.13)
95% CI of LS mean	(-5.11, 8.02)	(-8.99, 3.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.06 (-13.25, 5.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Week 16 (MMRM)		
n	19	16
LS mean (SE)	71.39 (4.19)	74.92 (4.51)
95% CI of LS mean	(62.84, 79.93)	(65.75, 84.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.54 (-9.02, 16.09)
Absolute Change at Week 16 (MMRM)		
n	17	16
LS mean (SE)	4.07 (3.73)	-4.45 (3.85)
95% CI of LS mean	(-3.56, 11.70)	(-12.29, 3.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.52 (-19.50, 2.45)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	71.97 (4.43)	78.47 (4.77)
95% CI of LS mean	(62.95, 80.99)	(68.77, 88.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.50 (-6.77, 19.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 24 (MMRM)		
n	17	16
LS mean (SE)	4.07 (4.41)	-0.62 (4.52)
95% CI of LS mean	(-4.93, 13.07)	(-9.83, 8.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.69 (-17.59, 8.22)
Week 52		
n	20	16
Mean (SD)	72.78 (19.24)	76.39 (20.64)
Absolute Change at Week 52		
n	18	16
Mean (SD)	4.94 (12.77)	-2.08 (12.97)
Week 52 (MMRM)		
n	19	15
LS mean (SE)	73.72 (4.29)	75.48 (4.69)
95% CI of LS mean	(64.98, 82.47)	(65.96, 85.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.76 (-11.20, 14.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 52 (MMRM)		
n	17	15
LS mean (SE)	4.72 (3.01)	-3.52 (3.26)
95% CI of LS mean	(-1.44, 10.88)	(-10.17, 3.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.25 (-17.36, 0.86)
Absolute Change through Week 52 (MMRM)		
n	17	17
LS mean (SE)	4.29 (2.59)	-2.86 (2.67)
95% CI of LS mean	(-1.00, 9.58)	(-8.29, 2.56)
P-value within Treatment	0.1082	0.2906
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.15 (-14.78, 0.48)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0652
Hedges' G (SE)		-0.64 (0.34)
Hedges' 95% CI		(-1.35, 0.06)
Hedges' P-value		0.0700

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Baseline		
n	22	22
Mean (SD)	62.12 (25.12)	72.22 (20.21)
Week 8 (MMRM)		
n	22	23
LS mean (SE)	65.03 (4.80)	65.34 (4.70)
95% CI of LS mean	(55.31, 74.75)	(55.84, 74.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.31 (-13.41, 14.02)
Absolute Change at Week 8 (MMRM)		
n	22	22
LS mean (SE)	1.87 (2.65)	-5.91 (2.65)
95% CI of LS mean	(-3.50, 7.24)	(-11.28, -0.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.78 (-15.44, -0.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Week 16 (MMRM)		
n	22	23
LS mean (SE)	60.48 (4.82)	61.95 (4.71)
95% CI of LS mean	(50.73, 70.23)	(52.42, 71.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.47 (-12.29, 15.23)
Absolute Change at Week 16 (MMRM)		
n	22	22
LS mean (SE)	-2.67 (3.84)	-9.45 (3.84)
95% CI of LS mean	(-10.42, 5.08)	(-17.20, -1.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.77 (-17.78, 4.23)
Week 24 (MMRM)		
n	22	22
LS mean (SE)	60.99 (4.96)	72.14 (4.87)
95% CI of LS mean	(50.97, 71.01)	(62.30, 81.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.15 (-3.01, 25.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 24 (MMRM)		
n	22	22
LS mean (SE)	-2.17 (2.70)	1.66 (2.70)
95% CI of LS mean	(-7.62, 3.28)	(-3.78, 7.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.83 (-3.94, 11.60)
Week 52		
n	22	23
Mean (SD)	64.14 (24.47)	72.95 (21.41)
Absolute Change at Week 52		
n	22	22
Mean (SD)	2.02 (11.70)	2.02 (14.40)
Week 52 (MMRM)		
n	22	23
LS mean (SE)	65.03 (4.69)	72.10 (4.59)
95% CI of LS mean	(55.53, 74.52)	(62.82, 81.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.07 (-6.33, 20.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 52 (MMRM)		
n	22	22
LS mean (SE)	1.87 (2.99)	2.17 (2.99)
95% CI of LS mean	(-4.19, 7.93)	(-3.89, 8.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.30 (-8.33, 8.92)
Absolute Change through Week 52 (MMRM)		
n	22	22
LS mean (SE)	-0.99 (2.53)	-1.87 (2.53)
95% CI of LS mean	(-6.12, 4.14)	(-7.00, 3.25)
P-value within Treatment	0.6982	0.4646
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.88 (-8.20, 6.43)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8087
Hedges' G (SE)		-0.07 (0.30)
Hedges' 95% CI		(-0.67, 0.52)
Hedges' P-value		0.8069

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Baseline		
n	21	20
Mean (SD)	73.02 (19.74)	68.33 (23.99)
Week 8 (MMRM)		
n	20	17
LS mean (SE)	73.99 (4.70)	68.75 (4.99)
95% CI of LS mean	(64.45, 83.54)	(58.61, 78.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.24 (-19.45, 8.98)
Absolute Change at Week 8 (MMRM)		
n	20	17
LS mean (SE)	2.90 (3.58)	-0.44 (3.82)
95% CI of LS mean	(-4.45, 10.25)	(-8.28, 7.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.35 (-14.21, 7.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Week 16 (MMRM)		
n	20	17
LS mean (SE)	69.55 (5.09)	68.76 (5.48)
95% CI of LS mean	(59.20, 79.89)	(57.63, 79.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.79 (-16.27, 14.69)
Absolute Change at Week 16 (MMRM)		
n	20	17
LS mean (SE)	-1.54 (3.15)	-0.96 (3.44)
95% CI of LS mean	(-7.94, 4.86)	(-7.94, 6.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-9.08, 10.23)
Week 24 (MMRM)		
n	20	16
LS mean (SE)	73.44 (4.79)	68.24 (5.15)
95% CI of LS mean	(63.68, 83.19)	(57.75, 78.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.20 (-19.82, 9.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 24 (MMRM)		
n	20	16
LS mean (SE)	2.35 (3.02)	-1.74 (3.30)
95% CI of LS mean	(-3.80, 8.50)	(-8.45, 4.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.09 (-13.37, 5.19)
Week 52		
n	21	17
Mean (SD)	77.25 (21.22)	69.28 (19.85)
Absolute Change at Week 52		
n	21	17
Mean (SD)	4.23 (16.28)	-1.96 (17.67)
Week 52 (MMRM)		
n	20	15
LS mean (SE)	75.66 (4.91)	68.72 (5.37)
95% CI of LS mean	(65.61, 85.70)	(57.77, 79.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.94 (-22.07, 8.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Health Perceptions

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	4.57 (4.27)	-0.84 (4.75)
95% CI of LS mean	(-4.15, 13.29)	(-10.51, 8.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.41 (-18.56, 7.74)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	1.79 (2.95)	-1.18 (3.21)
95% CI of LS mean	(-4.22, 7.81)	(-7.72, 5.36)
P-value within Treatment	0.5474	0.7155
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.97 (-12.06, 6.11)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5093
Hedges' G (SE)		-0.22 (0.32)
Hedges' 95% CI		(-0.88, 0.44)
Hedges' P-value		0.5007

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Baseline		
n	231	225
Mean (SD)	86.72 (15.71)	87.07 (16.61)
Week 8 (MMRM)		
n	230	222
LS mean (SE)	86.01 (1.07)	87.29 (1.09)
95% CI of LS mean	(83.90, 88.11)	(85.15, 89.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.28 (-1.72, 4.28)
Absolute Change at Week 8 (MMRM)		
n	224	219
LS mean (SE)	-0.71 (0.87)	0.15 (0.87)
95% CI of LS mean	(-2.41, 0.99)	(-1.57, 1.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-1.56, 3.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Week 16 (MMRM)		
n	225	218
LS mean (SE)	86.46 (1.11)	86.78 (1.12)
95% CI of LS mean	(84.28, 88.63)	(84.57, 88.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-2.78, 3.42)
Absolute Change at Week 16 (MMRM)		
n	219	215
LS mean (SE)	-0.18 (0.87)	-0.33 (0.88)
95% CI of LS mean	(-1.90, 1.54)	(-2.07, 1.40)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.15 (-2.59, 2.29)
Week 24 (MMRM)		
n	226	213
LS mean (SE)	85.26 (1.19)	85.93 (1.21)
95% CI of LS mean	(82.93, 87.60)	(83.54, 88.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.66 (-2.68, 4.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Absolute Change at Week 24 (MMRM)		
n	220	211
LS mean (SE)	-1.37 (1.01)	-1.19 (1.03)
95% CI of LS mean	(-3.37, 0.62)	(-3.22, 0.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.18 (-2.66, 3.03)
Week 52		
n	231	212
Mean (SD)	86.86 (17.45)	88.52 (14.44)
Absolute Change at Week 52		
n	225	209
Mean (SD)	0.21 (14.84)	0.92 (13.28)
Week 52 (MMRM)		
n	225	209
LS mean (SE)	86.83 (1.08)	88.30 (1.11)
95% CI of LS mean	(84.71, 88.94)	(86.13, 90.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.47 (-1.56, 4.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Absolute Change at Week 52 (MMRM)		
n	219	206
LS mean (SE)	0.02 (0.95)	1.17 (0.97)
95% CI of LS mean	(-1.84, 1.88)	(-0.74, 3.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.15 (-1.52, 3.81)
Absolute Change through Week 52 (MMRM)		
n	222	217
LS mean (SE)	-0.51 (0.75)	-0.12 (0.76)
95% CI of LS mean	(-1.99, 0.96)	(-1.62, 1.38)
P-value within Treatment	0.4955	0.8759
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.39 (-1.71, 2.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7134
Hedges' G (SE)		0.04 (0.10)
Hedges' 95% CI		(-0.15, 0.22)
Hedges' P-value		0.7133

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	38	41
Mean (SD)	86.18 (15.29)	84.96 (15.28)
Week 8 (MMRM)		
n	37	37
LS mean (SE)	89.24 (2.54)	87.83 (2.52)
95% CI of LS mean	(84.17, 94.31)	(82.79, 92.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.41 (-8.60, 5.77)
Absolute Change at Week 8 (MMRM)		
n	37	37
LS mean (SE)	3.91 (2.74)	2.49 (2.72)
95% CI of LS mean	(-1.57, 9.39)	(-2.95, 7.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.42 (-9.20, 6.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 16 (MMRM)		
n	36	37
LS mean (SE)	87.61 (2.54)	86.03 (2.51)
95% CI of LS mean	(82.55, 92.67)	(81.03, 91.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.58 (-8.73, 5.57)
Absolute Change at Week 16 (MMRM)		
n	36	37
LS mean (SE)	2.27 (2.98)	1.07 (2.95)
95% CI of LS mean	(-3.67, 8.22)	(-4.81, 6.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.21 (-9.64, 7.22)
Week 24 (MMRM)		
n	36	37
LS mean (SE)	90.58 (1.99)	88.24 (1.97)
95% CI of LS mean	(86.61, 94.55)	(84.30, 92.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.34 (-7.99, 3.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 24 (MMRM)		
n	36	37
LS mean (SE)	5.37 (2.70)	3.39 (2.67)
95% CI of LS mean	(-0.01, 10.76)	(-1.95, 8.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.99 (-9.64, 5.66)
Week 52		
n	35	38
Mean (SD)	89.05 (14.68)	91.45 (11.38)
Absolute Change at Week 52		
n	35	38
Mean (SD)	3.33 (16.57)	5.70 (12.87)
Week 52 (MMRM)		
n	34	35
LS mean (SE)	88.98 (2.21)	90.59 (2.17)
95% CI of LS mean	(84.57, 93.38)	(86.25, 94.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.61 (-4.61, 7.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 52 (MMRM)		
n	34	35
LS mean (SE)	3.89 (2.60)	5.55 (2.56)
95% CI of LS mean	(-1.30, 9.09)	(0.43, 10.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.66 (-5.70, 9.02)
Absolute Change through Week 52 (MMRM)		
n	37	37
LS mean (SE)	3.85 (2.38)	3.33 (2.36)
95% CI of LS mean	(-0.90, 8.60)	(-1.37, 8.04)
P-value within Treatment	0.1107	0.1617
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.51 (-7.28, 6.25)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8805
Hedges' G (SE)		-0.04 (0.23)
Hedges' 95% CI		(-0.49, 0.42)
Hedges' P-value		0.8791

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Baseline		
n	208	205
Mean (SD)	87.86 (14.90)	86.95 (16.32)
Week 8 (MMRM)		
n	206	200
LS mean (SE)	86.84 (1.12)	87.41 (1.13)
95% CI of LS mean	(84.64, 89.04)	(85.18, 89.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.56 (-2.56, 3.69)
Absolute Change at Week 8 (MMRM)		
n	202	198
LS mean (SE)	-0.97 (0.94)	0.26 (0.94)
95% CI of LS mean	(-2.81, 0.87)	(-1.59, 2.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-1.38, 3.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Week 16 (MMRM)		
n	200	199
LS mean (SE)	87.67 (1.11)	87.03 (1.12)
95% CI of LS mean	(85.48, 89.86)	(84.83, 89.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.64 (-3.75, 2.47)
Absolute Change at Week 16 (MMRM)		
n	196	197
LS mean (SE)	-0.24 (0.99)	0.05 (0.99)
95% CI of LS mean	(-2.19, 1.71)	(-1.89, 2.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.30 (-2.46, 3.06)
Week 24 (MMRM)		
n	201	197
LS mean (SE)	86.56 (1.22)	86.12 (1.23)
95% CI of LS mean	(84.16, 88.96)	(83.70, 88.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.44 (-3.85, 2.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Absolute Change at Week 24 (MMRM)		
n	197	195
LS mean (SE)	-1.24 (1.13)	-0.88 (1.14)
95% CI of LS mean	(-3.47, 0.98)	(-3.12, 1.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.36 (-2.80, 3.52)
Week 52		
n	203	194
Mean (SD)	87.59 (17.59)	88.62 (14.03)
Absolute Change at Week 52		
n	199	192
Mean (SD)	-0.06 (15.64)	1.04 (13.76)
Week 52 (MMRM)		
n	198	191
LS mean (SE)	87.54 (1.13)	88.61 (1.15)
95% CI of LS mean	(85.31, 89.77)	(86.35, 90.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.07 (-2.11, 4.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Absolute Change at Week 52 (MMRM)		
n	194	189
LS mean (SE)	-0.33 (1.06)	1.47 (1.07)
95% CI of LS mean	(-2.42, 1.75)	(-0.63, 3.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.81 (-1.16, 4.77)
Absolute Change through Week 52 (MMRM)		
n	200	198
LS mean (SE)	-0.61 (0.86)	0.22 (0.86)
95% CI of LS mean	(-2.30, 1.08)	(-1.48, 1.91)
P-value within Treatment	0.4808	0.8031
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.82 (-1.57, 3.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5006
Hedges' G (SE)		0.07 (0.10)
Hedges' 95% CI		(-0.13, 0.26)
Hedges' P-value		0.5004

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	18	19
Mean (SD)	81.94 (17.21)	91.67 (15.47)
Week 8 (MMRM)		
n	19	18
LS mean (SE)	84.88 (2.62)	92.81 (2.69)
95% CI of LS mean	(79.54, 90.22)	(87.32, 98.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.93 (0.25, 15.62)
Absolute Change at Week 8 (MMRM)		
n	17	18
LS mean (SE)	2.21 (3.47)	1.62 (3.37)
95% CI of LS mean	(-4.86, 9.28)	(-5.25, 8.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.59 (-10.47, 9.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Week 16 (MMRM)		
n	19	16
LS mean (SE)	81.81 (3.42)	92.82 (3.65)
95% CI of LS mean	(74.82, 88.80)	(85.39, 100.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.01 (0.79, 21.23)
Absolute Change at Week 16 (MMRM)		
n	17	16
LS mean (SE)	0.74 (2.46)	1.31 (2.54)
95% CI of LS mean	(-4.30, 5.78)	(-3.85, 6.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.58 (-6.69, 7.84)
Week 24 (MMRM)		
n	19	15
LS mean (SE)	81.81 (3.73)	89.94 (4.08)
95% CI of LS mean	(74.18, 89.44)	(81.63, 98.25)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.13 (-3.17, 19.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 24 (MMRM)		
n	17	15
LS mean (SE)	-0.24 (3.31)	-0.99 (3.48)
95% CI of LS mean	(-7.02, 6.53)	(-8.09, 6.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.74 (-10.59, 9.10)
Week 52		
n	20	16
Mean (SD)	82.92 (15.87)	93.23 (9.73)
Absolute Change at Week 52		
n	18	16
Mean (SD)	-0.46 (14.71)	1.56 (12.25)
Week 52 (MMRM)		
n	19	15
LS mean (SE)	82.25 (3.00)	93.27 (3.24)
95% CI of LS mean	(76.11, 88.39)	(86.67, 99.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.02 (1.99, 20.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 52 (MMRM)		
n	17	15
LS mean (SE)	-1.22 (3.36)	2.51 (3.40)
95% CI of LS mean	(-8.10, 5.65)	(-4.41, 9.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.74 (-6.05, 13.52)
Absolute Change through Week 52 (MMRM)		
n	17	17
LS mean (SE)	-0.24 (2.30)	0.95 (2.32)
95% CI of LS mean	(-4.93, 4.45)	(-3.77, 5.66)
P-value within Treatment	0.9172	0.6852
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.19 (-5.51, 7.88)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7200
Hedges' G (SE)		0.12 (0.34)
Hedges' 95% CI		(-0.56, 0.80)
Hedges' P-value		0.7183

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Baseline		
n	22	22
Mean (SD)	79.92 (17.38)	85.61 (16.90)
Week 8 (MMRM)		
n	22	23
LS mean (SE)	80.66 (4.22)	81.18 (4.13)
95% CI of LS mean	(72.11, 89.20)	(72.83, 89.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.53 (-11.52, 12.58)
Absolute Change at Week 8 (MMRM)		
n	22	22
LS mean (SE)	0.65 (3.24)	-4.82 (3.24)
95% CI of LS mean	(-5.91, 7.22)	(-11.39, 1.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.47 (-14.80, 3.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Week 16 (MMRM)		
n	22	23
LS mean (SE)	78.01 (4.61)	79.37 (4.51)
95% CI of LS mean	(68.69, 87.32)	(70.26, 88.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.37 (-11.75, 14.49)
Absolute Change at Week 16 (MMRM)		
n	22	22
LS mean (SE)	-2.00 (3.54)	-6.71 (3.54)
95% CI of LS mean	(-9.16, 5.16)	(-13.87, 0.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.72 (-14.88, 5.44)
Week 24 (MMRM)		
n	22	22
LS mean (SE)	80.28 (4.06)	84.51 (3.99)
95% CI of LS mean	(72.08, 88.47)	(76.45, 92.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.24 (-7.37, 15.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 24 (MMRM)		
n	22	22
LS mean (SE)	0.27 (2.86)	-1.03 (2.86)
95% CI of LS mean	(-5.50, 6.05)	(-6.81, 4.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.31 (-9.52, 6.91)
Week 52		
n	22	23
Mean (SD)	83.33 (16.67)	86.59 (18.76)
Absolute Change at Week 52		
n	22	22
Mean (SD)	3.41 (8.40)	1.52 (11.10)
Week 52 (MMRM)		
n	22	23
LS mean (SE)	84.07 (3.78)	85.89 (3.69)
95% CI of LS mean	(76.43, 91.70)	(78.43, 93.36)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.83 (-8.97, 12.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 52 (MMRM)		
n	22	22
LS mean (SE)	4.06 (2.03)	0.86 (2.03)
95% CI of LS mean	(-0.05, 8.17)	(-3.25, 4.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.20 (-9.08, 2.68)
Absolute Change through Week 52 (MMRM)		
n	22	22
LS mean (SE)	0.78 (2.29)	-2.30 (2.29)
95% CI of LS mean	(-3.86, 5.42)	(-6.94, 2.35)
P-value within Treatment	0.7358	0.3235
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.08 (-9.70, 3.55)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3537
Hedges' G (SE)		-0.28 (0.30)
Hedges' 95% CI		(-0.88, 0.32)
Hedges' P-value		0.3512

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Baseline		
n	21	20
Mean (SD)	85.71 (17.90)	81.25 (17.07)
Week 8 (MMRM)		
n	20	18
LS mean (SE)	89.79 (3.31)	90.05 (3.49)
95% CI of LS mean	(83.07, 96.51)	(82.96, 97.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.26 (-9.64, 10.15)
Absolute Change at Week 8 (MMRM)		
n	20	18
LS mean (SE)	4.46 (2.55)	9.86 (2.70)
95% CI of LS mean	(-0.73, 9.65)	(4.38, 15.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.40 (-2.30, 13.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Week 16 (MMRM)		
n	20	17
LS mean (SE)	89.79 (3.36)	86.57 (3.60)
95% CI of LS mean	(82.97, 96.61)	(79.28, 93.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.22 (-13.33, 6.90)
Absolute Change at Week 16 (MMRM)		
n	20	17
LS mean (SE)	4.46 (2.74)	6.74 (2.95)
95% CI of LS mean	(-1.12, 10.04)	(0.74, 12.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.28 (-6.06, 10.62)
Week 24 (MMRM)		
n	20	16
LS mean (SE)	90.21 (2.74)	87.56 (2.98)
95% CI of LS mean	(84.59, 95.82)	(81.47, 93.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.65 (-11.07, 5.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 24 (MMRM)		
n	20	16
LS mean (SE)	4.88 (2.92)	6.72 (3.19)
95% CI of LS mean	(-1.06, 10.81)	(0.24, 13.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.84 (-7.07, 10.76)
Week 52		
n	21	17
Mean (SD)	90.87 (12.88)	92.16 (9.07)
Absolute Change at Week 52		
n	21	17
Mean (SD)	5.16 (15.25)	8.82 (9.98)
Week 52 (MMRM)		
n	20	15
LS mean (SE)	90.62 (2.76)	89.70 (3.11)
95% CI of LS mean	(84.94, 96.31)	(83.32, 96.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.93 (-9.60, 7.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Role

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	5.29 (3.12)	8.52 (3.52)
95% CI of LS mean	(-1.06, 11.65)	(1.38, 15.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.23 (-6.45, 12.90)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	4.88 (2.54)	7.33 (2.77)
95% CI of LS mean	(-0.31, 10.06)	(1.70, 12.95)
P-value within Treatment	0.0643	0.0122
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.45 (-5.35, 10.25)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5272
Hedges' G (SE)		0.21 (0.32)
Hedges' 95% CI		(-0.45, 0.87)
Hedges' P-value		0.5198

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Baseline		
n	231	225
Mean (SD)	65.51 (19.02)	66.48 (19.15)
Week 8 (MMRM)		
n	229	223
LS mean (SE)	63.63 (1.37)	66.28 (1.38)
95% CI of LS mean	(60.94, 66.31)	(63.56, 69.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.65 (-1.17, 6.47)
Absolute Change at Week 8 (MMRM)		
n	224	220
LS mean (SE)	-1.56 (1.09)	-0.31 (1.10)
95% CI of LS mean	(-3.70, 0.58)	(-2.46, 1.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.25 (-1.79, 4.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Week 16 (MMRM)		
n	226	218
LS mean (SE)	63.42 (1.35)	65.50 (1.37)
95% CI of LS mean	(60.76, 66.07)	(62.81, 68.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.08 (-1.70, 5.87)
Absolute Change at Week 16 (MMRM)		
n	220	215
LS mean (SE)	-1.55 (1.02)	-1.06 (1.03)
95% CI of LS mean	(-3.56, 0.46)	(-3.09, 0.97)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.49 (-2.37, 3.35)
Week 24 (MMRM)		
n	225	214
LS mean (SE)	62.23 (1.39)	64.44 (1.42)
95% CI of LS mean	(59.49, 64.97)	(61.65, 67.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.21 (-1.70, 6.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Absolute Change at Week 24 (MMRM)		
n	219	212
LS mean (SE)	-3.17 (1.10)	-2.12 (1.12)
95% CI of LS mean	(-5.34, -1.01)	(-4.32, 0.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.05 (-2.04, 4.14)
Week 52		
n	231	212
Mean (SD)	64.21 (20.11)	67.65 (18.75)
Absolute Change at Week 52		
n	225	209
Mean (SD)	-0.96 (16.30)	0.72 (14.32)
Week 52 (MMRM)		
n	225	209
LS mean (SE)	63.92 (1.28)	66.83 (1.32)
95% CI of LS mean	(61.40, 66.44)	(64.25, 69.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.92 (-0.70, 6.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Absolute Change at Week 52 (MMRM)		
n	219	206
LS mean (SE)	-1.25 (1.04)	0.32 (1.07)
95% CI of LS mean	(-3.30, 0.79)	(-1.77, 2.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.58 (-1.35, 4.51)
Absolute Change through Week 52 (MMRM)		
n	222	217
LS mean (SE)	-1.99 (0.84)	-0.95 (0.85)
95% CI of LS mean	(-3.64, -0.35)	(-2.62, 0.71)
P-value within Treatment	0.0176	0.2621
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.04 (-1.30, 3.38)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3830
Hedges' G (SE)		0.08 (0.10)
Hedges' 95% CI		(-0.10, 0.27)
Hedges' P-value		0.3829

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	38	41
Mean (SD)	74.34 (17.59)	68.70 (17.56)
Week 8 (MMRM)		
n	37	38
LS mean (SE)	66.33 (3.21)	67.43 (3.16)
95% CI of LS mean	(59.93, 72.73)	(61.12, 73.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.11 (-7.96, 10.18)
Absolute Change at Week 8 (MMRM)		
n	37	38
LS mean (SE)	-6.79 (2.57)	-1.94 (2.54)
95% CI of LS mean	(-11.93, -1.65)	(-7.01, 3.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.85 (-2.44, 12.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 16 (MMRM)		
n	37	37
LS mean (SE)	66.55 (3.24)	66.25 (3.22)
95% CI of LS mean	(60.08, 73.02)	(59.82, 72.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.31 (-9.51, 8.90)
Absolute Change at Week 16 (MMRM)		
n	37	37
LS mean (SE)	-6.56 (2.83)	-3.01 (2.82)
95% CI of LS mean	(-12.20, -0.93)	(-8.63, 2.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.55 (-4.47, 11.57)
Week 24 (MMRM)		
n	36	37
LS mean (SE)	66.56 (3.29)	66.24 (3.25)
95% CI of LS mean	(60.00, 73.11)	(59.75, 72.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.32 (-9.62, 8.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 24 (MMRM)		
n	36	37
LS mean (SE)	-6.56 (3.31)	-3.03 (3.27)
95% CI of LS mean	(-13.16, 0.04)	(-9.56, 3.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.53 (-5.81, 12.87)
Week 52		
n	35	39
Mean (SD)	69.76 (18.31)	67.74 (16.90)
Absolute Change at Week 52		
n	35	39
Mean (SD)	-4.76 (15.82)	-0.43 (19.02)
Week 52 (MMRM)		
n	34	36
LS mean (SE)	68.69 (2.96)	67.23 (2.90)
95% CI of LS mean	(62.79, 74.59)	(61.45, 73.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.46 (-9.82, 6.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 52 (MMRM)		
n	34	36
LS mean (SE)	-4.49 (2.90)	-2.07 (2.83)
95% CI of LS mean	(-10.27, 1.29)	(-7.73, 3.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.41 (-5.74, 10.57)
Absolute Change through Week 52 (MMRM)		
n	37	37
LS mean (SE)	-5.87 (2.57)	-2.71 (2.55)
95% CI of LS mean	(-11.01, -0.74)	(-7.79, 2.38)
P-value within Treatment	0.0256	0.2923
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.17 (-4.14, 10.47)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3904
Hedges' G (SE)		0.20 (0.23)
Hedges' 95% CI		(-0.26, 0.66)
Hedges' P-value		0.3865

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Baseline		
n	208	205
Mean (SD)	68.07 (18.62)	67.56 (18.48)
Week 8 (MMRM)		
n	205	202
LS mean (SE)	64.65 (1.45)	66.98 (1.46)
95% CI of LS mean	(61.80, 67.50)	(64.11, 69.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.33 (-1.72, 6.38)
Absolute Change at Week 8 (MMRM)		
n	202	200
LS mean (SE)	-3.05 (1.17)	-0.83 (1.18)
95% CI of LS mean	(-5.35, -0.74)	(-3.15, 1.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.21 (-1.06, 5.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Week 16 (MMRM)		
n	202	199
LS mean (SE)	65.00 (1.43)	66.47 (1.44)
95% CI of LS mean	(62.20, 67.81)	(63.64, 69.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.46 (-2.52, 5.44)
Absolute Change at Week 16 (MMRM)		
n	198	197
LS mean (SE)	-2.70 (1.10)	-1.28 (1.10)
95% CI of LS mean	(-4.86, -0.53)	(-3.45, 0.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.42 (-1.65, 4.49)
Week 24 (MMRM)		
n	200	197
LS mean (SE)	63.45 (1.48)	64.37 (1.50)
95% CI of LS mean	(60.53, 66.37)	(61.42, 67.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.91 (-3.23, 5.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Absolute Change at Week 24 (MMRM)		
n	196	195
LS mean (SE)	-4.47 (1.24)	-3.34 (1.24)
95% CI of LS mean	(-6.91, -2.03)	(-5.79, -0.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.13 (-2.33, 4.58)
Week 52		
n	203	195
Mean (SD)	65.60 (19.73)	67.74 (18.75)
Absolute Change at Week 52		
n	199	193
Mean (SD)	-2.05 (16.32)	0.13 (14.84)
Week 52 (MMRM)		
n	198	192
LS mean (SE)	65.21 (1.34)	67.25 (1.36)
95% CI of LS mean	(62.57, 67.85)	(64.58, 69.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.04 (-1.72, 5.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Absolute Change at Week 52 (MMRM)		
n	194	190
LS mean (SE)	-2.44 (1.12)	-0.36 (1.13)
95% CI of LS mean	(-4.64, -0.25)	(-2.57, 1.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.08 (-1.03, 5.20)
Absolute Change through Week 52 (MMRM)		
n	200	198
LS mean (SE)	-3.20 (0.92)	-1.66 (0.92)
95% CI of LS mean	(-5.01, -1.39)	(-3.48, 0.16)
P-value within Treatment	0.0006	0.0734
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.54 (-1.02, 4.11)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2379
Hedges' G (SE)		0.12 (0.10)
Hedges' 95% CI		(-0.08, 0.32)
Hedges' P-value		0.2379

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	18	19
Mean (SD)	52.78 (12.78)	65.79 (18.19)
Week 8 (MMRM)		
n	19	18
LS mean (SE)	56.78 (3.50)	68.31 (3.59)
95% CI of LS mean	(49.65, 63.91)	(60.98, 75.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.52 (1.27, 21.78)
Absolute Change at Week 8 (MMRM)		
n	17	18
LS mean (SE)	3.03 (3.31)	3.62 (3.21)
95% CI of LS mean	(-3.72, 9.78)	(-2.94, 10.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.59 (-8.86, 10.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Week 16 (MMRM)		
n	19	16
LS mean (SE)	54.15 (3.45)	65.25 (3.72)
95% CI of LS mean	(47.08, 61.22)	(57.68, 72.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.10 (0.72, 21.49)
Absolute Change at Week 16 (MMRM)		
n	17	16
LS mean (SE)	3.03 (2.56)	-0.21 (2.65)
95% CI of LS mean	(-2.19, 8.26)	(-5.60, 5.18)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.24 (-10.81, 4.32)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	53.27 (4.04)	66.22 (4.33)
95% CI of LS mean	(45.01, 61.53)	(57.38, 75.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.95 (0.83, 25.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 24 (MMRM)		
n	17	16
LS mean (SE)	-0.89 (3.68)	0.62 (3.76)
95% CI of LS mean	(-8.41, 6.63)	(-7.07, 8.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.50 (-9.28, 12.29)
Week 52		
n	20	16
Mean (SD)	57.08 (16.94)	69.79 (16.07)
Absolute Change at Week 52		
n	18	16
Mean (SD)	3.24 (15.95)	1.56 (11.87)
Week 52 (MMRM)		
n	19	15
LS mean (SE)	56.34 (3.72)	67.48 (4.09)
95% CI of LS mean	(48.71, 63.97)	(59.14, 75.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.13 (-0.19, 22.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 52 (MMRM)		
n	17	15
LS mean (SE)	2.54 (3.40)	2.09 (3.59)
95% CI of LS mean	(-4.40, 9.48)	(-5.23, 9.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.45 (-10.57, 9.67)
Absolute Change through Week 52 (MMRM)		
n	17	17
LS mean (SE)	1.56 (2.58)	0.83 (2.65)
95% CI of LS mean	(-3.73, 6.85)	(-4.58, 6.24)
P-value within Treatment	0.5504	0.7560
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.73 (-8.34, 6.88)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8463
Hedges' G (SE)		-0.07 (0.33)
Hedges' 95% CI		(-0.75, 0.62)
Hedges' P-value		0.8452

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Baseline		
n	22	22
Mean (SD)	60.23 (21.35)	61.36 (19.68)
Week 8 (MMRM)		
n	22	23
LS mean (SE)	58.80 (4.31)	60.42 (4.21)
95% CI of LS mean	(50.09, 67.51)	(51.90, 68.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.62 (-10.67, 13.91)
Absolute Change at Week 8 (MMRM)		
n	22	22
LS mean (SE)	-1.68 (3.32)	-0.59 (3.32)
95% CI of LS mean	(-8.40, 5.04)	(-7.31, 6.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.09 (-8.51, 10.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Week 16 (MMRM)		
n	22	23
LS mean (SE)	56.53 (4.55)	61.15 (4.45)
95% CI of LS mean	(47.33, 65.73)	(52.15, 70.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.62 (-8.34, 17.58)
Absolute Change at Week 16 (MMRM)		
n	22	22
LS mean (SE)	-3.95 (3.98)	0.54 (3.98)
95% CI of LS mean	(-11.99, 4.08)	(-7.49, 8.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.50 (-6.95, 15.95)
Week 24 (MMRM)		
n	22	22
LS mean (SE)	59.18 (4.10)	66.02 (4.06)
95% CI of LS mean	(50.90, 67.46)	(57.83, 74.21)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.84 (-4.91, 18.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 24 (MMRM)		
n	22	22
LS mean (SE)	-1.30 (3.80)	5.09 (3.80)
95% CI of LS mean	(-8.98, 6.38)	(-2.59, 12.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.39 (-4.56, 17.34)
Week 52		
n	22	23
Mean (SD)	59.47 (22.02)	65.58 (19.67)
Absolute Change at Week 52		
n	22	22
Mean (SD)	-0.76 (17.61)	4.92 (18.66)
Week 52 (MMRM)		
n	22	23
LS mean (SE)	59.94 (4.45)	65.13 (4.35)
95% CI of LS mean	(50.96, 68.92)	(56.35, 73.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.20 (-7.46, 17.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 52 (MMRM)		
n	22	22
LS mean (SE)	-0.54 (3.96)	4.71 (3.96)
95% CI of LS mean	(-8.55, 7.47)	(-3.30, 12.72)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.26 (-6.16, 16.67)
Absolute Change through Week 52 (MMRM)		
n	22	22
LS mean (SE)	-1.93 (3.26)	3.45 (3.26)
95% CI of LS mean	(-8.53, 4.66)	(-3.14, 10.04)
P-value within Treatment	0.5565	0.2965
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.38 (-4.05, 14.81)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2553
Hedges' G (SE)		0.35 (0.30)
Hedges' 95% CI		(-0.26, 0.95)
Hedges' P-value		0.2532

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Baseline		
n	21	20
Mean (SD)	72.62 (19.39)	66.25 (23.02)
Week 8 (MMRM)		
n	20	18
LS mean (SE)	69.48 (4.33)	66.78 (4.58)
95% CI of LS mean	(60.67, 78.29)	(57.47, 76.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.70 (-15.79, 10.39)
Absolute Change at Week 8 (MMRM)		
n	20	18
LS mean (SE)	-1.31 (3.22)	0.07 (3.40)
95% CI of LS mean	(-7.86, 5.24)	(-6.85, 6.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.38 (-8.32, 11.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Week 16 (MMRM)		
n	20	17
LS mean (SE)	69.06 (4.47)	62.28 (4.80)
95% CI of LS mean	(59.96, 78.17)	(52.53, 72.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.79 (-20.40, 6.82)
Absolute Change at Week 16 (MMRM)		
n	20	17
LS mean (SE)	-1.73 (3.28)	-4.17 (3.55)
95% CI of LS mean	(-8.40, 4.94)	(-11.38, 3.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.43 (-12.44, 7.57)
Week 24 (MMRM)		
n	20	16
LS mean (SE)	69.06 (4.69)	66.07 (5.04)
95% CI of LS mean	(59.52, 78.61)	(55.83, 76.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.99 (-17.25, 11.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 24 (MMRM)		
n	20	16
LS mean (SE)	-1.73 (3.06)	-0.45 (3.33)
95% CI of LS mean	(-7.96, 4.50)	(-7.22, 6.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.28 (-8.10, 10.65)
Week 52		
n	21	17
Mean (SD)	71.83 (20.15)	67.65 (16.37)
Absolute Change at Week 52		
n	21	17
Mean (SD)	-0.79 (14.88)	-1.47 (16.20)
Week 52 (MMRM)		
n	20	15
LS mean (SE)	70.31 (4.43)	64.62 (4.83)
95% CI of LS mean	(61.26, 79.37)	(54.78, 74.47)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.69 (-19.31, 7.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Vitality

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	-0.48 (3.64)	-2.42 (4.03)
95% CI of LS mean	(-7.89, 6.93)	(-10.61, 5.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.94 (-13.13, 9.24)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	-1.31 (2.91)	-2.35 (3.15)
95% CI of LS mean	(-7.25, 4.62)	(-8.76, 4.06)
P-value within Treatment	0.6551	0.4620
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.03 (-9.96, 7.89)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8154
Hedges' G (SE)		-0.08 (0.32)
Hedges' 95% CI		(-0.73, 0.58)
Hedges' P-value		0.8114

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Baseline		
n	228	225
Mean (SD)	88.74 (23.93)	84.44 (27.09)
Week 8 (MMRM)		
n	225	223
LS mean (SE)	88.11 (1.68)	85.32 (1.70)
95% CI of LS mean	(84.80, 91.42)	(81.99, 88.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.79 (-7.49, 1.92)
Absolute Change at Week 8 (MMRM)		
n	221	220
LS mean (SE)	-1.24 (1.35)	0.72 (1.36)
95% CI of LS mean	(-3.90, 1.42)	(-1.95, 3.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.96 (-1.81, 5.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Week 16 (MMRM)		
n	221	218
LS mean (SE)	87.13 (1.76)	85.68 (1.78)
95% CI of LS mean	(83.67, 90.59)	(82.19, 89.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.45 (-6.37, 3.47)
Absolute Change at Week 16 (MMRM)		
n	217	215
LS mean (SE)	-2.24 (1.46)	1.11 (1.47)
95% CI of LS mean	(-5.11, 0.64)	(-1.78, 4.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.35 (-0.73, 7.42)
Week 24 (MMRM)		
n	221	214
LS mean (SE)	86.94 (1.79)	85.71 (1.81)
95% CI of LS mean	(83.43, 90.45)	(82.15, 89.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.23 (-6.23, 3.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Absolute Change at Week 24 (MMRM)		
n	217	212
LS mean (SE)	-2.25 (1.38)	1.31 (1.40)
95% CI of LS mean	(-4.97, 0.47)	(-1.43, 4.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.56 (-0.30, 7.43)
Week 52		
n	231	212
Mean (SD)	87.88 (25.58)	84.28 (28.00)
Absolute Change at Week 52		
n	222	209
Mean (SD)	-1.20 (22.16)	-0.32 (21.92)
Week 52 (MMRM)		
n	225	209
LS mean (SE)	87.67 (1.77)	84.27 (1.82)
95% CI of LS mean	(84.18, 91.16)	(80.70, 87.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.40 (-8.39, 1.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 237	VNZ/TEZ/D-IVA N = 228
Absolute Change at Week 52 (MMRM)		
n	216	206
LS mean (SE)	-1.63 (1.51)	-0.16 (1.53)
95% CI of LS mean	(-4.60, 1.33)	(-3.18, 2.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.47 (-2.76, 5.70)
Absolute Change through Week 52 (MMRM)		
n	219	217
LS mean (SE)	-2.04 (1.19)	0.75 (1.19)
95% CI of LS mean	(-4.37, 0.29)	(-1.59, 3.10)
P-value within Treatment	0.0861	0.5282
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.79 (-0.51, 6.10)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0977
Hedges' G (SE)		0.16 (0.10)
Hedges' 95% CI		(-0.03, 0.35)
Hedges' P-value		0.0980

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Baseline		
n	38	41
Mean (SD)	86.84 (25.16)	83.74 (27.00)
Week 8 (MMRM)		
n	37	37
LS mean (SE)	82.35 (5.48)	82.02 (5.44)
95% CI of LS mean	(71.42, 93.28)	(71.18, 92.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.33 (-15.87, 15.21)
Absolute Change at Week 8 (MMRM)		
n	37	37
LS mean (SE)	-4.85 (4.06)	-0.59 (4.04)
95% CI of LS mean	(-12.95, 3.24)	(-8.65, 7.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.26 (-7.27, 15.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Week 16 (MMRM)		
n	36	37
LS mean (SE)	81.80 (5.49)	85.90 (5.43)
95% CI of LS mean	(70.85, 92.76)	(75.07, 96.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.10 (-11.46, 19.66)
Absolute Change at Week 16 (MMRM)		
n	36	37
LS mean (SE)	-5.36 (4.59)	3.10 (4.53)
95% CI of LS mean	(-14.51, 3.78)	(-5.95, 12.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.46 (-4.50, 21.42)
Week 24 (MMRM)		
n	36	37
LS mean (SE)	81.51 (5.33)	82.32 (5.27)
95% CI of LS mean	(70.88, 92.15)	(71.81, 92.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.81 (-14.30, 15.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 24 (MMRM)		
n	36	37
LS mean (SE)	-5.69 (3.99)	-0.49 (3.95)
95% CI of LS mean	(-13.66, 2.27)	(-8.38, 7.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.20 (-6.12, 16.52)
Week 52		
n	35	38
Mean (SD)	81.90 (30.62)	84.21 (28.72)
Absolute Change at Week 52		
n	35	38
Mean (SD)	-5.71 (24.90)	0.88 (23.87)
Week 52 (MMRM)		
n	34	35
LS mean (SE)	80.27 (4.88)	84.04 (4.82)
95% CI of LS mean	(70.53, 90.01)	(74.43, 93.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.77 (-10.08, 17.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41
Absolute Change at Week 52 (MMRM)		
n	34	35
LS mean (SE)	-7.09 (4.25)	1.37 (4.20)
95% CI of LS mean	(-15.57, 1.39)	(-7.01, 9.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.46 (-3.57, 20.48)
Absolute Change through Week 52 (MMRM)		
n	37	37
LS mean (SE)	-6.05 (3.71)	1.32 (3.68)
95% CI of LS mean	(-13.45, 1.35)	(-6.01, 8.66)
P-value within Treatment	0.1076	0.7201
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.37 (-3.17, 17.92)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1677
Hedges' G (SE)		0.32 (0.23)
Hedges' 95% CI		(-0.14, 0.79)
Hedges' P-value		0.1654

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Baseline		
n	205	205
Mean (SD)	88.78 (23.54)	83.41 (27.93)
Week 8 (MMRM)		
n	201	202
LS mean (SE)	86.60 (1.90)	83.44 (1.91)
95% CI of LS mean	(82.86, 90.35)	(79.69, 87.19)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.16 (-8.47, 2.14)
Absolute Change at Week 8 (MMRM)		
n	199	200
LS mean (SE)	-2.68 (1.52)	-0.07 (1.51)
95% CI of LS mean	(-5.67, 0.30)	(-3.05, 2.90)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.61 (-1.61, 6.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Week 16 (MMRM)		
n	196	199
LS mean (SE)	86.09 (1.94)	84.73 (1.94)
95% CI of LS mean	(82.27, 89.90)	(80.91, 88.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.36 (-6.76, 4.04)
Absolute Change at Week 16 (MMRM)		
n	194	197
LS mean (SE)	-3.19 (1.58)	1.31 (1.57)
95% CI of LS mean	(-6.31, -0.08)	(-1.79, 4.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.50 (0.11, 8.90)
Week 24 (MMRM)		
n	196	197
LS mean (SE)	85.33 (2.02)	83.56 (2.02)
95% CI of LS mean	(81.36, 89.30)	(79.59, 87.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.76 (-7.39, 3.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Absolute Change at Week 24 (MMRM)		
n	194	195
LS mean (SE)	-3.77 (1.56)	0.25 (1.55)
95% CI of LS mean	(-6.84, -0.71)	(-2.80, 3.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.03 (-0.30, 8.35)
Week 52		
n	203	194
Mean (SD)	85.39 (27.75)	82.65 (29.43)
Absolute Change at Week 52		
n	196	192
Mean (SD)	-3.91 (23.67)	-0.52 (23.50)
Week 52 (MMRM)		
n	198	191
LS mean (SE)	84.91 (2.03)	82.48 (2.05)
95% CI of LS mean	(80.92, 88.89)	(78.44, 86.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.43 (-8.11, 3.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: F/F

	ELX/TEZ/IVA N = 212	VNZ/TEZ/D-IVA N = 207
Absolute Change at Week 52 (MMRM)		
n	191	189
LS mean (SE)	-4.37 (1.72)	-0.81 (1.72)
95% CI of LS mean	(-7.75, -0.99)	(-4.20, 2.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.56 (-1.23, 8.35)
Absolute Change through Week 52 (MMRM)		
n	197	198
LS mean (SE)	-3.78 (1.33)	0.25 (1.32)
95% CI of LS mean	(-6.39, -1.17)	(-2.35, 2.85)
P-value within Treatment	0.0047	0.8502
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.03 (0.34, 7.72)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0324
Hedges' G (SE)		0.22 (0.10)
Hedges' 95% CI		(0.02, 0.41)
Hedges' P-value		0.0327

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Baseline		
n	18	19
Mean (SD)	74.07 (33.44)	77.19 (33.43)
Week 8 (MMRM)		
n	19	18
LS mean (SE)	87.34 (6.94)	81.88 (7.13)
95% CI of LS mean	(73.20, 101.48)	(67.35, 96.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.46 (-25.81, 14.89)
Absolute Change at Week 8 (MMRM)		
n	17	18
LS mean (SE)	12.47 (3.08)	4.89 (2.99)
95% CI of LS mean	(6.18, 18.77)	(-1.23, 11.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.59 (-16.42, 1.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Week 16 (MMRM)		
n	19	16
LS mean (SE)	87.34 (7.19)	83.86 (7.44)
95% CI of LS mean	(72.70, 101.98)	(68.72, 98.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.49 (-24.61, 17.64)
Absolute Change at Week 16 (MMRM)		
n	17	16
LS mean (SE)	12.47 (4.77)	6.96 (4.73)
95% CI of LS mean	(2.73, 22.22)	(-2.68, 16.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.52 (-19.25, 8.22)
Week 24 (MMRM)		
n	19	16
LS mean (SE)	83.83 (7.83)	81.81 (8.13)
95% CI of LS mean	(67.89, 99.78)	(65.29, 98.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.02 (-25.05, 21.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 24 (MMRM)		
n	17	16
LS mean (SE)	8.55 (5.27)	4.67 (5.25)
95% CI of LS mean	(-2.19, 19.30)	(-6.01, 15.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.88 (-19.06, 11.30)
Week 52		
n	20	16
Mean (SD)	88.33 (27.09)	75.00 (33.33)
Absolute Change at Week 52		
n	18	16
Mean (SD)	12.96 (20.26)	-4.17 (20.64)
Week 52 (MMRM)		
n	19	15
LS mean (SE)	87.34 (7.06)	76.81 (7.48)
95% CI of LS mean	(72.94, 101.74)	(61.59, 92.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.53 (-31.55, 10.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: F/G

	ELX/TEZ/IVA N = 20	VNZ/TEZ/D-IVA N = 19
Absolute Change at Week 52 (MMRM)		
n	17	15
LS mean (SE)	12.47 (4.93)	0.21 (5.16)
95% CI of LS mean	(2.37, 22.57)	(-10.32, 10.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-12.26 (-26.89, 2.36)
Absolute Change through Week 52 (MMRM)		
n	17	17
LS mean (SE)	11.17 (4.41)	3.95 (4.40)
95% CI of LS mean	(2.15, 20.18)	(-5.02, 12.91)
P-value within Treatment	0.0170	0.3769
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.22 (-19.98, 5.54)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2572
Hedges' G (SE)		-0.39 (0.34)
Hedges' 95% CI		(-1.08, 0.30)
Hedges' P-value		0.2599

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Baseline		
n	22	22
Mean (SD)	96.97 (9.81)	90.91 (18.35)
Week 8 (MMRM)		
n	22	22
LS mean (SE)	92.43 (4.43)	92.75 (4.40)
95% CI of LS mean	(83.48, 101.37)	(83.87, 101.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.32 (-12.30, 12.94)
Absolute Change at Week 8 (MMRM)		
n	22	21
LS mean (SE)	-4.34 (3.84)	1.41 (3.91)
95% CI of LS mean	(-12.09, 3.41)	(-6.49, 9.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.75 (-5.34, 16.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Week 16 (MMRM)		
n	22	23
LS mean (SE)	90.91 (4.86)	89.85 (4.75)
95% CI of LS mean	(81.11, 100.71)	(80.27, 99.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.06 (-14.77, 12.66)
Absolute Change at Week 16 (MMRM)		
n	22	22
LS mean (SE)	-5.86 (5.42)	-1.72 (5.42)
95% CI of LS mean	(-16.79, 5.08)	(-12.66, 9.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.13 (-11.35, 19.62)
Week 24 (MMRM)		
n	22	22
LS mean (SE)	96.97 (2.29)	95.50 (2.30)
95% CI of LS mean	(92.33, 101.61)	(90.86, 100.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.47 (-8.07, 5.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 24 (MMRM)		
n	22	22
LS mean (SE)	0.21 (1.74)	4.34 (1.74)
95% CI of LS mean	(-3.32, 3.73)	(0.81, 7.87)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.13 (-0.90, 9.17)
Week 52		
n	22	23
Mean (SD)	96.97 (9.81)	97.10 (9.60)
Absolute Change at Week 52		
n	22	22
Mean (SD)	0.00 (14.55)	6.06 (16.70)
Week 52 (MMRM)		
n	22	23
LS mean (SE)	96.97 (2.15)	97.10 (2.10)
95% CI of LS mean	(92.62, 101.32)	(92.85, 101.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.13 (-5.99, 6.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: F/RF

	ELX/TEZ/IVA N = 22	VNZ/TEZ/D-IVA N = 23
Absolute Change at Week 52 (MMRM)		
n	22	22
LS mean (SE)	0.21 (3.17)	5.86 (3.17)
95% CI of LS mean	(-6.20, 6.61)	(-0.55, 12.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.65 (-3.44, 14.74)
Absolute Change through Week 52 (MMRM)		
n	22	22
LS mean (SE)	-1.81 (2.81)	2.83 (2.81)
95% CI of LS mean	(-7.50, 3.87)	(-2.86, 8.51)
P-value within Treatment	0.5227	0.3215
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.64 (-3.43, 12.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2524
Hedges' G (SE)		0.35 (0.30)
Hedges' 95% CI		(-0.26, 0.95)
Hedges' P-value		0.2539

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Baseline		
n	21	20
Mean (SD)	88.89 (26.53)	93.33 (13.68)
Week 8 (MMRM)		
n	20	18
LS mean (SE)	89.21 (5.36)	93.47 (5.66)
95% CI of LS mean	(78.32, 100.10)	(81.98, 104.96)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.26 (-11.77, 20.29)
Absolute Change at Week 8 (MMRM)		
n	20	18
LS mean (SE)	0.59 (3.26)	-0.66 (3.45)
95% CI of LS mean	(-6.05, 7.23)	(-7.67, 6.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.25 (-11.11, 8.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Week 16 (MMRM)		
n	20	17
LS mean (SE)	84.21 (6.35)	93.69 (6.80)
95% CI of LS mean	(71.27, 97.15)	(79.85, 107.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.48 (-9.63, 28.59)
Absolute Change at Week 16 (MMRM)		
n	20	17
LS mean (SE)	-4.41 (4.87)	-0.71 (5.27)
95% CI of LS mean	(-14.34, 5.52)	(-11.44, 10.03)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.70 (-11.05, 18.45)
Week 24 (MMRM)		
n	20	16
LS mean (SE)	85.88 (5.83)	93.66 (6.23)
95% CI of LS mean	(74.02, 97.74)	(81.01, 106.31)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.78 (-9.74, 25.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 24 (MMRM)		
n	20	16
LS mean (SE)	-2.74 (4.16)	-0.69 (4.49)
95% CI of LS mean	(-11.22, 5.73)	(-9.83, 8.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.05 (-10.56, 14.66)
Week 52		
n	21	17
Mean (SD)	92.06 (20.83)	94.12 (13.10)
Absolute Change at Week 52		
n	21	17
Mean (SD)	3.17 (14.55)	0.00 (11.79)
Week 52 (MMRM)		
n	20	15
LS mean (SE)	92.54 (4.02)	93.98 (4.31)
95% CI of LS mean	(84.36, 100.72)	(85.24, 102.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.44 (-10.78, 13.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.3.2.3
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups (Adolescents and Adults Only Domains)
Full Analysis Set

Version: 'Adolescents and Adults' Version
Domain: Weight

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 21	VNZ/TEZ/D-IVA N = 20
Absolute Change at Week 52 (MMRM)		
n	20	15
LS mean (SE)	3.93 (3.15)	-0.54 (3.48)
95% CI of LS mean	(-2.50, 10.36)	(-7.63, 6.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.47 (-14.22, 5.29)
Absolute Change through Week 52 (MMRM)		
n	20	17
LS mean (SE)	-1.07 (3.67)	-0.65 (3.96)
95% CI of LS mean	(-8.54, 6.39)	(-8.69, 7.40)
P-value within Treatment	0.7714	0.8714
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.43 (-10.72, 11.57)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9381
Hedges' G (SE)		0.03 (0.32)
Hedges' 95% CI		(-0.63, 0.68)
Hedges' P-value		0.9371

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.1055
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.1474
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.8496
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.3931
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.7479
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.0846
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.4636
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.3388
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.4644
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	-
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	-
Sex (Male vs. Female) [1]	0.3907
Region (North America vs. Rest of the World) [1]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for $ppFEV_1$, baseline sweat chloride, genotype group (F/F, F/G, F/RF, TCR/non-F) as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, baseline sweat chloride, and &geno. as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, baseline sweat chloride, and &geno. as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, baseline sweat chloride, and &geno. as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, baseline sweat chloride, and &geno. as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, baseline sweat chloride, and &geno. as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, baseline sweat chloride, and &geno. as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, baseline sweat chloride, and &geno. as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, baseline sweat chloride, and &geno. as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, baseline sweat chloride, and &geno. as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, baseline sweat chloride, and &geno. as covariates.
- [2] P-values are obtained from MMRM with treatment, visit, subgroup, treatment*visit, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15
Subgroup criteria are not met for this subgroup factor.		

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	87.04 (21.56)	77.78 (22.22)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	88.45 (8.50)	85.40 (9.31)
95% CI of LS mean	(70.27, 106.63)	(65.81, 104.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.05 (-31.32, 25.22)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	1.52 (11.47)	7.42 (12.06)
95% CI of LS mean	(-24.84, 27.88)	(-21.90, 36.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.90 (-35.90, 47.69)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	86.90 (8.30)	89.10 (9.31)
95% CI of LS mean	(69.04, 104.75)	(69.52, 108.69)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.20 (-25.66, 30.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	-7.20 (10.83)	18.53 (12.06)
95% CI of LS mean	(-32.24, 17.83)	(-10.79, 47.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	25.73 (-14.78, 66.24)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	85.02 (7.73)	80.20 (8.16)
95% CI of LS mean	(67.94, 102.10)	(62.48, 97.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.82 (-31.22, 21.58)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	-6.87 (9.09)	16.57 (10.71)
95% CI of LS mean	(-30.85, 17.11)	(-11.87, 45.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	23.44 (-17.03, 63.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	92.06 (16.62)	87.04 (12.99)
Absolute Change at Week 52		
n	5	3
Mean (SD)	2.22 (9.30)	18.52 (16.97)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	92.43 (7.73)	85.35 (7.73)
95% CI of LS mean	(75.35, 109.50)	(68.27, 102.43)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.08 (-33.06, 18.91)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	1.46 (9.09)	20.27 (10.71)
95% CI of LS mean	(-22.52, 25.45)	(-8.16, 48.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.81 (-21.66, 59.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	-4.20 (7.92)	18.46 (9.42)
95% CI of LS mean	(-31.22, 22.82)	(-13.59, 50.50)
P-value within Treatment	0.6364	0.1556
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	22.66 (-23.81, 69.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1991
Hedges' G (SE)		1.19 (0.72)
Hedges' 95% CI		(-0.65, 3.03)
Hedges' P-value		0.1581

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	72.22 (25.09)	88.89 (16.67)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	62.75 (8.82)	92.74 (7.15)
95% CI of LS mean	(43.52, 81.98)	(77.13, 108.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	29.99 (4.86, 55.11)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-7.44 (8.04)	2.49 (6.52)
95% CI of LS mean	(-24.99, 10.10)	(-11.75, 16.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.94 (-12.98, 32.86)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	76.90 (5.38)	99.03 (4.13)
95% CI of LS mean	(65.11, 88.69)	(89.92, 108.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	22.14 (6.50, 37.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	5.55 (8.87)	8.95 (7.25)
95% CI of LS mean	(-13.80, 24.91)	(-6.87, 24.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.39 (-21.83, 28.62)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	73.86 (4.85)	96.50 (3.93)
95% CI of LS mean	(63.20, 84.52)	(87.90, 105.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	22.64 (8.23, 37.06)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	3.67 (7.23)	6.36 (5.95)
95% CI of LS mean	(-12.18, 19.51)	(-6.63, 19.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.69 (-18.18, 23.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	91.67 (16.67)	95.24 (8.74)
Absolute Change at Week 52		
n	4	7
Mean (SD)	11.11 (30.09)	-1.59 (4.20)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	77.30 (8.41)	98.77 (6.67)
95% CI of LS mean	(57.93, 96.66)	(83.23, 114.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	21.48 (-3.60, 46.55)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	5.89 (10.41)	6.39 (8.14)
95% CI of LS mean	(-17.64, 29.42)	(-12.10, 24.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.50 (-29.61, 30.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	5.04 (7.99)	7.23 (6.46)
95% CI of LS mean	(-12.77, 22.85)	(-7.16, 21.63)
P-value within Treatment	0.5428	0.2892
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.20 (-21.02, 25.42)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8372
Hedges' G (SE)		0.11 (0.50)
Hedges' 95% CI		(-0.97, 1.18)
Hedges' P-value		0.8339

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	83.33 (15.32)	92.59 (12.83)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	83.02 (7.06)	89.91 (7.64)
95% CI of LS mean	(67.86, 98.18)	(73.78, 106.04)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.89 (-16.62, 30.40)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	4.35 (6.22)	4.31 (6.32)
95% CI of LS mean	(-9.43, 18.13)	(-10.04, 18.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.04 (-20.76, 20.68)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	80.44 (6.92)	82.50 (7.64)
95% CI of LS mean	(65.50, 95.38)	(66.37, 98.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.06 (-21.17, 25.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	-1.61 (5.81)	-12.36 (6.32)
95% CI of LS mean	(-14.43, 11.22)	(-26.71, 2.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.75 (-30.19, 8.69)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	87.14 (6.52)	89.52 (6.82)
95% CI of LS mean	(72.74, 101.55)	(74.68, 104.37)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.38 (-19.85, 24.61)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	6.62 (4.59)	-5.12 (5.39)
95% CI of LS mean	(-4.22, 17.45)	(-17.91, 7.67)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-11.74 (-29.71, 6.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	84.13 (15.53)	88.89 (9.94)
Absolute Change at Week 52		
n	5	3
Mean (SD)	0.00 (0.00)	3.70 (6.42)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	83.44 (6.52)	86.93 (6.52)
95% CI of LS mean	(69.03, 97.85)	(72.52, 101.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.49 (-18.45, 25.44)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	1.06 (4.59)	2.29 (5.39)
95% CI of LS mean	(-9.78, 11.90)	(-10.50, 15.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.23 (-16.74, 19.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	2.02 (3.69)	-5.06 (4.41)
95% CI of LS mean	(-8.94, 12.99)	(-18.15, 8.03)
P-value within Treatment	0.6175	0.3246
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.09 (-25.90, 11.73)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3235
Hedges' G (SE)		-0.80 (0.68)
Hedges' 95% CI		(-2.54, 0.94)
Hedges' P-value		0.2925

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	81.48 (20.69)	86.42 (9.26)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	78.30 (8.54)	82.37 (6.78)
95% CI of LS mean	(59.53, 97.06)	(67.48, 97.26)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.08 (-21.45, 29.60)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-0.98 (4.97)	-5.52 (3.97)
95% CI of LS mean	(-11.84, 9.88)	(-14.21, 3.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.54 (-19.11, 10.03)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	73.17 (8.79)	84.07 (6.65)
95% CI of LS mean	(53.96, 92.39)	(69.38, 98.76)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.90 (-15.00, 36.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-6.95 (6.27)	-4.27 (4.75)
95% CI of LS mean	(-20.69, 6.79)	(-14.87, 6.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.68 (-15.27, 20.64)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	65.33 (9.22)	92.19 (7.53)
95% CI of LS mean	(44.06, 86.61)	(74.91, 109.48)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	26.86 (-1.91, 55.63)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-13.94 (6.25)	4.20 (5.28)
95% CI of LS mean	(-28.41, 0.52)	(-7.95, 16.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.14 (-1.18, 37.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	80.56 (13.98)	80.95 (15.33)
Absolute Change at Week 52		
n	4	7
Mean (SD)	-11.11 (12.83)	-3.17 (8.40)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	64.15 (10.37)	80.74 (7.92)
95% CI of LS mean	(37.59, 90.71)	(59.46, 102.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	16.59 (-18.35, 51.53)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	-16.17 (8.06)	-7.42 (6.18)
95% CI of LS mean	(-35.13, 2.79)	(-22.43, 7.60)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.75 (-15.67, 33.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	-12.35 (5.25)	-2.49 (4.13)
95% CI of LS mean	(-24.90, 0.19)	(-12.62, 7.63)
P-value within Treatment	0.0526	0.5679
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.86 (-6.78, 26.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2029
Hedges' G (SE)		0.74 (0.51)
Hedges' 95% CI		(-0.37, 1.85)
Hedges' P-value		0.1744

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	97.22 (6.80)	88.89 (9.62)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	88.53 (5.57)	89.79 (6.27)
95% CI of LS mean	(76.96, 100.10)	(76.84, 102.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.26 (-16.83, 19.35)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	0.46 (3.98)	1.69 (4.33)
95% CI of LS mean	(-9.08, 10.01)	(-9.37, 12.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.22 (-14.46, 16.91)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	97.47 (5.39)	100.90 (6.27)
95% CI of LS mean	(86.25, 108.69)	(87.95, 113.85)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.43 (-14.19, 21.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	0.27 (3.83)	10.02 (4.33)
95% CI of LS mean	(-9.05, 9.60)	(-1.04, 21.08)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.75 (-5.82, 25.31)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	94.53 (4.83)	96.74 (5.21)
95% CI of LS mean	(84.31, 104.75)	(85.82, 107.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.21 (-13.66, 18.08)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	0.39 (3.40)	10.59 (4.01)
95% CI of LS mean	(-8.98, 9.76)	(-0.52, 21.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.20 (-5.61, 26.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	100.00 (0.00)	100.00 (0.00)
Absolute Change at Week 52		
n	5	3
Mean (SD)	0.00 (0.00)	11.11 (9.62)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	100.08 (4.83)	99.92 (4.83)
95% CI of LS mean	(89.86, 110.31)	(89.69, 110.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.17 (-15.56, 15.22)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	0.39 (3.40)	10.59 (4.01)
95% CI of LS mean	(-8.98, 9.76)	(-0.52, 21.71)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.20 (-5.61, 26.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	0.35 (3.12)	10.40 (3.71)
95% CI of LS mean	(-9.73, 10.43)	(-1.53, 22.34)
P-value within Treatment	0.9178	0.0691
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.05 (-7.05, 27.15)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1539
Hedges' G (SE)		1.34 (0.74)
Hedges' 95% CI		(-0.55, 3.23)
Hedges' P-value		0.1283

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	91.67 (20.41)	92.59 (16.90)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	82.94 (7.55)	98.41 (6.03)
95% CI of LS mean	(66.41, 99.47)	(85.18, 111.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	15.47 (-6.70, 37.65)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-8.88 (4.22)	5.92 (3.42)
95% CI of LS mean	(-18.01, 0.26)	(-1.49, 13.32)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.79 (2.84, 26.75)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	88.66 (7.13)	94.50 (5.75)
95% CI of LS mean	(73.02, 104.30)	(81.88, 107.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.84 (-15.30, 26.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-3.75 (2.78)	2.12 (2.25)
95% CI of LS mean	(-9.77, 2.26)	(-2.76, 7.00)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.87 (-2.25, 14.00)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	88.49 (6.53)	96.66 (5.23)
95% CI of LS mean	(74.00, 102.99)	(85.09, 108.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.17 (-11.61, 27.95)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-3.32 (3.94)	4.11 (3.41)
95% CI of LS mean	(-11.87, 5.23)	(-3.25, 11.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.43 (-4.06, 18.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	100.00 (0.00)	92.86 (13.11)
Absolute Change at Week 52		
n	4	7
Mean (SD)	0.00 (0.00)	-7.14 (13.11)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	84.87 (11.18)	89.04 (8.58)
95% CI of LS mean	(57.96, 111.78)	(67.80, 110.29)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.17 (-30.22, 38.57)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	2.00 (8.77)	-8.22 (5.78)
95% CI of LS mean	(-18.97, 22.96)	(-22.52, 6.09)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-10.21 (-35.70, 15.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	-1.69 (3.61)	-0.66 (2.54)
95% CI of LS mean	(-22.08, 18.69)	(-16.29, 14.96)
P-value within Treatment	0.6964	0.8255
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.03 (-24.44, 26.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8476
Hedges' G (SE)		0.12 (0.50)
Hedges' 95% CI		(-0.95, 1.19)
Hedges' P-value		0.8138

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14
Subgroup criteria are not met for this subgroup factor.		

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	86.67 (13.98)	80.00 (20.00)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	83.19 (7.26)	83.81 (7.65)
95% CI of LS mean	(67.26, 99.13)	(67.32, 100.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.62 (-23.96, 25.19)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	-0.32 (8.12)	8.25 (9.25)
95% CI of LS mean	(-22.16, 21.52)	(-18.02, 34.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.57 (-28.55, 45.68)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	84.74 (7.17)	88.25 (7.65)
95% CI of LS mean	(68.93, 100.56)	(71.76, 104.74)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.51 (-20.91, 27.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	12.01 (7.98)	8.25 (9.25)
95% CI of LS mean	(-9.88, 33.90)	(-18.02, 34.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.76 (-41.15, 33.63)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	81.13 (6.92)	86.81 (7.11)
95% CI of LS mean	(65.60, 96.66)	(71.04, 102.58)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.68 (-18.20, 29.56)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	-0.03 (7.57)	11.16 (8.95)
95% CI of LS mean	(-22.69, 22.62)	(-15.70, 38.01)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.19 (-27.00, 49.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	88.57 (12.00)	81.11 (14.86)
Absolute Change at Week 52		
n	5	3
Mean (SD)	1.33 (14.45)	4.44 (10.18)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	83.35 (6.92)	85.54 (6.92)
95% CI of LS mean	(67.82, 98.88)	(70.01, 101.07)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.19 (-21.54, 25.91)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	-0.03 (7.57)	8.93 (8.95)
95% CI of LS mean	(-22.69, 22.62)	(-17.92, 35.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.97 (-29.22, 47.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	3.98 (7.32)	9.45 (8.67)
95% CI of LS mean	(-19.53, 27.49)	(-18.37, 37.27)
P-value within Treatment	0.6249	0.3568
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.47 (-34.13, 45.06)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6864
Hedges' G (SE)		0.31 (0.65)
Hedges' 95% CI		(-1.36, 1.98)
Hedges' P-value		0.6517

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	77.78 (18.70)	79.26 (19.56)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	84.29 (5.83)	91.22 (4.70)
95% CI of LS mean	(71.34, 97.23)	(80.75, 101.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.93 (-10.12, 23.98)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	6.95 (6.89)	11.66 (5.52)
95% CI of LS mean	(-8.12, 22.03)	(-0.43, 23.75)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.71 (-15.43, 24.85)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	75.72 (7.98)	85.95 (6.56)
95% CI of LS mean	(57.90, 93.54)	(71.33, 100.57)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.22 (-13.03, 33.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-0.49 (6.75)	5.55 (5.44)
95% CI of LS mean	(-15.47, 14.50)	(-6.53, 17.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.04 (-14.04, 26.11)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	78.73 (7.48)	88.12 (6.16)
95% CI of LS mean	(62.17, 95.29)	(74.55, 101.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.39 (-12.32, 31.11)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	1.40 (7.60)	8.16 (6.20)
95% CI of LS mean	(-15.25, 18.04)	(-5.39, 21.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.76 (-15.40, 28.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	78.33 (11.39)	81.90 (10.69)
Absolute Change at Week 52		
n	4	7
Mean (SD)	-1.67 (19.91)	-4.76 (13.72)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	78.30 (5.53)	78.94 (4.05)
95% CI of LS mean	(65.90, 90.71)	(69.73, 88.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.64 (-15.41, 16.70)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	-0.91 (7.74)	-4.69 (5.62)
95% CI of LS mean	(-17.92, 16.11)	(-17.25, 7.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.78 (-25.79, 18.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	0.00 (6.11)	3.01 (4.82)
95% CI of LS mean	(-14.17, 14.18)	(-8.17, 14.18)
P-value within Treatment	0.9998	0.5505
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.00 (-16.11, 22.12)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7247
Hedges' G (SE)		0.19 (0.50)
Hedges' 95% CI		(-0.88, 1.27)
Hedges' P-value		0.7041

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12
Subgroup criteria are not met for this subgroup factor.		

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	87.04 (10.92)	88.89 (19.25)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	78.85 (9.02)	70.50 (9.90)
95% CI of LS mean	(59.62, 98.08)	(49.73, 91.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.34 (-38.26, 21.57)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	-14.70 (9.41)	-4.35 (9.94)
95% CI of LS mean	(-36.48, 7.09)	(-28.81, 20.10)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.34 (-24.47, 45.15)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	81.52 (8.80)	81.61 (9.90)
95% CI of LS mean	(62.65, 100.39)	(60.84, 102.38)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.09 (-29.37, 29.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	-0.37 (8.91)	-9.91 (9.94)
95% CI of LS mean	(-21.16, 20.41)	(-34.36, 14.54)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.54 (-43.45, 24.37)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	80.43 (8.18)	81.12 (8.64)
95% CI of LS mean	(62.43, 98.43)	(62.41, 99.83)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.69 (-27.14, 28.53)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	-8.30 (7.54)	-3.74 (8.89)
95% CI of LS mean	(-28.51, 11.90)	(-27.71, 20.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.56 (-29.58, 38.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	87.30 (10.00)	79.63 (16.36)
Absolute Change at Week 52		
n	5	3
Mean (SD)	-2.22 (14.49)	-11.11 (11.11)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	85.99 (8.18)	82.53 (8.18)
95% CI of LS mean	(67.99, 103.98)	(64.53, 100.53)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.45 (-30.82, 23.92)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	-2.75 (7.54)	-7.45 (8.89)
95% CI of LS mean	(-22.95, 17.46)	(-31.41, 16.52)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.70 (-38.84, 29.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	-3.81 (6.63)	-7.03 (7.89)
95% CI of LS mean	(-26.64, 19.02)	(-34.09, 20.03)
P-value within Treatment	0.6110	0.4460
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.22 (-42.43, 35.98)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7918
Hedges' G (SE)		-0.20 (0.65)
Hedges' 95% CI		(-1.86, 1.46)
Hedges' P-value		0.7666

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	72.22 (13.61)	71.60 (24.91)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	69.80 (7.01)	84.33 (5.66)
95% CI of LS mean	(54.59, 85.00)	(72.05, 96.62)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.54 (-5.50, 34.58)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-0.29 (8.86)	11.30 (7.11)
95% CI of LS mean	(-19.62, 19.04)	(-4.23, 26.84)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.59 (-14.13, 37.31)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	69.70 (8.27)	70.64 (6.06)
95% CI of LS mean	(51.57, 87.84)	(57.22, 84.06)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.93 (-22.17, 24.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-1.87 (8.96)	-0.22 (6.64)
95% CI of LS mean	(-21.50, 17.77)	(-14.96, 14.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.64 (-24.06, 27.35)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	77.20 (6.29)	83.58 (5.32)
95% CI of LS mean	(63.37, 91.03)	(71.93, 95.24)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.38 (-12.23, 25.00)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	7.12 (9.85)	11.81 (8.19)
95% CI of LS mean	(-14.39, 28.63)	(-6.01, 29.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.69 (-24.00, 33.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	86.11 (13.98)	82.54 (19.09)
Absolute Change at Week 52		
n	4	7
Mean (SD)	8.33 (10.64)	1.59 (23.51)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	80.35 (9.39)	82.06 (7.07)
95% CI of LS mean	(59.91, 100.78)	(66.53, 97.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-24.27, 27.69)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	10.23 (12.12)	11.34 (9.45)
95% CI of LS mean	(-17.08, 37.54)	(-10.20, 32.88)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.12 (-34.15, 36.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	5.16 (8.70)	7.64 (6.85)
95% CI of LS mean	(-13.85, 24.17)	(-7.39, 22.67)
P-value within Treatment	0.5645	0.2876
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.48 (-22.74, 27.71)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8336
Hedges' G (SE)		0.11 (0.50)
Hedges' 95% CI		(-0.96, 1.18)
Hedges' P-value		0.8248

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	88.89 (11.69)	97.22 (4.81)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	91.57 (4.40)	99.43 (4.81)
95% CI of LS mean	(82.25, 100.89)	(89.37, 109.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.86 (-6.64, 22.35)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	4.88 (2.97)	-1.01 (3.28)
95% CI of LS mean	(-2.46, 12.21)	(-9.65, 7.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.89 (-18.11, 6.34)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	91.19 (4.29)	99.43 (4.81)
95% CI of LS mean	(82.04, 100.34)	(89.37, 109.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.23 (-6.04, 22.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	5.56 (2.88)	-3.09 (3.28)
95% CI of LS mean	(-1.68, 12.80)	(-11.73, 5.55)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.65 (-20.88, 3.57)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	84.04 (4.00)	102.11 (4.22)
95% CI of LS mean	(75.33, 92.75)	(93.05, 111.16)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.07 (4.61, 31.53)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	3.11 (2.61)	1.41 (3.08)
95% CI of LS mean	(-4.30, 10.51)	(-7.37, 10.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.69 (-14.20, 10.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	91.07 (10.04)	99.31 (1.70)
Absolute Change at Week 52		
n	5	3
Mean (SD)	1.67 (9.13)	2.78 (4.81)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	90.29 (4.00)	102.07 (4.00)
95% CI of LS mean	(81.58, 99.00)	(93.36, 110.78)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.79 (-1.45, 25.02)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	6.23 (2.61)	1.41 (3.08)
95% CI of LS mean	(-1.17, 13.64)	(-7.37, 10.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.82 (-17.33, 7.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	4.97 (2.44)	-0.09 (2.89)
95% CI of LS mean	(-2.94, 12.88)	(-9.45, 9.27)
P-value within Treatment	0.1374	0.9776
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-5.05 (-18.44, 8.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3066
Hedges' G (SE)		-0.86 (0.68)
Hedges' 95% CI		(-2.62, 0.89)
Hedges' P-value		0.2618

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	83.33 (17.28)	81.48 (23.02)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	88.79 (5.19)	90.34 (4.14)
95% CI of LS mean	(77.36, 100.23)	(81.22, 99.46)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.55 (-13.87, 16.97)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	6.34 (6.05)	8.27 (4.93)
95% CI of LS mean	(-6.74, 19.42)	(-2.37, 18.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.93 (-14.99, 18.85)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	84.13 (5.94)	92.21 (4.76)
95% CI of LS mean	(71.11, 97.15)	(81.77, 102.65)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.08 (-9.27, 25.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	1.41 (6.32)	10.08 (5.12)
95% CI of LS mean	(-12.24, 15.05)	(-0.98, 21.14)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.68 (-8.94, 26.30)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	80.26 (5.67)	90.28 (4.75)
95% CI of LS mean	(67.68, 92.84)	(79.79, 100.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.02 (-7.03, 27.07)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-2.19 (8.95)	8.32 (7.41)
95% CI of LS mean	(-21.53, 17.15)	(-7.63, 24.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.51 (-14.60, 35.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	98.96 (2.08)	88.10 (15.11)
Absolute Change at Week 52		
n	4	7
Mean (SD)	10.42 (15.77)	-1.19 (7.87)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	93.98 (5.28)	87.47 (4.17)
95% CI of LS mean	(82.30, 105.66)	(78.22, 96.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.51 (-22.19, 9.17)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	10.27 (5.39)	3.41 (4.38)
95% CI of LS mean	(-1.41, 21.95)	(-6.06, 12.89)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.85 (-21.96, 8.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	3.16 (6.35)	7.27 (5.19)
95% CI of LS mean	(-10.57, 16.89)	(-3.93, 18.48)
P-value within Treatment	0.6272	0.1843
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.11 (-13.67, 21.89)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6258
Hedges' G (SE)		0.25 (0.50)
Hedges' 95% CI		(-0.83, 1.32)
Hedges' P-value		0.6260

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	84.72 (11.08)	86.11 (12.73)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	81.29 (6.97)	80.13 (7.63)
95% CI of LS mean	(66.49, 96.09)	(64.15, 96.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.16 (-24.18, 21.86)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	3.72 (7.01)	4.94 (7.57)
95% CI of LS mean	(-12.85, 20.29)	(-14.08, 23.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.22 (-25.77, 28.21)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	81.57 (6.80)	88.46 (7.63)
95% CI of LS mean	(67.04, 96.09)	(72.48, 104.45)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.90 (-15.77, 29.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	-8.83 (6.72)	4.94 (7.57)
95% CI of LS mean	(-24.93, 7.27)	(-14.08, 23.95)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	13.77 (-12.88, 40.42)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	81.42 (6.33)	83.67 (6.68)
95% CI of LS mean	(67.59, 95.26)	(69.28, 98.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.25 (-19.15, 23.64)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	-7.16 (5.89)	3.99 (6.95)
95% CI of LS mean	(-23.13, 8.81)	(-14.95, 22.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.14 (-15.80, 38.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	76.98 (14.05)	79.17 (12.64)
Absolute Change at Week 52		
n	5	3
Mean (SD)	-13.89 (14.57)	-2.78 (4.81)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	72.63 (6.33)	82.46 (6.33)
95% CI of LS mean	(58.79, 86.46)	(68.63, 96.30)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.84 (-11.19, 30.86)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	-18.27 (5.89)	1.21 (6.95)
95% CI of LS mean	(-34.24, -2.30)	(-17.73, 20.15)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	19.48 (-7.47, 46.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	-11.42 (5.36)	3.38 (6.36)
95% CI of LS mean	(-28.64, 5.80)	(-17.01, 23.76)
P-value within Treatment	0.1244	0.6327
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.80 (-14.44, 44.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2003
Hedges' G (SE)		1.15 (0.71)
Hedges' 95% CI		(-0.68, 2.98)
Hedges' P-value		0.1677

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	73.61 (31.81)	80.56 (16.14)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	68.43 (5.45)	86.79 (4.44)
95% CI of LS mean	(56.50, 80.35)	(77.08, 96.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.37 (2.91, 33.82)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-1.71 (8.43)	3.92 (6.83)
95% CI of LS mean	(-20.65, 17.23)	(-11.44, 19.27)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.62 (-19.18, 30.43)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	69.31 (7.28)	83.74 (6.08)
95% CI of LS mean	(53.33, 85.29)	(70.46, 97.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.43 (-6.44, 35.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-3.84 (6.23)	0.88 (4.95)
95% CI of LS mean	(-17.58, 9.89)	(-9.98, 11.73)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.72 (-13.57, 23.01)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	69.81 (9.87)	89.22 (8.12)
95% CI of LS mean	(48.44, 91.19)	(71.67, 106.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	19.40 (-8.30, 47.11)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-0.32 (8.52)	5.52 (7.22)
95% CI of LS mean	(-19.61, 18.97)	(-10.59, 21.64)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.84 (-19.71, 31.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	79.17 (25.00)	79.76 (17.25)
Absolute Change at Week 52		
n	4	7
Mean (SD)	-2.08 (23.94)	-5.95 (13.36)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	81.75 (10.39)	80.42 (8.34)
95% CI of LS mean	(59.14, 104.35)	(62.23, 98.61)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.32 (-30.41, 27.76)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	-3.96 (10.83)	-7.26 (7.79)
95% CI of LS mean	(-29.13, 21.20)	(-25.46, 10.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.30 (-35.01, 28.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	-2.71 (7.03)	-0.29 (5.44)
95% CI of LS mean	(-21.67, 16.26)	(-14.70, 14.13)
P-value within Treatment	0.7183	0.9602
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.42 (-22.37, 27.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8043
Hedges' G (SE)		0.14 (0.50)
Hedges' 95% CI		(-0.94, 1.21)
Hedges' P-value		0.7874

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	66.67 (31.43)	62.96 (12.83)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	60.86 (11.08)	82.82 (12.08)
95% CI of LS mean	(37.29, 84.44)	(57.47, 108.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	21.96 (-14.67, 58.59)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	6.12 (13.35)	16.92 (13.74)
95% CI of LS mean	(-23.83, 36.08)	(-15.15, 48.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.79 (-35.25, 56.83)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	55.30 (10.83)	82.82 (12.08)
95% CI of LS mean	(32.14, 78.47)	(57.47, 108.17)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	27.52 (-8.59, 63.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	-5.51 (12.48)	16.92 (13.74)
95% CI of LS mean	(-33.50, 22.48)	(-15.15, 48.98)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	22.42 (-21.29, 66.13)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	56.84 (10.13)	81.55 (10.65)
95% CI of LS mean	(34.71, 78.98)	(58.60, 104.51)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	24.71 (-9.49, 58.91)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	-5.67 (10.11)	18.68 (11.89)
95% CI of LS mean	(-30.76, 19.41)	(-11.00, 48.35)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	24.35 (-17.64, 66.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	66.67 (25.66)	68.52 (10.92)
Absolute Change at Week 52		
n	5	3
Mean (SD)	-4.44 (25.58)	11.11 (22.22)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	60.55 (10.13)	74.64 (10.13)
95% CI of LS mean	(38.41, 82.68)	(52.50, 96.77)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.09 (-19.57, 47.75)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	-2.90 (10.11)	11.27 (11.89)
95% CI of LS mean	(-27.98, 22.19)	(-18.41, 40.94)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.16 (-27.83, 56.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	-4.69 (8.44)	15.62 (10.07)
95% CI of LS mean	(-32.03, 22.64)	(-16.93, 48.17)
P-value within Treatment	0.6183	0.2210
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	20.31 (-26.88, 67.50)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2501
Hedges' G (SE)		1.00 (0.70)
Hedges' 95% CI		(-0.79, 2.79)
Hedges' P-value		0.2106

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	55.56 (32.20)	66.67 (22.22)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	73.69 (12.70)	65.69 (10.25)
95% CI of LS mean	(43.38, 104.00)	(41.15, 90.23)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.00 (-47.78, 31.79)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	13.80 (6.27)	1.91 (5.02)
95% CI of LS mean	(0.09, 27.52)	(-9.09, 12.91)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-11.90 (-30.23, 6.44)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	64.55 (9.21)	62.46 (7.11)
95% CI of LS mean	(42.79, 86.31)	(45.43, 79.49)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.09 (-31.16, 26.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-0.65 (8.91)	-0.88 (7.40)
95% CI of LS mean	(-20.97, 19.66)	(-17.95, 16.20)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.22 (-27.08, 26.64)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	58.87 (12.04)	69.68 (9.98)
95% CI of LS mean	(31.35, 86.39)	(46.97, 92.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.81 (-25.75, 47.37)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-1.01 (7.78)	6.00 (6.50)
95% CI of LS mean	(-18.88, 16.86)	(-8.86, 20.86)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.01 (-16.75, 30.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	61.11 (19.25)	69.84 (18.94)
Absolute Change at Week 52		
n	4	7
Mean (SD)	-2.78 (24.64)	0.00 (12.83)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	55.84 (11.84)	66.28 (9.12)
95% CI of LS mean	(27.36, 84.31)	(43.88, 88.68)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.44 (-26.74, 47.62)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	-4.11 (8.54)	3.30 (6.70)
95% CI of LS mean	(-22.82, 14.60)	(-11.52, 18.11)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.41 (-16.91, 31.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	-1.93 (7.18)	2.81 (5.87)
95% CI of LS mean	(-18.74, 14.89)	(-10.98, 16.59)
P-value within Treatment	0.7959	0.6465
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	4.73 (-17.49, 26.96)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6344
Hedges' G (SE)		0.25 (0.50)
Hedges' 95% CI		(-0.82, 1.33)
Hedges' P-value		0.6199

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	70.28 (22.96)	75.56 (15.40)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	73.41 (9.77)	72.03 (10.64)
95% CI of LS mean	(52.64, 94.19)	(49.71, 94.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.39 (-33.66, 30.88)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	18.29 (11.68)	1.65 (13.43)
95% CI of LS mean	(-13.89, 50.47)	(-37.04, 40.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-16.64 (-71.33, 38.05)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	74.72 (9.56)	74.25 (10.64)
95% CI of LS mean	(54.30, 95.14)	(51.94, 96.56)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.47 (-32.29, 31.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	27.37 (11.53)	-8.35 (13.43)
95% CI of LS mean	(-4.95, 59.68)	(-47.04, 30.34)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-35.72 (-90.77, 19.33)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	71.60 (8.94)	67.21 (9.40)
95% CI of LS mean	(52.09, 91.12)	(46.98, 87.44)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.39 (-34.54, 25.76)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	20.11 (11.08)	-9.58 (13.11)
95% CI of LS mean	(-13.13, 53.34)	(-48.98, 29.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-29.69 (-85.64, 26.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	79.05 (18.23)	77.78 (10.89)
Absolute Change at Week 52		
n	5	3
Mean (SD)	9.00 (20.67)	6.67 (11.55)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	76.05 (8.94)	79.51 (8.94)
95% CI of LS mean	(56.53, 95.56)	(59.99, 99.02)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.46 (-26.21, 33.14)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	16.77 (11.08)	-0.70 (13.11)
95% CI of LS mean	(-16.46, 50.01)	(-40.09, 38.70)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-17.47 (-73.42, 38.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	21.42 (10.81)	-6.21 (12.81)
95% CI of LS mean	(-12.70, 55.53)	(-46.58, 34.16)
P-value within Treatment	0.1406	0.6605
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-27.63 (-84.99, 29.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2237
Hedges' G (SE)		-1.06 (0.70)
Hedges' 95% CI		(-2.87, 0.74)
Hedges' P-value		0.1906

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	75.56 (13.11)	68.15 (18.19)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	76.21 (8.27)	75.12 (6.61)
95% CI of LS mean	(57.34, 95.08)	(59.96, 90.28)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.09 (-26.22, 24.04)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	0.49 (0.00)	7.08 (0.00)
95% CI of LS mean	(-, -)	(-, -)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.60 (-, -)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	83.37 (6.46)	67.91 (4.61)
95% CI of LS mean	(68.85, 97.89)	(57.60, 78.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-15.46 (-35.26, 4.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	8.32 (0.00)	0.70 (0.00)
95% CI of LS mean	(-, -)	(-, -)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-7.62 (-, -)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	69.54 (9.38)	71.77 (7.70)
95% CI of LS mean	(48.71, 90.37)	(54.73, 88.82)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	2.23 (-25.53, 29.99)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-6.18 (0.00)	4.35 (0.00)
95% CI of LS mean	(-, -)	(-, -)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	10.53 (-, -)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	85.00 (3.33)	72.38 (19.41)
Absolute Change at Week 52		
n	4	7
Mean (SD)	5.00 (13.74)	0.00 (12.17)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	82.89 (9.09)	70.90 (7.11)
95% CI of LS mean	(60.60, 105.18)	(52.68, 89.12)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-11.99 (-40.95, 16.97)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	15.78 (0.00)	12.29 (0.00)
95% CI of LS mean	(-, -)	(-, -)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.49 (-, -)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	5.97 (0.00)	5.78 (0.00)
95% CI of LS mean	(-, -)	(-, -)
P-value within Treatment	<0.0001	<0.0001
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.20 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	<0.0001
Hedges' G (SE)		-
Hedges' 95% CI		-
Hedges' P-value		-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 14

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	3
Mean (SD)	88.89 (17.21)	66.67 (33.33)
Week 8 (MMRM)		
n	4	3
LS mean (SE)	86.71 (14.77)	50.60 (16.22)
95% CI of LS mean	(54.95, 118.46)	(16.39, 84.81)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-36.11 (-85.50, 13.29)
Absolute Change at Week 8 (MMRM)		
n	2	2
LS mean (SE)	-8.89 (15.79)	-7.18 (14.66)
95% CI of LS mean	(-43.78, 26.00)	(-39.68, 25.33)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.71 (-47.39, 50.82)
Week 16 (MMRM)		
n	4	3
LS mean (SE)	89.27 (14.41)	61.71 (16.22)
95% CI of LS mean	(58.08, 120.46)	(27.50, 95.92)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-27.56 (-76.26, 21.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 16 (MMRM)		
n	2	2
LS mean (SE)	-7.74 (13.76)	9.49 (14.66)
95% CI of LS mean	(-37.73, 22.26)	(-23.01, 41.99)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	17.23 (-25.09, 59.54)
Week 24 (MMRM)		
n	6	5
LS mean (SE)	88.42 (13.40)	79.12 (14.16)
95% CI of LS mean	(58.50, 118.33)	(48.11, 110.13)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.30 (-55.56, 36.97)
Absolute Change at Week 24 (MMRM)		
n	4	3
LS mean (SE)	-10.72 (9.75)	14.29 (11.39)
95% CI of LS mean	(-32.37, 10.93)	(-11.09, 39.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	25.01 (-10.04, 60.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Week 52		
n	7	6
Mean (SD)	95.24 (12.60)	66.67 (42.16)
Absolute Change at Week 52		
n	5	3
Mean (SD)	0.00 (23.57)	22.22 (19.25)
Week 52 (MMRM)		
n	6	6
LS mean (SE)	99.53 (13.40)	61.58 (13.40)
95% CI of LS mean	(69.61, 129.45)	(31.67, 91.50)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-37.95 (-83.51, 7.62)
Absolute Change at Week 52 (MMRM)		
n	4	3
LS mean (SE)	-2.38 (9.75)	14.29 (11.39)
95% CI of LS mean	(-24.04, 19.27)	(-11.09, 39.66)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	16.67 (-18.38, 51.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Male

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 6
Absolute Change through Week 52 (MMRM)		
n	4	3
LS mean (SE)	-6.95 (6.33)	12.69 (7.66)
95% CI of LS mean	(-27.99, 14.10)	(-14.32, 39.70)
P-value within Treatment	0.3582	0.2119
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	19.63 (-21.17, 60.44)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1819
Hedges' G (SE)		1.28 (0.73)
Hedges' 95% CI		(-0.59, 3.15)
Hedges' P-value		0.1390

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Baseline		
n	6	9
Mean (SD)	83.33 (27.89)	85.19 (24.22)
Week 8 (MMRM)		
n	6	9
LS mean (SE)	73.56 (9.23)	88.00 (7.44)
95% CI of LS mean	(53.96, 93.16)	(72.21, 103.79)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	14.44 (-11.53, 40.41)
Absolute Change at Week 8 (MMRM)		
n	6	9
LS mean (SE)	-10.23 (13.34)	3.11 (10.74)
95% CI of LS mean	(-39.19, 18.74)	(-20.19, 26.41)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	13.34 (-25.14, 51.82)
Week 16 (MMRM)		
n	5	8
LS mean (SE)	79.04 (9.63)	87.31 (7.64)
95% CI of LS mean	(58.81, 99.27)	(71.19, 103.42)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	8.27 (-18.40, 34.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change at Week 16 (MMRM)		
n	5	8
LS mean (SE)	-4.34 (13.62)	2.56 (10.88)
95% CI of LS mean	(-33.68, 25.01)	(-20.94, 26.05)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.89 (-32.00, 45.79)
Week 24 (MMRM)		
n	6	8
LS mean (SE)	79.11 (9.23)	91.47 (7.64)
95% CI of LS mean	(59.51, 98.72)	(75.36, 107.59)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.36 (-13.80, 38.52)
Absolute Change at Week 24 (MMRM)		
n	6	8
LS mean (SE)	-4.67 (13.34)	6.72 (10.88)
95% CI of LS mean	(-33.64, 24.30)	(-16.77, 30.22)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.39 (-27.20, 49.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Week 52		
n	4	7
Mean (SD)	83.33 (33.33)	100.00 (0.00)
Absolute Change at Week 52		
n	4	7
Mean (SD)	-16.67 (33.33)	14.29 (26.23)
Week 52 (MMRM)		
n	4	7
LS mean (SE)	79.94 (10.13)	98.94 (7.86)
95% CI of LS mean	(58.87, 101.01)	(82.48, 115.39)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.99 (-8.49, 46.48)
Absolute Change at Week 52 (MMRM)		
n	4	7
LS mean (SE)	-4.61 (13.98)	13.93 (11.03)
95% CI of LS mean	(-34.47, 25.24)	(-9.77, 37.63)
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.55 (-20.85, 57.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Sex = Female

	ELX/TEZ/IVA N = 6	VNZ/TEZ/D-IVA N = 9
Absolute Change through Week 52 (MMRM)		
n	6	9
LS mean (SE)	-4.54 (12.79)	7.74 (10.26)
95% CI of LS mean	(-32.86, 23.78)	(-15.00, 30.48)
P-value within Treatment	0.7297	0.4675
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	12.28 (-25.40, 49.95)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4861
Hedges' G (SE)		0.37 (0.50)
Hedges' 95% CI		(-0.71, 1.45)
Hedges' P-value		0.4698

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Region = North America

	ELX/TEZ/IVA N = 3	VNZ/TEZ/D-IVA N = 3

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Region = Rest of World

	ELX/TEZ/IVA N = 11	VNZ/TEZ/D-IVA N = 12

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Genotype group: F/F

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Genotype group: F/G

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Body
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Genotype group: F/F

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Genotype group: F/G

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Digestion
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 2
Subgroup criteria are not met for this subgroup factor.		

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Genotype group: F/F

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Genotype group: F/G

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Eat
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Genotype group: F/F

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Genotype group: F/G

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Emotion
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 2
Subgroup criteria are not met for this subgroup factor.		

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Genotype group: F/F

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Genotype group: F/G

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Health Perceptions
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Genotype group: F/F

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Genotype group: F/G

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Physical
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Genotype group: F/F

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Genotype group: F/G

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: School
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
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- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Genotype group: F/F

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Genotype group: F/G

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Treatment Burden
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Genotype group: F/F

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Genotype group: F/G

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Vitality
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 13	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Genotype group: F/F

	ELX/TEZ/IVA N = 12	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Genotype group: F/G

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.9.4.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Version: Parents/Caregivers Version

Domain: Weight
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- Treatment effect through Week 52 is estimated by averaging Weeks 16, 24, and 52.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.0543
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.0409
Sex (Male vs. Female) [1]	0.8477
Region (North America vs. Rest of the World) [1]	0.7737

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.12.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.9848
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.6004
Sex (Male vs. Female) [1]	0.8520
Region (North America vs. Rest of the World) [1]	0.5898

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.12.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.7787
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.9212
Sex (Male vs. Female) [1]	0.8364
Region (North America vs. Rest of the World) [1]	0.8641

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Table 2.2.2.12.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for
MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction

Subgroup	P-value for Interaction
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4637
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.3046
Sex (Male vs. Female) [1]	0.7828
Region (North America vs. Rest of the World) [1]	0.3462

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype group (F/F, F/G, F/RF, TCR/non-F) and baseline sweat chloride and as covariates.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.2.2.12.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Effectiveness

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype and baseline sweat chloride and as covariates.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.12.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Side Effects

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype and baseline sweat chloride and as covariates.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.12.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Convenience

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype and baseline sweat chloride and as covariates.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.12.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Global Satisfaction

Subgroup	P-value for Interaction
Prior CFTR modulator use (yes vs. no) [1]	-
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [2]	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, genotype and baseline sweat chloride and as covariates.
- [1] P-values are obtained from MMRM with treatment, subgroup, and treatment*subgroup as fixed effects, with adjustment for baseline $ppFEV_1$, and baseline sweat chloride as covariates.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	6
Mean (SD)	79.63 (20.39)	73.15 (15.08)
Week 52		
n	5	6
Mean (SD)	75.56 (30.07)	84.26 (18.40)
Absolute Change at Week 52		
n	5	6
Mean (SD)	-10.00 (25.58)	11.11 (13.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52 (MMRM)		
n	4	6
LS mean (SE)	-5.50 (10.88)	5.52 (8.33)
95% CI of LS mean	(-33.47, 22.48)	(-15.91, 26.94)
P-value within Treatment	0.6349	0.5372
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	11.01 (-29.22, 51.25)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5130
Hedges' G (SE)		0.48 (0.59)
Hedges' 95% CI		(-0.89, 1.84)
Hedges' P-value		0.4457

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Baseline		
n	29	31
Mean (SD)	81.61 (17.00)	81.00 (18.07)
Week 52		
n	30	33
Mean (SD)	89.44 (11.88)	81.99 (19.84)
Absolute Change at Week 52		
n	28	30
Mean (SD)	8.13 (19.63)	1.48 (20.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 52 (MMRM)		
n	27	30
LS mean (SE)	9.08 (4.02)	0.53 (3.81)
95% CI of LS mean	(1.00, 17.17)	(-7.13, 8.18)
P-value within Treatment	0.0284	0.8902
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.55 (-19.88, 2.78)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1357
Hedges' G (SE)		-0.40 (0.26)
Hedges' 95% CI		(-0.93, 0.13)
Hedges' P-value		0.1323

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Baseline		
n	8	10
Mean (SD)	90.28 (13.85)	71.11 (22.95)
Week 52		
n	8	10
Mean (SD)	96.53 (6.60)	88.89 (17.57)
Absolute Change at Week 52		
n	8	9
Mean (SD)	6.25 (11.67)	16.05 (20.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	8	9
LS mean (SE)	1.82 (6.97)	19.99 (6.43)
95% CI of LS mean	(-13.72, 17.35)	(5.66, 34.32)
P-value within Treatment	0.7998	0.0111
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	18.17 (-6.58, 42.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1329
Hedges' G (SE)		0.88 (0.49)
Hedges' 95% CI		(-0.15, 1.92)
Hedges' P-value		0.0884

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Baseline		
n	25	28
Mean (SD)	79.11 (17.88)	82.14 (14.84)
Week 52		
n	25	29
Mean (SD)	85.11 (17.03)	80.08 (19.78)
Absolute Change at Week 52		
n	23	27
Mean (SD)	4.83 (24.69)	-1.23 (17.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Absolute Change at Week 52 (MMRM)		
n	23	27
LS mean (SE)	5.02 (4.48)	-1.40 (4.13)
95% CI of LS mean	(-4.02, 14.06)	(-9.72, 6.93)
P-value within Treatment	0.2690	0.7369
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-6.42 (-18.87, 6.04)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3046
Hedges' G (SE)		-0.29 (0.28)
Hedges' 95% CI		(-0.86, 0.27)
Hedges' P-value		0.3003

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Baseline		
n	20	13
Mean (SD)	80.56 (16.67)	80.34 (17.22)
Week 52		
n	20	15
Mean (SD)	90.00 (11.20)	79.26 (23.33)
Absolute Change at Week 52		
n	18	13
Mean (SD)	8.33 (16.42)	4.70 (15.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	16	13
LS mean (SE)	7.22 (4.29)	6.08 (4.79)
95% CI of LS mean	(-1.65, 16.08)	(-3.81, 15.96)
P-value within Treatment	0.1059	0.2168
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.14 (-14.75, 12.46)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8640
Hedges' G (SE)		-0.06 (0.36)
Hedges' 95% CI		(-0.81, 0.68)
Hedges' P-value		0.8605

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Baseline		
n	15	25
Mean (SD)	82.22 (18.69)	78.67 (18.26)
Week 52		
n	15	24
Mean (SD)	84.07 (20.45)	84.26 (16.76)
Absolute Change at Week 52		
n	15	23
Mean (SD)	1.85 (26.03)	2.17 (22.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	15	23
LS mean (SE)	2.45 (6.55)	1.78 (5.27)
95% CI of LS mean	(-10.90, 15.81)	(-8.96, 12.52)
P-value within Treatment	0.7107	0.7372
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.67 (-17.97, 16.64)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9377
Hedges' G (SE)		-0.03 (0.32)
Hedges' 95% CI		(-0.68, 0.63)
Hedges' P-value		0.9370

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Baseline		
n	9	13
Mean (SD)	85.19 (13.32)	76.07 (19.82)
Week 52		
n	9	13
Mean (SD)	91.36 (11.49)	84.19 (10.84)
Absolute Change at Week 52		
n	8	11
Mean (SD)	6.94 (16.47)	3.03 (12.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	8	11
LS mean (SE)	11.24 (5.63)	-0.09 (4.60)
95% CI of LS mean	(-0.83, 23.31)	(-9.97, 9.78)
P-value within Treatment	0.0656	0.9839
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-11.34 (-28.82, 6.15)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1861
Hedges' G (SE)		-0.70 (0.46)
Hedges' 95% CI		(-1.66, 0.27)
Hedges' P-value		0.1465

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Baseline		
n	26	25
Mean (SD)	79.91 (18.53)	80.89 (16.67)
Week 52		
n	26	26
Mean (SD)	86.11 (17.09)	81.41 (22.66)
Absolute Change at Week 52		
n	25	25
Mean (SD)	4.89 (22.81)	3.11 (22.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	23	25
LS mean (SE)	5.51 (4.94)	2.27 (4.73)
95% CI of LS mean	(-4.46, 15.47)	(-7.28, 11.81)
P-value within Treatment	0.2714	0.6343
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.24 (-17.24, 10.77)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6434
Hedges' G (SE)		-0.13 (0.28)
Hedges' 95% CI		(-0.71, 0.44)
Hedges' P-value		0.6388

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	6
Mean (SD)	100.00 (0.00)	93.75 (9.68)
Week 52		
n	5	6
Mean (SD)	100.00 (0.00)	97.92 (5.10)
Absolute Change at Week 52		
n	5	6
Mean (SD)	0.00 (0.00)	4.17 (7.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52 (MMRM)		
n	4	6
LS mean (SE)	0.39 (4.51)	3.91 (3.46)
95% CI of LS mean	(-11.21, 11.99)	(-4.98, 12.79)
P-value within Treatment	0.9343	0.3096
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	3.52 (-13.17, 20.20)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6113
Hedges' G (SE)		0.37 (0.59)
Hedges' 95% CI		(-0.99, 1.72)
Hedges' P-value		0.5516

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Baseline		
n	29	31
Mean (SD)	100.00 (0.00)	95.36 (12.81)
Week 52		
n	30	33
Mean (SD)	93.33 (15.91)	96.21 (14.06)
Absolute Change at Week 52		
n	28	30
Mean (SD)	-7.14 (16.38)	-0.42 (13.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 52 (MMRM)		
n	27	30
LS mean (SE)	-6.85 (3.01)	-0.92 (2.85)
95% CI of LS mean	(-12.90, -0.80)	(-6.64, 4.81)
P-value within Treatment	0.0272	0.7491
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.93 (-2.54, 14.41)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1660
Hedges' G (SE)		0.37 (0.26)
Hedges' 95% CI		(-0.15, 0.90)
Hedges' P-value		0.1617

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Baseline		
n	8	10
Mean (SD)	100.00 (0.00)	91.25 (11.86)
Week 52		
n	8	10
Mean (SD)	92.19 (14.85)	98.75 (3.95)
Absolute Change at Week 52		
n	8	9
Mean (SD)	-7.81 (14.85)	4.86 (8.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	8	9
LS mean (SE)	-4.93 (5.82)	2.30 (5.37)
95% CI of LS mean	(-17.90, 8.04)	(-9.66, 14.26)
P-value within Treatment	0.4168	0.6775
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.23 (-13.44, 27.90)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.4537
Hedges' G (SE)		0.42 (0.47)
Hedges' 95% CI		(-0.57, 1.42)
Hedges' P-value		0.3806

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Baseline		
n	25	28
Mean (SD)	100.00 (0.00)	96.65 (12.09)
Week 52		
n	25	29
Mean (SD)	94.50 (15.66)	95.69 (14.95)
Absolute Change at Week 52		
n	23	27
Mean (SD)	-5.98 (16.26)	-1.16 (13.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Absolute Change at Week 52 (MMRM)		
n	23	27
LS mean (SE)	-6.32 (3.27)	-0.87 (3.01)
95% CI of LS mean	(-12.91, 0.27)	(-6.94, 5.20)
P-value within Treatment	0.0598	0.7746
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.45 (-3.63, 14.53)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2326
Hedges' G (SE)		0.34 (0.28)
Hedges' 95% CI		(-0.22, 0.91)
Hedges' P-value		0.2292

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Baseline		
n	20	13
Mean (SD)	100.00 (0.00)	99.04 (3.47)
Week 52		
n	20	15
Mean (SD)	94.69 (16.38)	100.00 (0.00)
Absolute Change at Week 52		
n	18	13
Mean (SD)	-5.90 (17.21)	0.96 (3.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	16	13
LS mean (SE)	-7.55 (3.58)	2.08 (3.99)
95% CI of LS mean	(-14.94, -0.16)	(-6.16, 10.32)
P-value within Treatment	0.0455	0.6067
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	9.63 (-1.71, 20.97)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.0923
Hedges' G (SE)		0.65 (0.37)
Hedges' 95% CI		(-0.11, 1.42)
Hedges' P-value		0.0915

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Baseline		
n	15	25
Mean (SD)	100.00 (0.00)	93.25 (14.42)
Week 52		
n	15	24
Mean (SD)	93.75 (13.15)	94.27 (16.37)
Absolute Change at Week 52		
n	15	23
Mean (SD)	-6.25 (13.15)	0.00 (15.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	15	23
LS mean (SE)	-5.96 (3.93)	-0.19 (3.16)
95% CI of LS mean	(-13.98, 2.05)	(-6.63, 6.26)
P-value within Treatment	0.1393	0.9531
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	5.78 (-4.61, 16.16)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2654
Hedges' G (SE)		0.37 (0.33)
Hedges' 95% CI		(-0.29, 1.04)
Hedges' P-value		0.2632

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Baseline		
n	9	13
Mean (SD)	100.00 (0.00)	97.60 (8.67)
Week 52		
n	9	13
Mean (SD)	95.83 (12.50)	100.00 (0.00)
Absolute Change at Week 52		
n	8	11
Mean (SD)	-4.69 (13.26)	0.00 (0.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	8	11
LS mean (SE)	-2.49 (3.29)	-1.60 (2.69)
95% CI of LS mean	(-9.54, 4.57)	(-7.37, 4.17)
P-value within Treatment	0.4626	0.5613
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.88 (-9.34, 11.11)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8555
Hedges' G (SE)		0.09 (0.44)
Hedges' 95% CI		(-0.84, 1.03)
Hedges' P-value		0.8367

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Baseline		
n	26	25
Mean (SD)	100.00 (0.00)	94.00 (13.56)
Week 52		
n	26	26
Mean (SD)	93.75 (15.81)	94.71 (15.78)
Absolute Change at Week 52		
n	25	25
Mean (SD)	-6.50 (16.08)	0.50 (15.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	23	25
LS mean (SE)	-6.71 (3.45)	0.18 (3.31)
95% CI of LS mean	(-13.67, 0.25)	(-6.49, 6.84)
P-value within Treatment	0.0582	0.9578
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	6.89 (-2.89, 16.67)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.1626
Hedges' G (SE)		0.41 (0.29)
Hedges' 95% CI		(-0.17, 0.99)
Hedges' P-value		0.1605

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	5
Mean (SD)	71.30 (14.24)	92.22 (12.17)
Week 52		
n	5	6
Mean (SD)	74.44 (18.68)	87.04 (19.14)
Absolute Change at Week 52		
n	5	5
Mean (SD)	0.00 (17.12)	-4.44 (10.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52 (MMRM)		
n	4	5
LS mean (SE)	2.74 (11.25)	-6.64 (9.71)
95% CI of LS mean	(-28.50, 33.98)	(-33.60, 20.33)
P-value within Treatment	0.8194	0.5318
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-9.38 (-56.69, 37.93)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.6113
Hedges' G (SE)		-0.38 (0.60)
Hedges' 95% CI		(-1.80, 1.05)
Hedges' P-value		0.5505

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Baseline		
n	29	31
Mean (SD)	84.48 (14.88)	82.80 (15.20)
Week 52		
n	30	33
Mean (SD)	87.41 (13.21)	84.68 (11.95)
Absolute Change at Week 52		
n	28	30
Mean (SD)	2.98 (15.60)	0.56 (17.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 52 (MMRM)		
n	27	30
LS mean (SE)	2.87 (3.32)	0.38 (3.15)
95% CI of LS mean	(-3.81, 9.54)	(-5.93, 6.70)
P-value within Treatment	0.3924	0.9034
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.48 (-11.83, 6.87)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5963
Hedges' G (SE)		-0.14 (0.26)
Hedges' 95% CI		(-0.67, 0.38)
Hedges' P-value		0.5900

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Baseline		
n	8	9
Mean (SD)	88.19 (11.67)	83.33 (20.79)
Week 52		
n	8	10
Mean (SD)	90.97 (12.58)	87.22 (16.15)
Absolute Change at Week 52		
n	8	8
Mean (SD)	2.78 (9.85)	0.00 (12.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	8	8
LS mean (SE)	2.03 (4.21)	0.75 (4.21)
95% CI of LS mean	(-7.49, 11.54)	(-8.76, 10.27)
P-value within Treatment	0.6415	0.8621
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.27 (-17.23, 14.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8606
Hedges' G (SE)		-0.10 (0.47)
Hedges' 95% CI		(-1.12, 0.91)
Hedges' P-value		0.8336

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Baseline		
n	25	28
Mean (SD)	80.67 (16.44)	82.94 (14.89)
Week 52		
n	25	29
Mean (SD)	84.00 (14.73)	84.29 (11.98)
Absolute Change at Week 52		
n	23	27
Mean (SD)	2.17 (17.86)	-0.21 (17.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Absolute Change at Week 52 (MMRM)		
n	23	27
LS mean (SE)	1.41 (3.83)	0.44 (3.53)
95% CI of LS mean	(-6.31, 9.13)	(-6.67, 7.55)
P-value within Treatment	0.7144	0.9002
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-0.97 (-11.60, 9.67)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8556
Hedges' G (SE)		-0.05 (0.28)
Hedges' 95% CI		(-0.61, 0.51)
Hedges' P-value		0.8537

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Baseline		
n	20	13
Mean (SD)	85.56 (15.02)	88.03 (12.39)
Week 52		
n	20	15
Mean (SD)	88.33 (14.63)	86.67 (12.56)
Absolute Change at Week 52		
n	18	13
Mean (SD)	1.23 (13.00)	-0.43 (20.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	16	13
LS mean (SE)	0.13 (4.55)	0.27 (5.08)
95% CI of LS mean	(-9.27, 9.52)	(-10.21, 10.75)
P-value within Treatment	0.9778	0.9580
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.14 (-14.28, 14.56)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.9839
Hedges' G (SE)		0.01 (0.36)
Hedges' 95% CI		(-0.74, 0.75)
Hedges' P-value		0.9835

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Baseline		
n	15	24
Mean (SD)	77.78 (15.29)	80.32 (17.57)
Week 52		
n	15	24
Mean (SD)	81.85 (14.00)	84.03 (13.44)
Absolute Change at Week 52		
n	15	22
Mean (SD)	4.07 (18.60)	0.00 (13.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	15	22
LS mean (SE)	3.59 (4.30)	0.33 (3.54)
95% CI of LS mean	(-5.19, 12.37)	(-6.89, 7.55)
P-value within Treatment	0.4103	0.9261
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-3.26 (-14.74, 8.22)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5664
Hedges' G (SE)		-0.19 (0.33)
Hedges' 95% CI		(-0.86, 0.47)
Hedges' P-value		0.5626

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Baseline		
n	9	13
Mean (SD)	88.27 (14.01)	81.62 (19.95)
Week 52		
n	9	13
Mean (SD)	83.33 (17.79)	85.47 (13.90)
Absolute Change at Week 52		
n	8	11
Mean (SD)	-4.17 (16.99)	-4.04 (21.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	8	11
LS mean (SE)	-2.54 (9.08)	-5.22 (7.42)
95% CI of LS mean	(-22.00, 16.93)	(-21.14, 10.69)
P-value within Treatment	0.7838	0.4930
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.69 (-30.88, 25.51)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8411
Hedges' G (SE)		-0.10 (0.44)
Hedges' 95% CI		(-1.04, 0.83)
Hedges' P-value		0.8204

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Baseline		
n	26	24
Mean (SD)	80.13 (15.57)	83.80 (14.18)
Week 52		
n	26	26
Mean (SD)	86.32 (13.54)	84.83 (12.82)
Absolute Change at Week 52		
n	25	24
Mean (SD)	4.67 (14.84)	1.62 (13.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	23	24
LS mean (SE)	4.27 (3.11)	1.93 (3.04)
95% CI of LS mean	(-2.01, 10.55)	(-4.21, 8.07)
P-value within Treatment	0.1773	0.5300
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-2.34 (-11.25, 6.56)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5984
Hedges' G (SE)		-0.15 (0.29)
Hedges' 95% CI		(-0.73, 0.42)
Hedges' P-value		0.5938

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Baseline		
n	6	6
Mean (SD)	86.90 (10.51)	87.62 (15.95)
Week 52		
n	5	6
Mean (SD)	72.86 (35.14)	84.52 (18.85)
Absolute Change at Week 52		
n	5	6
Mean (SD)	-14.29 (28.12)	-3.10 (4.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 7	VNZ/TEZ/D-IVA N = 6
Absolute Change at Week 52 (MMRM)		
n	4	6
LS mean (SE)	-3.41 (5.44)	-11.54 (4.17)
95% CI of LS mean	(-17.39, 10.57)	(-22.24, -0.83)
P-value within Treatment	0.5583	0.0394
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-8.13 (-28.24, 11.98)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3465
Hedges' G (SE)		-0.70 (0.60)
Hedges' 95% CI		(-2.09, 0.69)
Hedges' P-value		0.2787

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Baseline		
n	29	31
Mean (SD)	86.21 (13.22)	86.41 (14.80)
Week 52		
n	30	33
Mean (SD)	92.62 (8.89)	89.39 (11.59)
Absolute Change at Week 52		
n	28	30
Mean (SD)	6.38 (15.59)	2.62 (17.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 31	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 52 (MMRM)		
n	27	30
LS mean (SE)	6.61 (3.27)	2.38 (3.10)
95% CI of LS mean	(0.04, 13.18)	(-3.84, 8.61)
P-value within Treatment	0.0487	0.4450
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-4.22 (-13.43, 4.99)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.3613
Hedges' G (SE)		-0.25 (0.26)
Hedges' 95% CI		(-0.77, 0.28)
Hedges' P-value		0.3542

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening <18 years

	ELX/TEZ/IVA N = 38	VNZ/TEZ/D-IVA N = 41

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening ≥18 years

	ELX/TEZ/IVA N = 0	VNZ/TEZ/D-IVA N = 0

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment,and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Baseline		
n	8	10
Mean (SD)	87.50 (17.39)	81.86 (19.55)
Week 52		
n	8	10
Mean (SD)	94.64 (9.92)	90.00 (16.56)
Absolute Change at Week 52		
n	8	9
Mean (SD)	7.14 (22.26)	7.46 (19.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 8	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 52 (MMRM)		
n	8	9
LS mean (SE)	3.23 (7.78)	10.94 (7.18)
95% CI of LS mean	(-14.11, 20.56)	(-5.05, 26.93)
P-value within Treatment	0.6873	0.1583
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	7.72 (-19.91, 35.34)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.5475
Hedges' G (SE)		0.34 (0.46)
Hedges' 95% CI		(-0.65, 1.33)
Hedges' P-value		0.4799

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Baseline		
n	25	28
Mean (SD)	86.57 (11.54)	87.50 (13.13)
Week 52		
n	25	29
Mean (SD)	89.14 (17.87)	88.18 (11.50)
Absolute Change at Week 52		
n	23	27
Mean (SD)	2.17 (18.83)	-0.26 (15.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 30
Absolute Change at Week 52 (MMRM)		
n	23	27
LS mean (SE)	1.52 (3.23)	0.29 (2.97)
95% CI of LS mean	(-4.99, 8.03)	(-5.70, 6.29)
P-value within Treatment	0.6404	0.9217
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-1.22 (-10.19, 7.74)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7844
Hedges' G (SE)		-0.08 (0.28)
Hedges' 95% CI		(-0.64, 0.48)
Hedges' P-value		0.7815

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Baseline		
n	20	13
Mean (SD)	85.71 (12.26)	86.26 (16.61)
Week 52		
n	20	15
Mean (SD)	93.21 (9.41)	90.00 (11.71)
Absolute Change at Week 52		
n	18	13
Mean (SD)	7.54 (15.97)	5.49 (14.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Male

	ELX/TEZ/IVA N = 23	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	16	13
LS mean (SE)	6.83 (3.47)	7.53 (3.87)
95% CI of LS mean	(-0.35, 14.00)	(-0.46, 15.53)
P-value within Treatment	0.0612	0.0637
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.71 (-10.30, 11.72)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8954
Hedges' G (SE)		0.05 (0.36)
Hedges' 95% CI		(-0.70, 0.79)
Hedges' P-value		0.8927

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Baseline		
n	15	25
Mean (SD)	87.14 (13.55)	85.89 (14.46)
Week 52		
n	15	24
Mean (SD)	85.24 (21.84)	87.80 (13.57)
Absolute Change at Week 52		
n	15	23
Mean (SD)	-1.90 (21.51)	-0.50 (17.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Sex = Female

	ELX/TEZ/IVA N = 15	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	15	23
LS mean (SE)	-1.57 (4.72)	-0.71 (3.79)
95% CI of LS mean	(-11.20, 8.05)	(-8.45, 7.03)
P-value within Treatment	0.7408	0.8524
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	0.86 (-11.61, 13.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.8887
Hedges' G (SE)		0.05 (0.32)
Hedges' 95% CI		(-0.61, 0.71)
Hedges' P-value		0.8874

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Baseline		
n	9	13
Mean (SD)	86.51 (16.15)	86.26 (15.28)
Week 52		
n	9	13
Mean (SD)	96.03 (9.52)	87.36 (10.17)
Absolute Change at Week 52		
n	8	11
Mean (SD)	10.71 (21.26)	-3.25 (16.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = North America

	ELX/TEZ/IVA N = 10	VNZ/TEZ/D-IVA N = 15
Absolute Change at Week 52 (MMRM)		
n	8	11
LS mean (SE)	10.91 (7.72)	-3.39 (6.31)
95% CI of LS mean	(-5.65, 27.47)	(-16.93, 10.15)
P-value within Treatment	0.1794	0.5997
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	-14.30 (-38.28, 9.68)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.2217
Hedges' G (SE)		-0.64 (0.46)
Hedges' 95% CI		(-1.60, 0.32)
Hedges' P-value		0.1777

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Baseline		
n	26	25
Mean (SD)	86.26 (11.59)	85.89 (15.18)
Week 52		
n	26	26
Mean (SD)	87.64 (17.56)	89.29 (14.03)
Absolute Change at Week 52		
n	25	25
Mean (SD)	0.86 (18.01)	3.83 (16.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = Rest of World

	ELX/TEZ/IVA N = 28	VNZ/TEZ/D-IVA N = 26
Absolute Change at Week 52 (MMRM)		
n	23	25
LS mean (SE)	1.69 (3.49)	3.13 (3.34)
95% CI of LS mean	(-5.35, 8.73)	(-3.61, 9.87)
P-value within Treatment	0.6304	0.3544
LS mean Diff (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), 95% CI	-	1.44 (-8.45, 11.33)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority	-	0.7706
Hedges' G (SE)		0.08 (0.28)
Hedges' 95% CI		(-0.49, 0.66)
Hedges' P-value		0.7673

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Effectiveness
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 37	VNZ/TEZ/D-IVA N = 36

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Effectiveness
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Effectiveness
Genotype group: F/F

	ELX/TEZ/IVA N = 33	VNZ/TEZ/D-IVA N = 34

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Effectiveness
Genotype group: F/G

	ELX/TEZ/IVA N = 2	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Effectiveness
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Effectiveness
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 2	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Side Effects
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 37	VNZ/TEZ/D-IVA N = 36

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Side Effects
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Side Effects
Genotype group: F/F

	ELX/TEZ/IVA N = 33	VNZ/TEZ/D-IVA N = 34

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Side Effects
Genotype group: F/G

	ELX/TEZ/IVA N = 2	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
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- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Side Effects
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
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- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Side Effects
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 2	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
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- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Convenience
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 37	VNZ/TEZ/D-IVA N = 36

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
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- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Convenience
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Convenience
Genotype group: F/F

	ELX/TEZ/IVA N = 33	VNZ/TEZ/D-IVA N = 34

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
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- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Convenience
Genotype group: F/G

	ELX/TEZ/IVA N = 2	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Convenience
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
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- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Convenience
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 2	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
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- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Global Satisfaction
Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 37	VNZ/TEZ/D-IVA N = 36

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Global Satisfaction
Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Full Analysis Set

Domain: Global Satisfaction
Genotype group: F/F

	ELX/TEZ/IVA N = 33	VNZ/TEZ/D-IVA N = 34

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Global Satisfaction
Genotype group: F/G

	ELX/TEZ/IVA N = 2	VNZ/TEZ/D-IVA N = 2

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Global Satisfaction
Genotype group: F/RF

	ELX/TEZ/IVA N = 1	VNZ/TEZ/D-IVA N = 1

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.2.2.12.1.2.1
Study VX20-121-103: MMRM Analysis of Absolute Change from Baseline in TSQM Domain Score at Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent for Additional Subgroups
Full Analysis Set

Domain: Global Satisfaction
Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 2	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

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- N is the number of subjects in each subgroup in the Full Analysis Set who are ≥12 to <18 years of age at the date of informed consent.
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- CI: Confidence interval; LS Mean Diff: Least Squares Mean difference; SD: Standard deviation; SE: Standard error.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Genotype group" subgroup factor, genotype covariate is removed from MMRM.
- SMD (standardized mean difference) is the LS mean difference (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA) divided by the pooled standard deviation. The unbiased estimate of Hedges' G is the product of SMD and the correction factor 1-3/(4m-1), where m is the degree of freedom.
- N/C: model does not converge.

Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any TEAEs	271 (93.77)	274 (96.48)
Relative Risk (RR) (95% CI)		1.0289 (0.9914, 1.0678)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1327
Odds Ratio (OR) (95% CI)		1.8199 (0.8251, 4.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1379
Risk Difference (RD) (95% CI)		0.0271 (-0.0081, 0.0622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1312
Infections and infestations	208 (71.97)	199 (70.07)
Relative Risk (RR) (95% CI)		0.9736 (0.8768, 1.0810)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6160
Odds Ratio (OR) (95% CI)		0.9117 (0.6354, 1.3082)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6159
Risk Difference (RD) (95% CI)		-0.0190 (-0.0933, 0.0553)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6158

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
COVID-19	73 (25.26)	58 (20.42)
Relative Risk (RR) (95% CI)		0.8085 (0.5969, 1.0951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1697
Odds Ratio (OR) (95% CI)		0.7594 (0.5131, 1.1238)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1687
Risk Difference (RD) (95% CI)		-0.0484 (-0.1170, 0.0202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1671
Nasopharyngitis	60 (20.76)	57 (20.07)
Relative Risk (RR) (95% CI)		0.9667 (0.6996, 1.3359)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8375
Odds Ratio (OR) (95% CI)		0.9584 (0.6384, 1.4388)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8375

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0729, 0.0591)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8375

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Upper respiratory tract infection	40 (13.84)	55 (19.37)
Relative Risk (RR) (95% CI)		1.3992 (0.9637, 2.0316)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0775
Odds Ratio (OR) (95% CI)		1.4951 (0.9580, 2.3332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0765
Risk Difference (RD) (95% CI)		0.0553 (-0.0056, 0.1161)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0749
Influenza	16 (5.54)	33 (11.62)
Relative Risk (RR) (95% CI)		2.0988 (1.1820, 3.7268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0114
Odds Ratio (OR) (95% CI)		2.2433 (1.2053, 4.1750)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0108

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0608 (0.0152, 0.1065)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0090

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Viral upper respiratory tract infection	17 (5.88)	20 (7.04)
Relative Risk (RR) (95% CI)		1.1972 (0.6405, 2.2377)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5728
Odds Ratio (OR) (95% CI)		1.2121 (0.6213, 2.3649)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5727
Risk Difference (RD) (95% CI)		0.0116 (-0.0287, 0.0519)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5724
Sinusitis	26 (9.00)	9 (3.17)
Relative Risk (RR) (95% CI)		0.3522 (0.1680, 0.7384)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0057
Odds Ratio (OR) (95% CI)		0.3310 (0.1523, 0.7197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0053

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0583 (-0.0970, -0.0195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0032

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Urinary tract infection	10 (3.46)	9 (3.17)
Relative Risk (RR) (95% CI)		0.9158 (0.3778, 2.2202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8457
Odds Ratio (OR) (95% CI)		0.9131 (0.3654, 2.2816)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8457
Risk Difference (RD) (95% CI)		-0.0029 (-0.0322, 0.0264)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8456
Rhinitis	11 (3.81)	8 (2.82)
Relative Risk (RR) (95% CI)		0.7401 (0.3021, 1.8128)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5102
Odds Ratio (OR) (95% CI)		0.7325 (0.2902, 1.8489)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5100

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0099 (-0.0392, 0.0194)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5077

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Bronchitis	8 (2.77)	7 (2.46)
Relative Risk (RR) (95% CI)		0.8904 (0.3272, 2.4230)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8202
Odds Ratio (OR) (95% CI)		0.8876 (0.3176, 2.4810)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8202
Risk Difference (RD) (95% CI)		-0.0030 (-0.0292, 0.0231)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8200
Gastroenteritis	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Conjunctivitis	12 (4.15)	5 (1.76)
Relative Risk (RR) (95% CI)		0.4240 (0.1513, 1.1881)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1026
Odds Ratio (OR) (95% CI)		0.4137 (0.1438, 1.1898)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1015
Risk Difference (RD) (95% CI)		-0.0239 (-0.0515, 0.0037)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0897
Pharyngitis	8 (2.77)	5 (1.76)
Relative Risk (RR) (95% CI)		0.6360 (0.2106, 1.9208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4223
Odds Ratio (OR) (95% CI)		0.6295 (0.2034, 1.9478)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4219

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0101 (-0.0344, 0.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4169

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Vulvovaginal mycotic infection	7 (2.42)	5 (1.76)
Relative Risk (RR) (95% CI)		0.7269 (0.2334, 2.2634)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5820
Odds Ratio (OR) (95% CI)		0.7220 (0.2264, 2.3019)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5819
Risk Difference (RD) (95% CI)		-0.0066 (-0.0300, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5797
Otitis media	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pneumonia	8 (2.77)	4 (1.41)
Relative Risk (RR) (95% CI)		0.5088 (0.1549, 1.6708)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2654
Odds Ratio (OR) (95% CI)		0.5018 (0.1494, 1.6854)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2646
Risk Difference (RD) (95% CI)		-0.0136 (-0.0370, 0.0098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2539
Respiratory, thoracic and mediastinal disorders	153 (52.94)	145 (51.06)
Relative Risk (RR) (95% CI)		0.9644 (0.8239, 1.1288)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6517
Odds Ratio (OR) (95% CI)		0.9273 (0.6681, 1.2870)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6516
Risk Difference (RD) (95% CI)		-0.0188 (-0.1007, 0.0630)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6516

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Cough	60 (20.76)	63 (22.18)
Relative Risk (RR) (95% CI)		1.0685 (0.7811, 1.4617)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6786
Odds Ratio (OR) (95% CI)		1.0880 (0.7301, 1.6214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6786
Risk Difference (RD) (95% CI)		0.0142 (-0.0530, 0.0815)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6786
Oropharyngeal pain	37 (12.80)	45 (15.85)
Relative Risk (RR) (95% CI)		1.2376 (0.8272, 1.8518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2997
Odds Ratio (OR) (95% CI)		1.2824 (0.8018, 2.0509)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2992

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0304 (-0.0269, 0.0878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2984

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nasal congestion	23 (7.96)	29 (10.21)
Relative Risk (RR) (95% CI)		1.2831 (0.7612, 2.1629)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3495
Odds Ratio (OR) (95% CI)		1.3153 (0.7412, 2.3341)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3491
Risk Difference (RD) (95% CI)		0.0225 (-0.0245, 0.0696)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3480
Sputum increased	29 (10.03)	27 (9.51)
Relative Risk (RR) (95% CI)		0.9474 (0.5758, 1.5588)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8316
Odds Ratio (OR) (95% CI)		0.9419 (0.5425, 1.6355)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8316

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0053 (-0.0539, 0.0433)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8316

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Sinus congestion	10 (3.46)	18 (6.34)
Relative Risk (RR) (95% CI)		1.8317 (0.8605, 3.8990)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1164
Odds Ratio (OR) (95% CI)		1.8880 (0.8559, 4.1643)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1154
Risk Difference (RD) (95% CI)		0.0288 (-0.0065, 0.0641)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1102
Haemoptysis	22 (7.61)	17 (5.99)
Relative Risk (RR) (95% CI)		0.7863 (0.4267, 1.4492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4409
Odds Ratio (OR) (95% CI)		0.7727 (0.4013, 1.4880)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4406

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0163 (-0.0574, 0.0249)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4389

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Productive cough	19 (6.57)	16 (5.63)
Relative Risk (RR) (95% CI)		0.8569 (0.4498, 1.6326)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6387
Odds Ratio (OR) (95% CI)		0.8484 (0.4272, 1.6850)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6386
Risk Difference (RD) (95% CI)		-0.0094 (-0.0486, 0.0298)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6380
Rhinorrhoea	22 (7.61)	16 (5.63)
Relative Risk (RR) (95% CI)		0.7401 (0.3970, 1.3796)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3435
Odds Ratio (OR) (95% CI)		0.7246 (0.3723, 1.4102)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3430

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0198 (-0.0605, 0.0209)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3403

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Dyspnoea	21 (7.27)	11 (3.87)
Relative Risk (RR) (95% CI)		0.5330 (0.2618, 1.0851)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0828
Odds Ratio (OR) (95% CI)		0.5142 (0.2432, 1.0872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0817
Risk Difference (RD) (95% CI)		-0.0339 (-0.0713, 0.0035)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0754
Lower respiratory tract congestion	5 (1.73)	9 (3.17)
Relative Risk (RR) (95% CI)		1.8317 (0.6215, 5.3985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2724
Odds Ratio (OR) (95% CI)		1.8589 (0.6152, 5.6165)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2718

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Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0144 (-0.0109, 0.0397)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2653

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Respiration abnormal	7 (2.42)	9 (3.17)
Relative Risk (RR) (95% CI)		1.3084 (0.4940, 3.4654)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5886
Odds Ratio (OR) (95% CI)		1.3184 (0.4843, 3.5896)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5885
Risk Difference (RD) (95% CI)		0.0075 (-0.0195, 0.0345)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5878
Wheezing	7 (2.42)	8 (2.82)
Relative Risk (RR) (95% CI)		1.1630 (0.4274, 3.1647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7675
Odds Ratio (OR) (95% CI)		1.1677 (0.4178, 3.2638)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7675

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0039 (-0.0222, 0.0301)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7674

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Upper-airway cough syndrome	8 (2.77)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2544 (0.0545, 1.1876)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0816
Odds Ratio (OR) (95% CI)		0.2491 (0.0524, 1.1834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0804
Risk Difference (RD) (95% CI)		-0.0206 (-0.0419, 0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0572
Gastrointestinal disorders	111 (38.41)	114 (40.14)
Relative Risk (RR) (95% CI)		1.0451 (0.8525, 1.2812)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6712
Odds Ratio (OR) (95% CI)		1.0754 (0.7689, 1.5039)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6711
Risk Difference (RD) (95% CI)		0.0173 (-0.0626, 0.0973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6711

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Diarrhoea	44 (15.22)	37 (13.03)
Relative Risk (RR) (95% CI)		0.8557 (0.5705, 1.2834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4512
Odds Ratio (OR) (95% CI)		0.8341 (0.5205, 1.3366)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4509
Risk Difference (RD) (95% CI)		-0.0220 (-0.0790, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4500
Nausea	13 (4.50)	22 (7.75)
Relative Risk (RR) (95% CI)		1.7221 (0.8849, 3.3513)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1096
Odds Ratio (OR) (95% CI)		1.7827 (0.8798, 3.6122)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1086

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0325 (-0.0067, 0.0717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1045

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Abdominal pain	23 (7.96)	15 (5.28)
Relative Risk (RR) (95% CI)		0.6637 (0.3536, 1.2455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2018
Odds Ratio (OR) (95% CI)		0.6449 (0.3293, 1.2631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2009
Risk Difference (RD) (95% CI)		-0.0268 (-0.0674, 0.0139)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1966
Constipation	20 (6.92)	15 (5.28)
Relative Risk (RR) (95% CI)		0.7632 (0.3988, 1.4607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4145
Odds Ratio (OR) (95% CI)		0.7500 (0.3760, 1.4960)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4141

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0164 (-0.0555, 0.0228)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4120

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Abdominal pain upper	13 (4.50)	14 (4.93)
Relative Risk (RR) (95% CI)		1.0959 (0.5245, 2.2899)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8076
Odds Ratio (OR) (95% CI)		1.1009 (0.5080, 2.3855)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8076
Risk Difference (RD) (95% CI)		0.0043 (-0.0304, 0.0390)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8076
Vomiting	19 (6.57)	12 (4.23)
Relative Risk (RR) (95% CI)		0.6427 (0.3179, 1.2993)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2183
Odds Ratio (OR) (95% CI)		0.6269 (0.2985, 1.3167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2175

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0235 (-0.0604, 0.0134)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2125

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Abdominal distension	5 (1.73)	6 (2.11)
Relative Risk (RR) (95% CI)		1.2211 (0.3769, 3.9560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7391
Odds Ratio (OR) (95% CI)		1.2259 (0.3699, 4.0631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7390
Risk Difference (RD) (95% CI)		0.0038 (-0.0187, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7388
Gastrooesophageal reflux disease	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Flatulence	8 (2.77)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2544 (0.0545, 1.1876)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0816
Odds Ratio (OR) (95% CI)		0.2491 (0.0524, 1.1834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0804
Risk Difference (RD) (95% CI)		-0.0206 (-0.0419, 0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0572
Investigations	94 (32.53)	104 (36.62)
Relative Risk (RR) (95% CI)		1.1259 (0.8983, 1.4111)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3035
Odds Ratio (OR) (95% CI)		1.1986 (0.8491, 1.6919)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3031
Risk Difference (RD) (95% CI)		0.0409 (-0.0369, 0.1188)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3025

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Alanine aminotransferase increased	18 (6.23)	25 (8.80)
Relative Risk (RR) (95% CI)		1.4133 (0.7887, 2.5327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2451
Odds Ratio (OR) (95% CI)		1.4532 (0.7745, 2.7268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2444
Risk Difference (RD) (95% CI)		0.0257 (-0.0174, 0.0689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2423
Blood creatine phosphokinase increased	17 (5.88)	25 (8.80)
Relative Risk (RR) (95% CI)		1.4965 (0.8262, 2.7104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1835
Odds Ratio (OR) (95% CI)		1.5444 (0.8150, 2.9266)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1826

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0292 (-0.0135, 0.0719)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1799

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Aspartate aminotransferase increased	18 (6.23)	21 (7.39)
Relative Risk (RR) (95% CI)		1.1872 (0.6464, 2.1804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5801
Odds Ratio (OR) (95% CI)		1.2022 (0.6263, 2.3074)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5800
Risk Difference (RD) (95% CI)		0.0117 (-0.0296, 0.0529)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5797
Bacterial test positive	13 (4.50)	7 (2.46)
Relative Risk (RR) (95% CI)		0.5479 (0.2219, 1.3533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1922
Odds Ratio (OR) (95% CI)		0.5365 (0.2109, 1.3650)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1913

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0203 (-0.0503, 0.0096)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1831

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood alkaline phosphatase increased	6 (2.08)	7 (2.46)
Relative Risk (RR) (95% CI)		1.1872 (0.4040, 3.4892)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7551
Odds Ratio (OR) (95% CI)		1.1919 (0.3956, 3.5913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7550
Risk Difference (RD) (95% CI)		0.0039 (-0.0205, 0.0283)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7549
Blood glucose increased	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gamma-glutamyltransferase increased	8 (2.77)	6 (2.11)
Relative Risk (RR) (95% CI)		0.7632 (0.2682, 2.1717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6125
Odds Ratio (OR) (95% CI)		0.7581 (0.2597, 2.2132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6124
Risk Difference (RD) (95% CI)		-0.0066 (-0.0318, 0.0187)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6109
SARS-CoV-2 test positive	8 (2.77)	6 (2.11)
Relative Risk (RR) (95% CI)		0.7632 (0.2682, 2.1717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6125
Odds Ratio (OR) (95% CI)		0.7581 (0.2597, 2.2132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6124

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0066 (-0.0318, 0.0187)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6109

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Weight decreased	5 (1.73)	6 (2.11)
Relative Risk (RR) (95% CI)		1.2211 (0.3769, 3.9560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7391
Odds Ratio (OR) (95% CI)		1.2259 (0.3699, 4.0631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7390
Risk Difference (RD) (95% CI)		0.0038 (-0.0187, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7388
Blood bilirubin increased	10 (3.46)	5 (1.76)
Relative Risk (RR) (95% CI)		0.5088 (0.1761, 1.4700)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2119
Odds Ratio (OR) (95% CI)		0.5000 (0.1687, 1.4816)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2111

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0170 (-0.0430, 0.0090)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2008

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
General disorders and administration site conditions	72 (24.91)	86 (30.28)
Relative Risk (RR) (95% CI)		1.2155 (0.9308, 1.5872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1518
Odds Ratio (OR) (95% CI)		1.3091 (0.9064, 1.8906)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1510
Risk Difference (RD) (95% CI)		0.0537 (-0.0194, 0.1268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1500
Fatigue	30 (10.38)	33 (11.62)
Relative Risk (RR) (95% CI)		1.1194 (0.7020, 1.7848)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6357
Odds Ratio (OR) (95% CI)		1.1351 (0.6721, 1.9169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6356
Risk Difference (RD) (95% CI)		0.0124 (-0.0389, 0.0636)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6355

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pyrexia	29 (10.03)	28 (9.86)
Relative Risk (RR) (95% CI)		0.9825 (0.6002, 1.6083)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9441
Odds Ratio (OR) (95% CI)		0.9806 (0.5673, 1.6949)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9441
Risk Difference (RD) (95% CI)		-0.0018 (-0.0508, 0.0473)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9441
Pain	3 (1.04)	10 (3.52)
Relative Risk (RR) (95% CI)		3.3920 (0.9433, 12.1971)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0614
Odds Ratio (OR) (95% CI)		3.4793 (0.9475, 12.7769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0603

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0248 (0.0004, 0.0492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0462

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Influenza like illness	5 (1.73)	7 (2.46)
Relative Risk (RR) (95% CI)		1.4246 (0.4575, 4.4363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5414
Odds Ratio (OR) (95% CI)		1.4354 (0.4502, 4.5765)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5412
Risk Difference (RD) (95% CI)		0.0073 (-0.0161, 0.0308)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5396
Malaise	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nervous system disorders	64 (22.15)	72 (25.35)
Relative Risk (RR) (95% CI)		1.1448 (0.8530, 1.5364)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3676
Odds Ratio (OR) (95% CI)		1.1940 (0.8121, 1.7555)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3673
Risk Difference (RD) (95% CI)		0.0321 (-0.0376, 0.1017)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3669
Headache	41 (14.19)	51 (17.96)
Relative Risk (RR) (95% CI)		1.2658 (0.8682, 1.8456)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2205
Odds Ratio (OR) (95% CI)		1.3240 (0.8456, 2.0729)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2199
Risk Difference (RD) (95% CI)		0.0377 (-0.0224, 0.0978)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2187

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Dizziness	13 (4.50)	9 (3.17)
Relative Risk (RR) (95% CI)		0.7045 (0.3060, 1.6221)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4104
Odds Ratio (OR) (95% CI)		0.6948 (0.2922, 1.6521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4100
Risk Difference (RD) (95% CI)		-0.0133 (-0.0447, 0.0181)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4067
Migraine	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Skin and subcutaneous tissue disorders	52 (17.99)	68 (23.94)
Relative Risk (RR) (95% CI)		1.3307 (0.9646, 1.8358)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0818
Odds Ratio (OR) (95% CI)		1.4348 (0.9566, 2.1521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0809
Risk Difference (RD) (95% CI)		0.0595 (-0.0070, 0.1260)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0795
Rash	13 (4.50)	25 (8.80)
Relative Risk (RR) (95% CI)		1.9569 (1.0217, 3.7481)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0429
Odds Ratio (OR) (95% CI)		2.0493 (1.0265, 4.0911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0419
Risk Difference (RD) (95% CI)		0.0430 (0.0023, 0.0838)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0382

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Acne	12 (4.15)	11 (3.87)
Relative Risk (RR) (95% CI)		0.9328 (0.4185, 2.0793)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8649
Odds Ratio (OR) (95% CI)		0.9301 (0.4035, 2.1438)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8649
Risk Difference (RD) (95% CI)		-0.0028 (-0.0349, 0.0293)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8649
Pruritus	6 (2.08)	9 (3.17)
Relative Risk (RR) (95% CI)		1.5264 (0.5505, 4.2327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4164
Odds Ratio (OR) (95% CI)		1.5436 (0.5422, 4.3946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4160

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0109 (-0.0152, 0.0371)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4132

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Alopecia	6 (2.08)	5 (1.76)
Relative Risk (RR) (95% CI)		0.8480 (0.2618, 2.7472)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7834
Odds Ratio (OR) (95% CI)		0.8453 (0.2550, 2.8016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7834
Risk Difference (RD) (95% CI)		-0.0032 (-0.0256, 0.0193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7830
Musculoskeletal and connective tissue disorders	71 (24.57)	55 (19.37)
Relative Risk (RR) (95% CI)		0.7883 (0.5772, 1.0766)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1346
Odds Ratio (OR) (95% CI)		0.7374 (0.4953, 1.0978)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1336
Risk Difference (RD) (95% CI)		-0.0520 (-0.1197, 0.0156)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1318

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Back pain	15 (5.19)	16 (5.63)
Relative Risk (RR) (95% CI)		1.0854 (0.5471, 2.1535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8145
Odds Ratio (OR) (95% CI)		1.0905 (0.5286, 2.2500)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8145
Risk Difference (RD) (95% CI)		0.0044 (-0.0326, 0.0415)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8145
Arthralgia	25 (8.65)	14 (4.93)
Relative Risk (RR) (95% CI)		0.5699 (0.3025, 1.0736)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0818
Odds Ratio (OR) (95% CI)		0.5476 (0.2785, 1.0764)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0807

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0372 (-0.0782, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0756

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Myalgia	7 (2.42)	10 (3.52)
Relative Risk (RR) (95% CI)		1.4537 (0.5611, 3.7660)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4411
Odds Ratio (OR) (95% CI)		1.4703 (0.5518, 3.9178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4408
Risk Difference (RD) (95% CI)		0.0110 (-0.0168, 0.0388)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4387
Pain in extremity	7 (2.42)	6 (2.11)
Relative Risk (RR) (95% CI)		0.8722 (0.2968, 2.5635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8037
Odds Ratio (OR) (95% CI)		0.8695 (0.2886, 2.6197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8037

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0031 (-0.0275, 0.0213)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8034

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Musculoskeletal chest pain	7 (2.42)	4 (1.41)
Relative Risk (RR) (95% CI)		0.5815 (0.1721, 1.9647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3828
Odds Ratio (OR) (95% CI)		0.5755 (0.1666, 1.9878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3823
Risk Difference (RD) (95% CI)		-0.0101 (-0.0325, 0.0123)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3752
Injury, poisoning and procedural complications	53 (18.34)	46 (16.20)
Relative Risk (RR) (95% CI)		0.8832 (0.6166, 1.2652)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4982
Odds Ratio (OR) (95% CI)		0.8606 (0.5576, 1.3284)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4980
Risk Difference (RD) (95% CI)		-0.0214 (-0.0833, 0.0404)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4974

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Psychiatric disorders	36 (12.46)	41 (14.44)
Relative Risk (RR) (95% CI)		1.1589 (0.7640, 1.7579)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4877
Odds Ratio (OR) (95% CI)		1.1858 (0.7330, 1.9183)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4875
Risk Difference (RD) (95% CI)		0.0198 (-0.0361, 0.0757)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4873
Anxiety	6 (2.08)	16 (5.63)
Relative Risk (RR) (95% CI)		2.7136 (1.0773, 6.8356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0342
Odds Ratio (OR) (95% CI)		2.8159 (1.0858, 7.3032)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0332
Risk Difference (RD) (95% CI)		0.0356 (0.0041, 0.0670)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0266

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Insomnia	14 (4.84)	11 (3.87)
Relative Risk (RR) (95% CI)		0.7995 (0.3693, 1.7312)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5703
Odds Ratio (OR) (95% CI)		0.7915 (0.3531, 1.7743)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5702
Risk Difference (RD) (95% CI)		-0.0097 (-0.0431, 0.0237)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5689
Depression	3 (1.04)	10 (3.52)
Relative Risk (RR) (95% CI)		3.3920 (0.9433, 12.1971)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0614
Odds Ratio (OR) (95% CI)		3.4793 (0.9475, 12.7769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0603

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0248 (0.0004, 0.0492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0462

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Metabolism and nutrition disorders	25 (8.65)	25 (8.80)
Relative Risk (RR) (95% CI)		1.0176 (0.5992, 1.7282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9485
Odds Ratio (OR) (95% CI)		1.0193 (0.5706, 1.8210)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9485
Risk Difference (RD) (95% CI)		0.0015 (-0.0447, 0.0477)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9485
Decreased appetite	8 (2.77)	3 (1.06)
Relative Risk (RR) (95% CI)		0.3816 (0.1023, 1.4239)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1516
Odds Ratio (OR) (95% CI)		0.3750 (0.0985, 1.4281)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1505
Risk Difference (RD) (95% CI)		-0.0171 (-0.0395, 0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1332

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Eye disorders	18 (6.23)	17 (5.99)
Relative Risk (RR) (95% CI)		0.9611 (0.5056, 1.8269)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9036
Odds Ratio (OR) (95% CI)		0.9586 (0.4837, 1.8999)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9036
Risk Difference (RD) (95% CI)		-0.0024 (-0.0416, 0.0368)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9035
Renal and urinary disorders	15 (5.19)	10 (3.52)
Relative Risk (RR) (95% CI)		0.6784 (0.3100, 1.4847)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3316
Odds Ratio (OR) (95% CI)		0.6667 (0.2944, 1.5099)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3310
Risk Difference (RD) (95% CI)		-0.0167 (-0.0501, 0.0167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3269

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nephrolithiasis	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409
Reproductive system and breast disorders	19 (6.57)	10 (3.52)
Relative Risk (RR) (95% CI)		0.5356 (0.2535, 1.1316)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1018
Odds Ratio (OR) (95% CI)		0.5186 (0.2368, 1.1359)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1007
Risk Difference (RD) (95% CI)		-0.0305 (-0.0663, 0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0939

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Ear and labyrinth disorders	11 (3.81)	9 (3.17)
Relative Risk (RR) (95% CI)		0.8326 (0.3504, 1.9786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6782
Odds Ratio (OR) (95% CI)		0.8271 (0.3374, 2.0274)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6782
Risk Difference (RD) (95% CI)		-0.0064 (-0.0364, 0.0237)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6775
Congenital, familial and genetic disorders	5 (1.73)	8 (2.82)
Relative Risk (RR) (95% CI)		1.6282 (0.5391, 4.9172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3874
Odds Ratio (OR) (95% CI)		1.6464 (0.5321, 5.0944)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3870
Risk Difference (RD) (95% CI)		0.0109 (-0.0136, 0.0353)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3830

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Immune system disorders	8 (2.77)	8 (2.82)
Relative Risk (RR) (95% CI)		1.0176 (0.3872, 2.6742)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9718
Odds Ratio (OR) (95% CI)		1.0181 (0.3768, 2.7509)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9718
Risk Difference (RD) (95% CI)		0.0005 (-0.0265, 0.0275)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9718
Seasonal allergy	6 (2.08)	7 (2.46)
Relative Risk (RR) (95% CI)		1.1872 (0.4040, 3.4892)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7551
Odds Ratio (OR) (95% CI)		1.1919 (0.3956, 3.5913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7550
Risk Difference (RD) (95% CI)		0.0039 (-0.0205, 0.0283)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7549

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Cardiac disorders	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467
Vascular disorders	9 (3.11)	5 (1.76)
Relative Risk (RR) (95% CI)		0.5653 (0.1918, 1.6662)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3010
Odds Ratio (OR) (95% CI)		0.5575 (0.1845, 1.6846)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3004
Risk Difference (RD) (95% CI)		-0.0135 (-0.0387, 0.0117)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2924

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Table 2.3.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Hepatobiliary disorders	9 (3.11)	4 (1.41)
Relative Risk (RR) (95% CI)		0.4523 (0.1409, 1.4519)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1824
Odds Ratio (OR) (95% CI)		0.4444 (0.1353, 1.4600)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1814
Risk Difference (RD) (95% CI)		-0.0171 (-0.0413, 0.0072)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1683

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any TEAEs	271 (93.77)	274 (96.48)
Relative Risk (RR) (95% CI)		1.0289 (0.9914, 1.0678)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1327
Odds Ratio (OR) (95% CI)		1.8199 (0.8251, 4.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1379
Risk Difference (RD) (95% CI)		0.0271 (-0.0081, 0.0622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1312
Grade 1/Mild	89 (30.80)	103 (36.27)
Relative Risk (RR) (95% CI)		1.1777 (0.9342, 1.4846)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1664
Odds Ratio (OR) (95% CI)		1.2788 (0.9032, 1.8105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1657

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0547 (-0.0225, 0.1319)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1648

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	153 (52.94)	147 (51.76)
Relative Risk (RR) (95% CI)		0.9777 (0.8363, 1.1431)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7773
Odds Ratio (OR) (95% CI)		0.9538 (0.6871, 1.3239)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7772
Risk Difference (RD) (95% CI)		-0.0118 (-0.0936, 0.0700)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7772
Grade 3/Severe	28 (9.69)	24 (8.45)
Relative Risk (RR) (95% CI)		0.8722 (0.5185, 1.4672)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6064
Odds Ratio (OR) (95% CI)		0.8604 (0.4858, 1.5240)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6063

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0124 (-0.0594, 0.0346)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6057

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Infections and infestations	208 (71.97)	199 (70.07)
Relative Risk (RR) (95% CI)		0.9736 (0.8768, 1.0810)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6160
Odds Ratio (OR) (95% CI)		0.9117 (0.6354, 1.3082)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6159
Risk Difference (RD) (95% CI)		-0.0190 (-0.0933, 0.0553)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6158
Grade 1/Mild	102 (35.29)	108 (38.03)
Relative Risk (RR) (95% CI)		1.0775 (0.8686, 1.3365)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4973
Odds Ratio (OR) (95% CI)		1.1250 (0.8007, 1.5806)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4972

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0273 (-0.0515, 0.1062)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4970

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	100 (34.60)	86 (30.28)
Relative Risk (RR) (95% CI)		0.8751 (0.6903, 1.1094)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2705
Odds Ratio (OR) (95% CI)		0.8209 (0.5782, 1.1654)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2697
Risk Difference (RD) (95% CI)		-0.0432 (-0.1198, 0.0334)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2688
Grade 3/Severe	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
COVID-19	73 (25.26)	58 (20.42)
Relative Risk (RR) (95% CI)		0.8085 (0.5969, 1.0951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1697
Odds Ratio (OR) (95% CI)		0.7594 (0.5131, 1.1238)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1687
Risk Difference (RD) (95% CI)		-0.0484 (-0.1170, 0.0202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1671
Grade 1/Mild	47 (16.26)	37 (13.03)
Relative Risk (RR) (95% CI)		0.8011 (0.5378, 1.1932)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2753
Odds Ratio (OR) (95% CI)		0.7713 (0.4841, 1.2289)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2746

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0323 (-0.0902, 0.0255)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2728

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	25 (8.65)	21 (7.39)
Relative Risk (RR) (95% CI)		0.8548 (0.4899, 1.4913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5806
Odds Ratio (OR) (95% CI)		0.8432 (0.4606, 1.5437)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5804
Risk Difference (RD) (95% CI)		-0.0126 (-0.0570, 0.0319)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5797
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nasopharyngitis	60 (20.76)	57 (20.07)
Relative Risk (RR) (95% CI)		0.9667 (0.6996, 1.3359)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8375
Odds Ratio (OR) (95% CI)		0.9584 (0.6384, 1.4388)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8375
Risk Difference (RD) (95% CI)		-0.0069 (-0.0729, 0.0591)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8375
Grade 1/Mild	39 (13.49)	49 (17.25)
Relative Risk (RR) (95% CI)		1.2785 (0.8679, 1.8835)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2138
Odds Ratio (OR) (95% CI)		1.3366 (0.8465, 2.1104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2131

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0376 (-0.0214, 0.0966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2119

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	21 (7.27)	8 (2.82)
Relative Risk (RR) (95% CI)		0.3877 (0.1746, 0.8608)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0199
Odds Ratio (OR) (95% CI)		0.3699 (0.1611, 0.8496)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0191
Risk Difference (RD) (95% CI)		-0.0445 (-0.0801, -0.0089)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0142
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Upper respiratory tract infection	40 (13.84)	55 (19.37)
Relative Risk (RR) (95% CI)		1.3992 (0.9637, 2.0316)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0775
Odds Ratio (OR) (95% CI)		1.4951 (0.9580, 2.3332)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0765
Risk Difference (RD) (95% CI)		0.0553 (-0.0056, 0.1161)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0749
Grade 1/Mild	27 (9.34)	40 (14.08)
Relative Risk (RR) (95% CI)		1.5076 (0.9518, 2.3878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0802
Odds Ratio (OR) (95% CI)		1.5908 (0.9473, 2.6714)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0792

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0474 (-0.0051, 0.1000)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0770

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	13 (4.50)	15 (5.28)
Relative Risk (RR) (95% CI)		1.1742 (0.5690, 2.4229)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6640
Odds Ratio (OR) (95% CI)		1.1839 (0.5529, 2.5351)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6639
Risk Difference (RD) (95% CI)		0.0078 (-0.0275, 0.0432)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6638
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Influenza	16 (5.54)	33 (11.62)
Relative Risk (RR) (95% CI)		2.0988 (1.1820, 3.7268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0114
Odds Ratio (OR) (95% CI)		2.2433 (1.2053, 4.1750)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0108
Risk Difference (RD) (95% CI)		0.0608 (0.0152, 0.1065)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0090
Grade 1/Mild	6 (2.08)	14 (4.93)
Relative Risk (RR) (95% CI)		2.3744 (0.9254, 6.0921)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0721
Odds Ratio (OR) (95% CI)		2.4457 (0.9264, 6.4567)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0710

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0285 (-0.0015, 0.0586)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0629

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	9 (3.11)	17 (5.99)
Relative Risk (RR) (95% CI)		1.9221 (0.8713, 4.2403)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1055
Odds Ratio (OR) (95% CI)		1.9809 (0.8679, 4.5208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1045
Risk Difference (RD) (95% CI)		0.0287 (-0.0054, 0.0628)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0987
Grade 3/Severe	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Viral upper respiratory tract infection	17 (5.88)	20 (7.04)
Relative Risk (RR) (95% CI)		1.1972 (0.6405, 2.2377)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5728
Odds Ratio (OR) (95% CI)		1.2121 (0.6213, 2.3649)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5727
Risk Difference (RD) (95% CI)		0.0116 (-0.0287, 0.0519)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5724
Grade 1/Mild	15 (5.19)	15 (5.28)
Relative Risk (RR) (95% CI)		1.0176 (0.5070, 2.0424)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9608
Odds Ratio (OR) (95% CI)		1.0186 (0.4883, 2.1246)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9608

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0009 (-0.0356, 0.0374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9608

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	5 (1.76)
Relative Risk (RR) (95% CI)		2.5440 (0.4976, 13.0055)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2620
Odds Ratio (OR) (95% CI)		2.5717 (0.4948, 13.3651)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2613
Risk Difference (RD) (95% CI)		0.0107 (-0.0074, 0.0287)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2456
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Sinusitis	26 (9.00)	9 (3.17)
Relative Risk (RR) (95% CI)		0.3522 (0.1680, 0.7384)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0057
Odds Ratio (OR) (95% CI)		0.3310 (0.1523, 0.7197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0053
Risk Difference (RD) (95% CI)		-0.0583 (-0.0970, -0.0195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0032
Grade 1/Mild	17 (5.88)	5 (1.76)
Relative Risk (RR) (95% CI)		0.2993 (0.1119, 0.8003)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0162
Odds Ratio (OR) (95% CI)		0.2867 (0.1043, 0.7881)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0154

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0412 (-0.0724, -0.0101)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0095

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	9 (3.11)	4 (1.41)
Relative Risk (RR) (95% CI)		0.4523 (0.1409, 1.4519)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1824
Odds Ratio (OR) (95% CI)		0.4444 (0.1353, 1.4600)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1814
Risk Difference (RD) (95% CI)		-0.0171 (-0.0413, 0.0072)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1683
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Urinary tract infection	10 (3.46)	9 (3.17)
Relative Risk (RR) (95% CI)		0.9158 (0.3778, 2.2202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8457
Odds Ratio (OR) (95% CI)		0.9131 (0.3654, 2.2816)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8457
Risk Difference (RD) (95% CI)		-0.0029 (-0.0322, 0.0264)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8456
Grade 1/Mild	6 (2.08)	6 (2.11)
Relative Risk (RR) (95% CI)		1.0176 (0.3321, 3.1178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9756
Odds Ratio (OR) (95% CI)		1.0180 (0.3244, 3.1946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9756

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0004 (-0.0231, 0.0238)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9756

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	4 (1.38)	3 (1.06)
Relative Risk (RR) (95% CI)		0.7632 (0.1724, 3.3795)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7219
Odds Ratio (OR) (95% CI)		0.7607 (0.1687, 3.4296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7218
Risk Difference (RD) (95% CI)		-0.0033 (-0.0212, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7207
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Rhinitis	11 (3.81)	8 (2.82)
Relative Risk (RR) (95% CI)		0.7401 (0.3021, 1.8128)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5102
Odds Ratio (OR) (95% CI)		0.7325 (0.2902, 1.8489)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5100
Risk Difference (RD) (95% CI)		-0.0099 (-0.0392, 0.0194)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5077
Grade 1/Mild	9 (3.11)	8 (2.82)
Relative Risk (RR) (95% CI)		0.9045 (0.3540, 2.3114)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8340
Odds Ratio (OR) (95% CI)		0.9018 (0.3430, 2.3712)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8340

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- [3] Risk difference estimate from 2x2 table.
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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0030 (-0.0307, 0.0248)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8338

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0069 (-0.0165, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1559
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Bronchitis	8 (2.77)	7 (2.46)
Relative Risk (RR) (95% CI)		0.8904 (0.3272, 2.4230)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8202
Odds Ratio (OR) (95% CI)		0.8876 (0.3176, 2.4810)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8202
Risk Difference (RD) (95% CI)		-0.0030 (-0.0292, 0.0231)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8200
Grade 1/Mild	3 (1.04)	2 (0.70)
Relative Risk (RR) (95% CI)		0.6784 (0.1142, 4.0296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6695
Odds Ratio (OR) (95% CI)		0.6761 (0.1121, 4.0770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6694

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0033 (-0.0185, 0.0119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6669

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gastroenteritis	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467
Grade 1/Mild	2 (0.69)	6 (2.11)
Relative Risk (RR) (95% CI)		3.0528 (0.6214, 14.9988)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1694
Odds Ratio (OR) (95% CI)		3.0971 (0.6198, 15.4754)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1684

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0142 (-0.0051, 0.0335)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1483

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Conjunctivitis	12 (4.15)	5 (1.76)
Relative Risk (RR) (95% CI)		0.4240 (0.1513, 1.1881)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1026
Odds Ratio (OR) (95% CI)		0.4137 (0.1438, 1.1898)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1015
Risk Difference (RD) (95% CI)		-0.0239 (-0.0515, 0.0037)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0897
Grade 1/Mild	5 (1.73)	4 (1.41)
Relative Risk (RR) (95% CI)		0.8141 (0.2209, 3.0007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7573
Odds Ratio (OR) (95% CI)		0.8114 (0.2157, 3.0531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7573

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0032 (-0.0236, 0.0171)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7566

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	7 (2.42)	1 (0.35)
Relative Risk (RR) (95% CI)		0.1454 (0.0180, 1.1740)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0704
Odds Ratio (OR) (95% CI)		0.1424 (0.0174, 1.1645)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0691
Risk Difference (RD) (95% CI)		-0.0207 (-0.0397, -0.0017)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0329
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pharyngitis	8 (2.77)	5 (1.76)
Relative Risk (RR) (95% CI)		0.6360 (0.2106, 1.9208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4223
Odds Ratio (OR) (95% CI)		0.6295 (0.2034, 1.9478)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4219
Risk Difference (RD) (95% CI)		-0.0101 (-0.0344, 0.0142)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4169
Grade 1/Mild	5 (1.73)	4 (1.41)
Relative Risk (RR) (95% CI)		0.8141 (0.2209, 3.0007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7573
Odds Ratio (OR) (95% CI)		0.8114 (0.2157, 3.0531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7573

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0032 (-0.0236, 0.0171)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7566

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	1 (0.35)
Relative Risk (RR) (95% CI)		0.3392 (0.0355, 3.2416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3478
Odds Ratio (OR) (95% CI)		0.3369 (0.0348, 3.2578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3473
Risk Difference (RD) (95% CI)		-0.0069 (-0.0204, 0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3216
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Vulvovaginal mycotic infection	7 (2.42)	5 (1.76)
Relative Risk (RR) (95% CI)		0.7269 (0.2334, 2.2634)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5820
Odds Ratio (OR) (95% CI)		0.7220 (0.2264, 2.3019)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5819
Risk Difference (RD) (95% CI)		-0.0066 (-0.0300, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5797
Grade 1/Mild	2 (0.69)	2 (0.70)
Relative Risk (RR) (95% CI)		1.0176 (0.1443, 7.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9860
Odds Ratio (OR) (95% CI)		1.0177 (0.1424, 7.2748)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9860

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0135, 0.0138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9860

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	5 (1.73)	3 (1.06)
Relative Risk (RR) (95% CI)		0.6106 (0.1473, 2.5309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4965
Odds Ratio (OR) (95% CI)		0.6064 (0.1436, 2.5616)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4962
Risk Difference (RD) (95% CI)		-0.0067 (-0.0259, 0.0124)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4908
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Otitis media	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409
Grade 1/Mild	3 (1.04)	2 (0.70)
Relative Risk (RR) (95% CI)		0.6784 (0.1142, 4.0296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6695
Odds Ratio (OR) (95% CI)		0.6761 (0.1121, 4.0770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6694

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0033 (-0.0185, 0.0119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6669

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	2 (0.70)
Relative Risk (RR) (95% CI)		0.6784 (0.1142, 4.0296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6695
Odds Ratio (OR) (95% CI)		0.6761 (0.1121, 4.0770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6694
Risk Difference (RD) (95% CI)		-0.0033 (-0.0185, 0.0119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6669
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pneumonia	8 (2.77)	4 (1.41)
Relative Risk (RR) (95% CI)		0.5088 (0.1549, 1.6708)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2654
Odds Ratio (OR) (95% CI)		0.5018 (0.1494, 1.6854)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2646
Risk Difference (RD) (95% CI)		-0.0136 (-0.0370, 0.0098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2539
Grade 1/Mild	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	4 (1.38)	2 (0.70)
Relative Risk (RR) (95% CI)		0.5088 (0.0939, 2.7560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4331
Odds Ratio (OR) (95% CI)		0.5053 (0.0918, 2.7809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4328
Risk Difference (RD) (95% CI)		-0.0068 (-0.0234, 0.0098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4225
Grade 3/Severe	2 (0.69)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0165, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1559

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Respiratory, thoracic and mediastinal disorders	153 (52.94)	145 (51.06)
Relative Risk (RR) (95% CI)		0.9644 (0.8239, 1.1288)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6517
Odds Ratio (OR) (95% CI)		0.9273 (0.6681, 1.2870)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6516
Risk Difference (RD) (95% CI)		-0.0188 (-0.1007, 0.0630)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6516
Grade 1/Mild	102 (35.29)	104 (36.62)
Relative Risk (RR) (95% CI)		1.0376 (0.8338, 1.2911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7409
Odds Ratio (OR) (95% CI)		1.0593 (0.7530, 1.4901)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7409

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0133 (-0.0653, 0.0918)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7409

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	48 (16.61)	40 (14.08)
Relative Risk (RR) (95% CI)		0.8480 (0.5763, 1.2479)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4029
Odds Ratio (OR) (95% CI)		0.8231 (0.5218, 1.2984)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4025
Risk Difference (RD) (95% CI)		-0.0252 (-0.0842, 0.0337)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4015
Grade 3/Severe	3 (1.04)	1 (0.35)
Relative Risk (RR) (95% CI)		0.3392 (0.0355, 3.2416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3478
Odds Ratio (OR) (95% CI)		0.3369 (0.0348, 3.2578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3473

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0204, 0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3216

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Cough	60 (20.76)	63 (22.18)
Relative Risk (RR) (95% CI)		1.0685 (0.7811, 1.4617)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6786
Odds Ratio (OR) (95% CI)		1.0880 (0.7301, 1.6214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6786
Risk Difference (RD) (95% CI)		0.0142 (-0.0530, 0.0815)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6786
Grade 1/Mild	44 (15.22)	50 (17.61)
Relative Risk (RR) (95% CI)		1.1564 (0.7983, 1.6751)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4422
Odds Ratio (OR) (95% CI)		1.1898 (0.7640, 1.8529)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4420

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0238 (-0.0368, 0.0845)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4416

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	15 (5.19)	13 (4.58)
Relative Risk (RR) (95% CI)		0.8819 (0.4274, 1.8199)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7339
Odds Ratio (OR) (95% CI)		0.8763 (0.4092, 1.8764)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7339
Risk Difference (RD) (95% CI)		-0.0061 (-0.0414, 0.0292)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7335
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Oropharyngeal pain	37 (12.80)	45 (15.85)
Relative Risk (RR) (95% CI)		1.2376 (0.8272, 1.8518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2997
Odds Ratio (OR) (95% CI)		1.2824 (0.8018, 2.0509)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2992
Risk Difference (RD) (95% CI)		0.0304 (-0.0269, 0.0878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2984
Grade 1/Mild	27 (9.34)	34 (11.97)
Relative Risk (RR) (95% CI)		1.2814 (0.7945, 2.0667)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3092
Odds Ratio (OR) (95% CI)		1.3197 (0.7736, 2.2514)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3087

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0263 (-0.0242, 0.0768)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3076

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	10 (3.46)	11 (3.87)
Relative Risk (RR) (95% CI)		1.1194 (0.4830, 2.5943)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7926
Odds Ratio (OR) (95% CI)		1.1242 (0.4698, 2.6900)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7926
Risk Difference (RD) (95% CI)		0.0041 (-0.0267, 0.0349)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7926
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nasal congestion	23 (7.96)	29 (10.21)
Relative Risk (RR) (95% CI)		1.2831 (0.7612, 2.1629)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3495
Odds Ratio (OR) (95% CI)		1.3153 (0.7412, 2.3341)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3491
Risk Difference (RD) (95% CI)		0.0225 (-0.0245, 0.0696)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3480
Grade 1/Mild	21 (7.27)	27 (9.51)
Relative Risk (RR) (95% CI)		1.3084 (0.7577, 2.2592)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3349
Odds Ratio (OR) (95% CI)		1.3407 (0.7392, 2.4317)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3344

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0224 (-0.0230, 0.0678)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3332

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	2 (0.70)
Relative Risk (RR) (95% CI)		1.0176 (0.1443, 7.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9860
Odds Ratio (OR) (95% CI)		1.0177 (0.1424, 7.2748)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9860
Risk Difference (RD) (95% CI)		0.0001 (-0.0135, 0.0138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9860
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Sputum increased	29 (10.03)	27 (9.51)
Relative Risk (RR) (95% CI)		0.9474 (0.5758, 1.5588)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8316
Odds Ratio (OR) (95% CI)		0.9419 (0.5425, 1.6355)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8316
Risk Difference (RD) (95% CI)		-0.0053 (-0.0539, 0.0433)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8316
Grade 1/Mild	21 (7.27)	17 (5.99)
Relative Risk (RR) (95% CI)		0.8238 (0.4440, 1.5285)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5388
Odds Ratio (OR) (95% CI)		0.8126 (0.4193, 1.5745)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5386

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0128 (-0.0535, 0.0279)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5375

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	8 (2.77)	10 (3.52)
Relative Risk (RR) (95% CI)		1.2720 (0.5094, 3.1764)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6064
Odds Ratio (OR) (95% CI)		1.2819 (0.4985, 3.2964)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6063
Risk Difference (RD) (95% CI)		0.0075 (-0.0211, 0.0361)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6057
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Sinus congestion	10 (3.46)	18 (6.34)
Relative Risk (RR) (95% CI)		1.8317 (0.8605, 3.8990)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1164
Odds Ratio (OR) (95% CI)		1.8880 (0.8559, 4.1643)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1154
Risk Difference (RD) (95% CI)		0.0288 (-0.0065, 0.0641)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1102
Grade 1/Mild	9 (3.11)	17 (5.99)
Relative Risk (RR) (95% CI)		1.9221 (0.8713, 4.2403)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1055
Odds Ratio (OR) (95% CI)		1.9809 (0.8679, 4.5208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1045

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0287 (-0.0054, 0.0628)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0987

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Haemoptysis	22 (7.61)	17 (5.99)
Relative Risk (RR) (95% CI)		0.7863 (0.4267, 1.4492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4409
Odds Ratio (OR) (95% CI)		0.7727 (0.4013, 1.4880)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4406
Risk Difference (RD) (95% CI)		-0.0163 (-0.0574, 0.0249)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4389
Grade 1/Mild	11 (3.81)	12 (4.23)
Relative Risk (RR) (95% CI)		1.1101 (0.4980, 2.4745)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7984
Odds Ratio (OR) (95% CI)		1.1150 (0.4837, 2.5699)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7984

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0042 (-0.0280, 0.0363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7984

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	10 (3.46)	4 (1.41)
Relative Risk (RR) (95% CI)		0.4070 (0.1292, 1.2828)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1249
Odds Ratio (OR) (95% CI)		0.3986 (0.1235, 1.2859)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1238
Risk Difference (RD) (95% CI)		-0.0205 (-0.0457, 0.0046)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1096
Grade 3/Severe	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Productive cough	19 (6.57)	16 (5.63)
Relative Risk (RR) (95% CI)		0.8569 (0.4498, 1.6326)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6387
Odds Ratio (OR) (95% CI)		0.8484 (0.4272, 1.6850)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6386
Risk Difference (RD) (95% CI)		-0.0094 (-0.0486, 0.0298)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6380
Grade 1/Mild	16 (5.54)	13 (4.58)
Relative Risk (RR) (95% CI)		0.8268 (0.4052, 1.6872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6013
Odds Ratio (OR) (95% CI)		0.8185 (0.3863, 1.7343)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6011

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0096 (-0.0454, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6002

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	3 (1.06)
Relative Risk (RR) (95% CI)		1.5264 (0.2570, 9.0666)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6418
Odds Ratio (OR) (95% CI)		1.5320 (0.2541, 9.2381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6417
Risk Difference (RD) (95% CI)		0.0036 (-0.0116, 0.0189)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6398
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Rhinorrhoea	22 (7.61)	16 (5.63)
Relative Risk (RR) (95% CI)		0.7401 (0.3970, 1.3796)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3435
Odds Ratio (OR) (95% CI)		0.7246 (0.3723, 1.4102)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3430
Risk Difference (RD) (95% CI)		-0.0198 (-0.0605, 0.0209)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3403
Grade 1/Mild	20 (6.92)	14 (4.93)
Relative Risk (RR) (95% CI)		0.7123 (0.3670, 1.3824)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3160
Odds Ratio (OR) (95% CI)		0.6974 (0.3451, 1.4094)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3154

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0199 (-0.0585, 0.0187)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3121

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	2 (0.70)
Relative Risk (RR) (95% CI)		1.0176 (0.1443, 7.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9860
Odds Ratio (OR) (95% CI)		1.0177 (0.1424, 7.2748)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9860
Risk Difference (RD) (95% CI)		0.0001 (-0.0135, 0.0138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9860
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Dyspnoea	21 (7.27)	11 (3.87)
Relative Risk (RR) (95% CI)		0.5330 (0.2618, 1.0851)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0828
Odds Ratio (OR) (95% CI)		0.5142 (0.2432, 1.0872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0817
Risk Difference (RD) (95% CI)		-0.0339 (-0.0713, 0.0035)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0754
Grade 1/Mild	11 (3.81)	9 (3.17)
Relative Risk (RR) (95% CI)		0.8326 (0.3504, 1.9786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6782
Odds Ratio (OR) (95% CI)		0.8271 (0.3374, 2.0274)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6782

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0064 (-0.0364, 0.0237)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6775

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	10 (3.46)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2035 (0.0450, 0.9207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0387
Odds Ratio (OR) (95% CI)		0.1979 (0.0430, 0.9112)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0376
Risk Difference (RD) (95% CI)		-0.0276 (-0.0508, -0.0044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0199
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Lower respiratory tract congestion	5 (1.73)	9 (3.17)
Relative Risk (RR) (95% CI)		1.8317 (0.6215, 5.3985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2724
Odds Ratio (OR) (95% CI)		1.8589 (0.6152, 5.6165)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2718
Risk Difference (RD) (95% CI)		0.0144 (-0.0109, 0.0397)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2653
Grade 1/Mild	3 (1.04)	8 (2.82)
Relative Risk (RR) (95% CI)		2.7136 (0.7273, 10.1253)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1373
Odds Ratio (OR) (95% CI)		2.7633 (0.7256, 10.5233)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1363

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0178 (-0.0047, 0.0403)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1215

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Respiration abnormal	7 (2.42)	9 (3.17)
Relative Risk (RR) (95% CI)		1.3084 (0.4940, 3.4654)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5886
Odds Ratio (OR) (95% CI)		1.3184 (0.4843, 3.5896)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5885
Risk Difference (RD) (95% CI)		0.0075 (-0.0195, 0.0345)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5878
Grade 1/Mild	3 (1.04)	8 (2.82)
Relative Risk (RR) (95% CI)		2.7136 (0.7273, 10.1253)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1373
Odds Ratio (OR) (95% CI)		2.7633 (0.7256, 10.5233)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1363

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0178 (-0.0047, 0.0403)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1215

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	4 (1.38)	1 (0.35)
Relative Risk (RR) (95% CI)		0.2544 (0.0286, 2.2622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2195
Odds Ratio (OR) (95% CI)		0.2518 (0.0280, 2.2665)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2186
Risk Difference (RD) (95% CI)		-0.0103 (-0.0254, 0.0048)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1813
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Wheezing	7 (2.42)	8 (2.82)
Relative Risk (RR) (95% CI)		1.1630 (0.4274, 3.1647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7675
Odds Ratio (OR) (95% CI)		1.1677 (0.4178, 3.2638)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7675
Risk Difference (RD) (95% CI)		0.0039 (-0.0222, 0.0301)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7674
Grade 1/Mild	6 (2.08)	5 (1.76)
Relative Risk (RR) (95% CI)		0.8480 (0.2618, 2.7472)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7834
Odds Ratio (OR) (95% CI)		0.8453 (0.2550, 2.8016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7834

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0032 (-0.0256, 0.0193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7830

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	3 (1.06)
Relative Risk (RR) (95% CI)		3.0528 (0.3194, 29.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3325
Odds Ratio (OR) (95% CI)		3.0747 (0.3179, 29.7357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3320
Risk Difference (RD) (95% CI)		0.0071 (-0.0066, 0.0208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3089
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Upper-airway cough syndrome	8 (2.77)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2544 (0.0545, 1.1876)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0816
Odds Ratio (OR) (95% CI)		0.2491 (0.0524, 1.1834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0804
Risk Difference (RD) (95% CI)		-0.0206 (-0.0419, 0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0572
Grade 1/Mild	8 (2.77)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2544 (0.0545, 1.1876)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0816
Odds Ratio (OR) (95% CI)		0.2491 (0.0524, 1.1834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0804

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0206 (-0.0419, 0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0572

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gastrointestinal disorders	111 (38.41)	114 (40.14)
Relative Risk (RR) (95% CI)		1.0451 (0.8525, 1.2812)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6712
Odds Ratio (OR) (95% CI)		1.0754 (0.7689, 1.5039)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6711
Risk Difference (RD) (95% CI)		0.0173 (-0.0626, 0.0973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6711
Grade 1/Mild	57 (19.72)	70 (24.65)
Relative Risk (RR) (95% CI)		1.2497 (0.9175, 1.7021)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1574
Odds Ratio (OR) (95% CI)		1.3314 (0.8961, 1.9781)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1566

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0492 (-0.0187, 0.1172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1554

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	49 (16.96)	40 (14.08)
Relative Risk (RR) (95% CI)		0.8307 (0.5657, 1.2198)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3440
Odds Ratio (OR) (95% CI)		0.8029 (0.5099, 1.2644)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3435
Risk Difference (RD) (95% CI)		-0.0287 (-0.0879, 0.0305)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3422
Grade 3/Severe	5 (1.73)	4 (1.41)
Relative Risk (RR) (95% CI)		0.8141 (0.2209, 3.0007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7573
Odds Ratio (OR) (95% CI)		0.8114 (0.2157, 3.0531)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7573

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0032 (-0.0236, 0.0171)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7566

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Diarrhoea	44 (15.22)	37 (13.03)
Relative Risk (RR) (95% CI)		0.8557 (0.5705, 1.2834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4512
Odds Ratio (OR) (95% CI)		0.8341 (0.5205, 1.3366)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4509
Risk Difference (RD) (95% CI)		-0.0220 (-0.0790, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4500
Grade 1/Mild	31 (10.73)	30 (10.56)
Relative Risk (RR) (95% CI)		0.9848 (0.6127, 1.5827)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9495
Odds Ratio (OR) (95% CI)		0.9830 (0.5780, 1.6717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9495

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0016 (-0.0521, 0.0489)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9495

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	12 (4.15)	7 (2.46)
Relative Risk (RR) (95% CI)		0.5936 (0.2371, 1.4860)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2653
Odds Ratio (OR) (95% CI)		0.5833 (0.2263, 1.5037)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2646
Risk Difference (RD) (95% CI)		-0.0169 (-0.0461, 0.0124)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2578
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nausea	13 (4.50)	22 (7.75)
Relative Risk (RR) (95% CI)		1.7221 (0.8849, 3.3513)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1096
Odds Ratio (OR) (95% CI)		1.7827 (0.8798, 3.6122)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1086
Risk Difference (RD) (95% CI)		0.0325 (-0.0067, 0.0717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1045
Grade 1/Mild	12 (4.15)	16 (5.63)
Relative Risk (RR) (95% CI)		1.3568 (0.6536, 2.8164)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4129
Odds Ratio (OR) (95% CI)		1.3781 (0.6399, 2.9677)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4125

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0148 (-0.0205, 0.0501)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4111

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	6 (2.11)
Relative Risk (RR) (95% CI)		6.1056 (0.7397, 50.3940)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0929
Odds Ratio (OR) (95% CI)		6.2158 (0.7436, 51.9617)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0917
Risk Difference (RD) (95% CI)		0.0177 (-0.0004, 0.0357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0550
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Abdominal pain	23 (7.96)	15 (5.28)
Relative Risk (RR) (95% CI)		0.6637 (0.3536, 1.2455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2018
Odds Ratio (OR) (95% CI)		0.6449 (0.3293, 1.2631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2009
Risk Difference (RD) (95% CI)		-0.0268 (-0.0674, 0.0139)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1966
Grade 1/Mild	11 (3.81)	11 (3.87)
Relative Risk (RR) (95% CI)		1.0176 (0.4484, 2.3094)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9667
Odds Ratio (OR) (95% CI)		1.0183 (0.4343, 2.3879)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9667

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0007 (-0.0308, 0.0321)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9667

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	11 (3.81)	4 (1.41)
Relative Risk (RR) (95% CI)		0.3700 (0.1192, 1.1485)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0854
Odds Ratio (OR) (95% CI)		0.3610 (0.1136, 1.1475)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0842
Risk Difference (RD) (95% CI)		-0.0240 (-0.0499, 0.0020)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0704
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Constipation	20 (6.92)	15 (5.28)
Relative Risk (RR) (95% CI)		0.7632 (0.3988, 1.4607)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4145
Odds Ratio (OR) (95% CI)		0.7500 (0.3760, 1.4960)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4141
Risk Difference (RD) (95% CI)		-0.0164 (-0.0555, 0.0228)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4120
Grade 1/Mild	10 (3.46)	7 (2.46)
Relative Risk (RR) (95% CI)		0.7123 (0.2750, 1.8454)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4849
Odds Ratio (OR) (95% CI)		0.7051 (0.2646, 1.8787)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4846

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0100 (-0.0377, 0.0178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4818

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	9 (3.11)	8 (2.82)
Relative Risk (RR) (95% CI)		0.9045 (0.3540, 2.3114)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8340
Odds Ratio (OR) (95% CI)		0.9018 (0.3430, 2.3712)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8340
Risk Difference (RD) (95% CI)		-0.0030 (-0.0307, 0.0248)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8338
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Abdominal pain upper	13 (4.50)	14 (4.93)
Relative Risk (RR) (95% CI)		1.0959 (0.5245, 2.2899)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8076
Odds Ratio (OR) (95% CI)		1.1009 (0.5080, 2.3855)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8076
Risk Difference (RD) (95% CI)		0.0043 (-0.0304, 0.0390)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8076
Grade 1/Mild	8 (2.77)	10 (3.52)
Relative Risk (RR) (95% CI)		1.2720 (0.5094, 3.1764)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6064
Odds Ratio (OR) (95% CI)		1.2819 (0.4985, 3.2964)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6063

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- [1] Relative risk from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0075 (-0.0211, 0.0361)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6057

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	5 (1.73)	3 (1.06)
Relative Risk (RR) (95% CI)		0.6106 (0.1473, 2.5309)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4965
Odds Ratio (OR) (95% CI)		0.6064 (0.1436, 2.5616)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4962
Risk Difference (RD) (95% CI)		-0.0067 (-0.0259, 0.0124)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4908
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Vomiting	19 (6.57)	12 (4.23)
Relative Risk (RR) (95% CI)		0.6427 (0.3179, 1.2993)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2183
Odds Ratio (OR) (95% CI)		0.6269 (0.2985, 1.3167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2175
Risk Difference (RD) (95% CI)		-0.0235 (-0.0604, 0.0134)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2125
Grade 1/Mild	10 (3.46)	10 (3.52)
Relative Risk (RR) (95% CI)		1.0176 (0.4301, 2.4074)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9683
Odds Ratio (OR) (95% CI)		1.0182 (0.4172, 2.4851)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9683

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0006 (-0.0294, 0.0307)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9683

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	9 (3.11)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2261 (0.0493, 1.0375)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0558
Odds Ratio (OR) (95% CI)		0.2206 (0.0473, 1.0303)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0546
Risk Difference (RD) (95% CI)		-0.0241 (-0.0464, -0.0018)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0339
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Abdominal distension	5 (1.73)	6 (2.11)
Relative Risk (RR) (95% CI)		1.2211 (0.3769, 3.9560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7391
Odds Ratio (OR) (95% CI)		1.2259 (0.3699, 4.0631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7390
Risk Difference (RD) (95% CI)		0.0038 (-0.0187, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7388
Grade 1/Mild	2 (0.69)	5 (1.76)
Relative Risk (RR) (95% CI)		2.5440 (0.4976, 13.0055)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2620
Odds Ratio (OR) (95% CI)		2.5717 (0.4948, 13.3651)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2613

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0107 (-0.0074, 0.0287)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2456

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	1 (0.35)
Relative Risk (RR) (95% CI)		0.3392 (0.0355, 3.2416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3478
Odds Ratio (OR) (95% CI)		0.3369 (0.0348, 3.2578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3473
Risk Difference (RD) (95% CI)		-0.0069 (-0.0204, 0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3216
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gastrooesophageal reflux disease	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409
Grade 1/Mild	3 (1.04)	3 (1.06)
Relative Risk (RR) (95% CI)		1.0176 (0.2071, 4.9996)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9829
Odds Ratio (OR) (95% CI)		1.0178 (0.2037, 5.0855)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9829

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0002 (-0.0165, 0.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9829

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Flatulence	8 (2.77)	2 (0.70)
Relative Risk (RR) (95% CI)		0.2544 (0.0545, 1.1876)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0816
Odds Ratio (OR) (95% CI)		0.2491 (0.0524, 1.1834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0804
Risk Difference (RD) (95% CI)		-0.0206 (-0.0419, 0.0006)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0572
Grade 1/Mild	5 (1.73)	2 (0.70)
Relative Risk (RR) (95% CI)		0.4070 (0.0796, 2.0809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2803
Odds Ratio (OR) (95% CI)		0.4028 (0.0775, 2.0935)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2796

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0103 (-0.0282, 0.0076)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2614

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- [2] Odds ratio from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0104 (-0.0221, 0.0013)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0817
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Investigations	94 (32.53)	104 (36.62)
Relative Risk (RR) (95% CI)		1.1259 (0.8983, 1.4111)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3035
Odds Ratio (OR) (95% CI)		1.1986 (0.8491, 1.6919)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3031
Risk Difference (RD) (95% CI)		0.0409 (-0.0369, 0.1188)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3025
Grade 1/Mild	55 (19.03)	64 (22.54)
Relative Risk (RR) (95% CI)		1.1841 (0.8590, 1.6323)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3021
Odds Ratio (OR) (95% CI)		1.2377 (0.8258, 1.8550)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3017

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0350 (-0.0314, 0.1014)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3010

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	34 (11.76)	35 (12.32)
Relative Risk (RR) (95% CI)		1.0475 (0.6729, 1.6308)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8371
Odds Ratio (OR) (95% CI)		1.0542 (0.6374, 1.7437)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8371
Risk Difference (RD) (95% CI)		0.0056 (-0.0477, 0.0589)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8371
Grade 3/Severe	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Alanine aminotransferase increased	18 (6.23)	25 (8.80)
Relative Risk (RR) (95% CI)		1.4133 (0.7887, 2.5327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2451
Odds Ratio (OR) (95% CI)		1.4532 (0.7745, 2.7268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2444
Risk Difference (RD) (95% CI)		0.0257 (-0.0174, 0.0689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2423
Grade 1/Mild	8 (2.77)	15 (5.28)
Relative Risk (RR) (95% CI)		1.9080 (0.8218, 4.4298)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1328
Odds Ratio (OR) (95% CI)		1.9586 (0.8171, 4.6948)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1318

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0251 (-0.0070, 0.0573)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1256

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	10 (3.46)	6 (2.11)
Relative Risk (RR) (95% CI)		0.6106 (0.2249, 1.6577)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3330
Odds Ratio (OR) (95% CI)		0.6022 (0.2159, 1.6794)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3324
Risk Difference (RD) (95% CI)		-0.0135 (-0.0404, 0.0134)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3262
Grade 3/Severe	0	4 (1.41)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0141 (0.0004, 0.0278)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0440

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood creatine phosphokinase increased	17 (5.88)	25 (8.80)
Relative Risk (RR) (95% CI)		1.4965 (0.8262, 2.7104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1835
Odds Ratio (OR) (95% CI)		1.5444 (0.8150, 2.9266)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1826
Risk Difference (RD) (95% CI)		0.0292 (-0.0135, 0.0719)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1799
Grade 1/Mild	10 (3.46)	16 (5.63)
Relative Risk (RR) (95% CI)		1.6282 (0.7517, 3.5268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2164
Odds Ratio (OR) (95% CI)		1.6657 (0.7427, 3.7356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2157

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0217 (-0.0124, 0.0558)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2116

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	6 (2.08)	8 (2.82)
Relative Risk (RR) (95% CI)		1.3568 (0.4768, 3.8609)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5674
Odds Ratio (OR) (95% CI)		1.3671 (0.4683, 3.9914)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5673
Risk Difference (RD) (95% CI)		0.0074 (-0.0179, 0.0327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5662
Grade 3/Severe	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Aspartate aminotransferase increased	18 (6.23)	21 (7.39)
Relative Risk (RR) (95% CI)		1.1872 (0.6464, 2.1804)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5801
Odds Ratio (OR) (95% CI)		1.2022 (0.6263, 2.3074)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5800
Risk Difference (RD) (95% CI)		0.0117 (-0.0296, 0.0529)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5797
Grade 1/Mild	10 (3.46)	11 (3.87)
Relative Risk (RR) (95% CI)		1.1194 (0.4830, 2.5943)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7926
Odds Ratio (OR) (95% CI)		1.1242 (0.4698, 2.6900)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7926

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0041 (-0.0267, 0.0349)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7926

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	8 (2.77)	8 (2.82)
Relative Risk (RR) (95% CI)		1.0176 (0.3872, 2.6742)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9718
Odds Ratio (OR) (95% CI)		1.0181 (0.3768, 2.7509)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9718
Risk Difference (RD) (95% CI)		0.0005 (-0.0265, 0.0275)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9718
Grade 3/Severe	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Bacterial test positive	13 (4.50)	7 (2.46)
Relative Risk (RR) (95% CI)		0.5479 (0.2219, 1.3533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1922
Odds Ratio (OR) (95% CI)		0.5365 (0.2109, 1.3650)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1913
Risk Difference (RD) (95% CI)		-0.0203 (-0.0503, 0.0096)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1831
Grade 1/Mild	11 (3.81)	6 (2.11)
Relative Risk (RR) (95% CI)		0.5551 (0.2081, 1.4806)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2396
Odds Ratio (OR) (95% CI)		0.5455 (0.1990, 1.4954)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2388

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0169 (-0.0446, 0.0107)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2305

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood alkaline phosphatase increased	6 (2.08)	7 (2.46)
Relative Risk (RR) (95% CI)		1.1872 (0.4040, 3.4892)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7551
Odds Ratio (OR) (95% CI)		1.1919 (0.3956, 3.5913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7550
Risk Difference (RD) (95% CI)		0.0039 (-0.0205, 0.0283)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7549
Grade 1/Mild	2 (0.69)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0165, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1559

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	7 (2.46)
Relative Risk (RR) (95% CI)		3.5616 (0.7462, 16.9985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1112
Odds Ratio (OR) (95% CI)		3.6264 (0.7469, 17.6078)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1101
Risk Difference (RD) (95% CI)		0.0177 (-0.0027, 0.0381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0887
Grade 3/Severe	2 (0.69)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0165, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1559

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood glucose increased	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467
Grade 1/Mild	4 (1.38)	4 (1.41)
Relative Risk (RR) (95% CI)		1.0176 (0.2570, 4.0295)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9802
Odds Ratio (OR) (95% CI)		1.0179 (0.2521, 4.1098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9802

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0002 (-0.0190, 0.0195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9802

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	3 (1.06)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0106 (-0.0013, 0.0225)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0816
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gamma-glutamyltransferase increased	8 (2.77)	6 (2.11)
Relative Risk (RR) (95% CI)		0.7632 (0.2682, 2.1717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6125
Odds Ratio (OR) (95% CI)		0.7581 (0.2597, 2.2132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6124
Risk Difference (RD) (95% CI)		-0.0066 (-0.0318, 0.0187)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6109
Grade 1/Mild	4 (1.38)	2 (0.70)
Relative Risk (RR) (95% CI)		0.5088 (0.0939, 2.7560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4331
Odds Ratio (OR) (95% CI)		0.5053 (0.0918, 2.7809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4328

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0068 (-0.0234, 0.0098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4225

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	2 (0.70)
Relative Risk (RR) (95% CI)		0.6784 (0.1142, 4.0296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6695
Odds Ratio (OR) (95% CI)		0.6761 (0.1121, 4.0770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6694
Risk Difference (RD) (95% CI)		-0.0033 (-0.0185, 0.0119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6669
Grade 3/Severe	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
SARS-CoV-2 test positive	8 (2.77)	6 (2.11)
Relative Risk (RR) (95% CI)		0.7632 (0.2682, 2.1717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6125
Odds Ratio (OR) (95% CI)		0.7581 (0.2597, 2.2132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6124
Risk Difference (RD) (95% CI)		-0.0066 (-0.0318, 0.0187)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6109
Grade 1/Mild	7 (2.42)	6 (2.11)
Relative Risk (RR) (95% CI)		0.8722 (0.2968, 2.5635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8037
Odds Ratio (OR) (95% CI)		0.8695 (0.2886, 2.6197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8037

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0031 (-0.0275, 0.0213)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8034

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Weight decreased	5 (1.73)	6 (2.11)
Relative Risk (RR) (95% CI)		1.2211 (0.3769, 3.9560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7391
Odds Ratio (OR) (95% CI)		1.2259 (0.3699, 4.0631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7390
Risk Difference (RD) (95% CI)		0.0038 (-0.0187, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7388
Grade 1/Mild	4 (1.38)	4 (1.41)
Relative Risk (RR) (95% CI)		1.0176 (0.2570, 4.0295)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9802
Odds Ratio (OR) (95% CI)		1.0179 (0.2521, 4.1098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9802

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0002 (-0.0190, 0.0195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9802

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood bilirubin increased	10 (3.46)	5 (1.76)
Relative Risk (RR) (95% CI)		0.5088 (0.1761, 1.4700)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2119
Odds Ratio (OR) (95% CI)		0.5000 (0.1687, 1.4816)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2111
Risk Difference (RD) (95% CI)		-0.0170 (-0.0430, 0.0090)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2008
Grade 1/Mild	5 (1.73)	2 (0.70)
Relative Risk (RR) (95% CI)		0.4070 (0.0796, 2.0809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2803
Odds Ratio (OR) (95% CI)		0.4028 (0.0775, 2.0935)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2796

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0103 (-0.0282, 0.0076)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2614

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	4 (1.38)	1 (0.35)
Relative Risk (RR) (95% CI)		0.2544 (0.0286, 2.2622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2195
Odds Ratio (OR) (95% CI)		0.2518 (0.0280, 2.2665)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2186
Risk Difference (RD) (95% CI)		-0.0103 (-0.0254, 0.0048)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1813
Grade 3/Severe	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607

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Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535

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(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
General disorders and administration site conditions	72 (24.91)	86 (30.28)
Relative Risk (RR) (95% CI)		1.2155 (0.9308, 1.5872)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1518
Odds Ratio (OR) (95% CI)		1.3091 (0.9064, 1.8906)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1510
Risk Difference (RD) (95% CI)		0.0537 (-0.0194, 0.1268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1500
Grade 1/Mild	54 (18.69)	59 (20.77)
Relative Risk (RR) (95% CI)		1.1118 (0.7987, 1.5478)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5300
Odds Ratio (OR) (95% CI)		1.1412 (0.7559, 1.7228)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5298

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0209 (-0.0443, 0.0861)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5297

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	18 (6.23)	25 (8.80)
Relative Risk (RR) (95% CI)		1.4133 (0.7887, 2.5327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2451
Odds Ratio (OR) (95% CI)		1.4532 (0.7745, 2.7268)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2444
Risk Difference (RD) (95% CI)		0.0257 (-0.0174, 0.0689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2423
Grade 3/Severe	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Fatigue	30 (10.38)	33 (11.62)
Relative Risk (RR) (95% CI)		1.1194 (0.7020, 1.7848)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6357
Odds Ratio (OR) (95% CI)		1.1351 (0.6721, 1.9169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6356
Risk Difference (RD) (95% CI)		0.0124 (-0.0389, 0.0636)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6355
Grade 1/Mild	26 (9.00)	26 (9.15)
Relative Risk (RR) (95% CI)		1.0176 (0.6060, 1.7088)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9474
Odds Ratio (OR) (95% CI)		1.0194 (0.5764, 1.8027)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9474

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0016 (-0.0455, 0.0486)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9474

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	4 (1.38)	6 (2.11)
Relative Risk (RR) (95% CI)		1.5264 (0.4354, 5.3518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5088
Odds Ratio (OR) (95% CI)		1.5378 (0.4293, 5.5081)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5086
Risk Difference (RD) (95% CI)		0.0073 (-0.0142, 0.0288)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5061
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pyrexia	29 (10.03)	28 (9.86)
Relative Risk (RR) (95% CI)		0.9825 (0.6002, 1.6083)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9441
Odds Ratio (OR) (95% CI)		0.9806 (0.5673, 1.6949)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9441
Risk Difference (RD) (95% CI)		-0.0018 (-0.0508, 0.0473)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9441
Grade 1/Mild	18 (6.23)	18 (6.34)
Relative Risk (RR) (95% CI)		1.0176 (0.5406, 1.9154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9569
Odds Ratio (OR) (95% CI)		1.0188 (0.5188, 2.0007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9569

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0011 (-0.0386, 0.0408)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9569

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	11 (3.81)	10 (3.52)
Relative Risk (RR) (95% CI)		0.9251 (0.3991, 2.1441)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8559
Odds Ratio (OR) (95% CI)		0.9224 (0.3855, 2.2070)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8559
Risk Difference (RD) (95% CI)		-0.0029 (-0.0336, 0.0279)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8558
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pain	3 (1.04)	10 (3.52)
Relative Risk (RR) (95% CI)		3.3920 (0.9433, 12.1971)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0614
Odds Ratio (OR) (95% CI)		3.4793 (0.9475, 12.7769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0603
Risk Difference (RD) (95% CI)		0.0248 (0.0004, 0.0492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0462
Grade 1/Mild	3 (1.04)	9 (3.17)
Relative Risk (RR) (95% CI)		3.0528 (0.8350, 11.1608)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0915
Odds Ratio (OR) (95% CI)		3.1200 (0.8359, 11.6455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0904

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0213 (-0.0022, 0.0448)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0754

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Influenza like illness	5 (1.73)	7 (2.46)
Relative Risk (RR) (95% CI)		1.4246 (0.4575, 4.4363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5414
Odds Ratio (OR) (95% CI)		1.4354 (0.4502, 4.5765)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5412
Risk Difference (RD) (95% CI)		0.0073 (-0.0161, 0.0308)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5396
Grade 1/Mild	3 (1.04)	1 (0.35)
Relative Risk (RR) (95% CI)		0.3392 (0.0355, 3.2416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3478
Odds Ratio (OR) (95% CI)		0.3369 (0.0348, 3.2578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3473

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0204, 0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3216

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	5 (1.76)
Relative Risk (RR) (95% CI)		2.5440 (0.4976, 13.0055)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2620
Odds Ratio (OR) (95% CI)		2.5717 (0.4948, 13.3651)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2613
Risk Difference (RD) (95% CI)		0.0107 (-0.0074, 0.0287)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2456
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Malaise	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467
Grade 1/Mild	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nervous system disorders	64 (22.15)	72 (25.35)
Relative Risk (RR) (95% CI)		1.1448 (0.8530, 1.5364)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3676
Odds Ratio (OR) (95% CI)		1.1940 (0.8121, 1.7555)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3673
Risk Difference (RD) (95% CI)		0.0321 (-0.0376, 0.1017)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3669
Grade 1/Mild	40 (13.84)	47 (16.55)
Relative Risk (RR) (95% CI)		1.1957 (0.8107, 1.7634)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3673
Odds Ratio (OR) (95% CI)		1.2345 (0.7812, 1.9509)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3669

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0271 (-0.0317, 0.0858)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3663

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	20 (6.92)	21 (7.39)
Relative Risk (RR) (95% CI)		1.0685 (0.5923, 1.9277)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8258
Odds Ratio (OR) (95% CI)		1.0740 (0.5688, 2.0276)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8258
Risk Difference (RD) (95% CI)		0.0047 (-0.0375, 0.0470)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8259
Grade 3/Severe	4 (1.38)	4 (1.41)
Relative Risk (RR) (95% CI)		1.0176 (0.2570, 4.0295)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9802
Odds Ratio (OR) (95% CI)		1.0179 (0.2521, 4.1098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9802

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0002 (-0.0190, 0.0195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9802

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Headache	41 (14.19)	51 (17.96)
Relative Risk (RR) (95% CI)		1.2658 (0.8682, 1.8456)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2205
Odds Ratio (OR) (95% CI)		1.3240 (0.8456, 2.0729)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2199
Risk Difference (RD) (95% CI)		0.0377 (-0.0224, 0.0978)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2187
Grade 1/Mild	27 (9.34)	37 (13.03)
Relative Risk (RR) (95% CI)		1.3945 (0.8731, 2.2273)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1640
Odds Ratio (OR) (95% CI)		1.4536 (0.8593, 2.4588)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1631

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0369 (-0.0147, 0.0884)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1612

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	12 (4.15)	14 (4.93)
Relative Risk (RR) (95% CI)		1.1872 (0.5589, 2.5220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6553
Odds Ratio (OR) (95% CI)		1.1969 (0.5437, 2.6348)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6553
Risk Difference (RD) (95% CI)		0.0078 (-0.0263, 0.0419)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6550
Grade 3/Severe	2 (0.69)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0069 (-0.0165, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1559

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Dizziness	13 (4.50)	9 (3.17)
Relative Risk (RR) (95% CI)		0.7045 (0.3060, 1.6221)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4104
Odds Ratio (OR) (95% CI)		0.6948 (0.2922, 1.6521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4100
Risk Difference (RD) (95% CI)		-0.0133 (-0.0447, 0.0181)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4067
Grade 1/Mild	9 (3.11)	8 (2.82)
Relative Risk (RR) (95% CI)		0.9045 (0.3540, 2.3114)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8340
Odds Ratio (OR) (95% CI)		0.9018 (0.3430, 2.3712)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8340

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0030 (-0.0307, 0.0248)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8338

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	4 (1.38)	1 (0.35)
Relative Risk (RR) (95% CI)		0.2544 (0.0286, 2.2622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2195
Odds Ratio (OR) (95% CI)		0.2518 (0.0280, 2.2665)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2186
Risk Difference (RD) (95% CI)		-0.0103 (-0.0254, 0.0048)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1813
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Migraine	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778
Grade 1/Mild	2 (0.69)	2 (0.70)
Relative Risk (RR) (95% CI)		1.0176 (0.1443, 7.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9860
Odds Ratio (OR) (95% CI)		1.0177 (0.1424, 7.2748)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9860

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0135, 0.0138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9860

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	1 (0.35)
Relative Risk (RR) (95% CI)		0.3392 (0.0355, 3.2416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3478
Odds Ratio (OR) (95% CI)		0.3369 (0.0348, 3.2578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3473
Risk Difference (RD) (95% CI)		-0.0069 (-0.0204, 0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3216
Grade 3/Severe	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Skin and subcutaneous tissue disorders	52 (17.99)	68 (23.94)
Relative Risk (RR) (95% CI)		1.3307 (0.9646, 1.8358)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0818
Odds Ratio (OR) (95% CI)		1.4348 (0.9566, 2.1521)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0809
Risk Difference (RD) (95% CI)		0.0595 (-0.0070, 0.1260)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0795
Grade 1/Mild	38 (13.15)	45 (15.85)
Relative Risk (RR) (95% CI)		1.2051 (0.8081, 1.7969)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3602
Odds Ratio (OR) (95% CI)		1.2437 (0.7798, 1.9834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3598

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0270 (-0.0307, 0.0846)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3592

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	14 (4.84)	22 (7.75)
Relative Risk (RR) (95% CI)		1.5991 (0.8350, 3.0624)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1568
Odds Ratio (OR) (95% CI)		1.6494 (0.8264, 3.2921)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1559
Risk Difference (RD) (95% CI)		0.0290 (-0.0107, 0.0688)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1523
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Rash	13 (4.50)	25 (8.80)
Relative Risk (RR) (95% CI)		1.9569 (1.0217, 3.7481)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0429
Odds Ratio (OR) (95% CI)		2.0493 (1.0265, 4.0911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0419
Risk Difference (RD) (95% CI)		0.0430 (0.0023, 0.0838)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0382
Grade 1/Mild	5 (1.73)	17 (5.99)
Relative Risk (RR) (95% CI)		3.4599 (1.2939, 9.2518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0134
Odds Ratio (OR) (95% CI)		3.6165 (1.3158, 9.9396)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0127

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0426 (0.0111, 0.0740)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0079

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	8 (2.77)	7 (2.46)
Relative Risk (RR) (95% CI)		0.8904 (0.3272, 2.4230)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8202
Odds Ratio (OR) (95% CI)		0.8876 (0.3176, 2.4810)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8202
Risk Difference (RD) (95% CI)		-0.0030 (-0.0292, 0.0231)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8200
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Acne	12 (4.15)	11 (3.87)
Relative Risk (RR) (95% CI)		0.9328 (0.4185, 2.0793)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8649
Odds Ratio (OR) (95% CI)		0.9301 (0.4035, 2.1438)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8649
Risk Difference (RD) (95% CI)		-0.0028 (-0.0349, 0.0293)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8649
Grade 1/Mild	12 (4.15)	8 (2.82)
Relative Risk (RR) (95% CI)		0.6784 (0.2815, 1.6347)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3872
Odds Ratio (OR) (95% CI)		0.6691 (0.2693, 1.6622)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3868

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0134 (-0.0433, 0.0166)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3828

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	3 (1.06)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0106 (-0.0013, 0.0225)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0816
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pruritus	6 (2.08)	9 (3.17)
Relative Risk (RR) (95% CI)		1.5264 (0.5505, 4.2327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4164
Odds Ratio (OR) (95% CI)		1.5436 (0.5422, 4.3946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4160
Risk Difference (RD) (95% CI)		0.0109 (-0.0152, 0.0371)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4132
Grade 1/Mild	4 (1.38)	6 (2.11)
Relative Risk (RR) (95% CI)		1.5264 (0.4354, 5.3518)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5088
Odds Ratio (OR) (95% CI)		1.5378 (0.4293, 5.5081)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5086

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0073 (-0.0142, 0.0288)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5061

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	3 (1.06)
Relative Risk (RR) (95% CI)		1.5264 (0.2570, 9.0666)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6418
Odds Ratio (OR) (95% CI)		1.5320 (0.2541, 9.2381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6417
Risk Difference (RD) (95% CI)		0.0036 (-0.0116, 0.0189)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6398
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Alopecia	6 (2.08)	5 (1.76)
Relative Risk (RR) (95% CI)		0.8480 (0.2618, 2.7472)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7834
Odds Ratio (OR) (95% CI)		0.8453 (0.2550, 2.8016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7834
Risk Difference (RD) (95% CI)		-0.0032 (-0.0256, 0.0193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7830
Grade 1/Mild	6 (2.08)	3 (1.06)
Relative Risk (RR) (95% CI)		0.5088 (0.1285, 2.0148)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3359
Odds Ratio (OR) (95% CI)		0.5036 (0.1247, 2.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3353

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0102 (-0.0305, 0.0101)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3245

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Musculoskeletal and connective tissue disorders	71 (24.57)	55 (19.37)
Relative Risk (RR) (95% CI)		0.7883 (0.5772, 1.0766)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1346
Odds Ratio (OR) (95% CI)		0.7374 (0.4953, 1.0978)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1336
Risk Difference (RD) (95% CI)		-0.0520 (-0.1197, 0.0156)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1318
Grade 1/Mild	42 (14.53)	36 (12.68)
Relative Risk (RR) (95% CI)		0.8722 (0.5766, 1.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5175
Odds Ratio (OR) (95% CI)		0.8537 (0.5289, 1.3779)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5172

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0186 (-0.0747, 0.0375)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5166

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	29 (10.03)	18 (6.34)
Relative Risk (RR) (95% CI)		0.6316 (0.3590, 1.1111)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1109
Odds Ratio (OR) (95% CI)		0.6067 (0.3288, 1.1193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1098
Risk Difference (RD) (95% CI)		-0.0370 (-0.0817, 0.0078)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1055
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Back pain	15 (5.19)	16 (5.63)
Relative Risk (RR) (95% CI)		1.0854 (0.5471, 2.1535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8145
Odds Ratio (OR) (95% CI)		1.0905 (0.5286, 2.2500)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8145
Risk Difference (RD) (95% CI)		0.0044 (-0.0326, 0.0415)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8145
Grade 1/Mild	9 (3.11)	10 (3.52)
Relative Risk (RR) (95% CI)		1.1307 (0.4664, 2.7410)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7858
Odds Ratio (OR) (95% CI)		1.1354 (0.4544, 2.8373)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7857

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0041 (-0.0253, 0.0334)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7857

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	6 (2.08)	6 (2.11)
Relative Risk (RR) (95% CI)		1.0176 (0.3321, 3.1178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9756
Odds Ratio (OR) (95% CI)		1.0180 (0.3244, 3.1946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9756
Risk Difference (RD) (95% CI)		0.0004 (-0.0231, 0.0238)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9756
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Arthralgia	25 (8.65)	14 (4.93)
Relative Risk (RR) (95% CI)		0.5699 (0.3025, 1.0736)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0818
Odds Ratio (OR) (95% CI)		0.5476 (0.2785, 1.0764)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0807
Risk Difference (RD) (95% CI)		-0.0372 (-0.0782, 0.0038)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0756
Grade 1/Mild	18 (6.23)	10 (3.52)
Relative Risk (RR) (95% CI)		0.5653 (0.2656, 1.2034)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1390
Odds Ratio (OR) (95% CI)		0.5495 (0.2491, 1.2120)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1379

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0271 (-0.0622, 0.0081)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1312

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	7 (2.42)	3 (1.06)
Relative Risk (RR) (95% CI)		0.4361 (0.1139, 1.6698)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2257
Odds Ratio (OR) (95% CI)		0.4301 (0.1101, 1.6800)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2249
Risk Difference (RD) (95% CI)		-0.0137 (-0.0350, 0.0077)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2098
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Myalgia	7 (2.42)	10 (3.52)
Relative Risk (RR) (95% CI)		1.4537 (0.5611, 3.7660)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4411
Odds Ratio (OR) (95% CI)		1.4703 (0.5518, 3.9178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4408
Risk Difference (RD) (95% CI)		0.0110 (-0.0168, 0.0388)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4387
Grade 1/Mild	6 (2.08)	9 (3.17)
Relative Risk (RR) (95% CI)		1.5264 (0.5505, 4.2327)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4164
Odds Ratio (OR) (95% CI)		1.5436 (0.5422, 4.3946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4160

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0109 (-0.0152, 0.0371)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4132

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pain in extremity	7 (2.42)	6 (2.11)
Relative Risk (RR) (95% CI)		0.8722 (0.2968, 2.5635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8037
Odds Ratio (OR) (95% CI)		0.8695 (0.2886, 2.6197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8037
Risk Difference (RD) (95% CI)		-0.0031 (-0.0275, 0.0213)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8034
Grade 1/Mild	4 (1.38)	5 (1.76)
Relative Risk (RR) (95% CI)		1.2720 (0.3451, 4.6886)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7177
Odds Ratio (OR) (95% CI)		1.2769 (0.3394, 4.8044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7177

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0038 (-0.0166, 0.0241)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7173

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	1 (0.35)
Relative Risk (RR) (95% CI)		0.3392 (0.0355, 3.2416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3478
Odds Ratio (OR) (95% CI)		0.3369 (0.0348, 3.2578)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3473
Risk Difference (RD) (95% CI)		-0.0069 (-0.0204, 0.0067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3216
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Musculoskeletal chest pain	7 (2.42)	4 (1.41)
Relative Risk (RR) (95% CI)		0.5815 (0.1721, 1.9647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3828
Odds Ratio (OR) (95% CI)		0.5755 (0.1666, 1.9878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3823
Risk Difference (RD) (95% CI)		-0.0101 (-0.0325, 0.0123)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3752
Grade 1/Mild	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Injury, poisoning and procedural complications	53 (18.34)	46 (16.20)
Relative Risk (RR) (95% CI)		0.8832 (0.6166, 1.2652)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4982
Odds Ratio (OR) (95% CI)		0.8606 (0.5576, 1.3284)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4980
Risk Difference (RD) (95% CI)		-0.0214 (-0.0833, 0.0404)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4974
Grade 1/Mild	31 (10.73)	27 (9.51)
Relative Risk (RR) (95% CI)		0.8863 (0.5434, 1.4457)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6287
Odds Ratio (OR) (95% CI)		0.8744 (0.5075, 1.5065)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6286

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0122 (-0.0616, 0.0372)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6282

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	20 (6.92)	18 (6.34)
Relative Risk (RR) (95% CI)		0.9158 (0.4950, 1.6946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7795
Odds Ratio (OR) (95% CI)		0.9102 (0.4709, 1.7591)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7795
Risk Difference (RD) (95% CI)		-0.0058 (-0.0466, 0.0349)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7793
Grade 3/Severe	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Psychiatric disorders	36 (12.46)	41 (14.44)
Relative Risk (RR) (95% CI)		1.1589 (0.7640, 1.7579)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4877
Odds Ratio (OR) (95% CI)		1.1858 (0.7330, 1.9183)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4875
Risk Difference (RD) (95% CI)		0.0198 (-0.0361, 0.0757)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4873
Grade 1/Mild	17 (5.88)	23 (8.10)
Relative Risk (RR) (95% CI)		1.3768 (0.7517, 2.5215)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3004
Odds Ratio (OR) (95% CI)		1.4100 (0.7364, 2.6994)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2998

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0222 (-0.0196, 0.0639)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2981

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	17 (5.88)	16 (5.63)
Relative Risk (RR) (95% CI)		0.9577 (0.4937, 1.8581)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8984
Odds Ratio (OR) (95% CI)		0.9552 (0.4728, 1.9298)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8984
Risk Difference (RD) (95% CI)		-0.0025 (-0.0406, 0.0357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8984
Grade 3/Severe	2 (0.69)	2 (0.70)
Relative Risk (RR) (95% CI)		1.0176 (0.1443, 7.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9860
Odds Ratio (OR) (95% CI)		1.0177 (0.1424, 7.2748)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9860

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0135, 0.0138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9860

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Anxiety	6 (2.08)	16 (5.63)
Relative Risk (RR) (95% CI)		2.7136 (1.0773, 6.8356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0342
Odds Ratio (OR) (95% CI)		2.8159 (1.0858, 7.3032)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0332
Risk Difference (RD) (95% CI)		0.0356 (0.0041, 0.0670)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0266
Grade 1/Mild	3 (1.04)	9 (3.17)
Relative Risk (RR) (95% CI)		3.0528 (0.8350, 11.1608)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0915
Odds Ratio (OR) (95% CI)		3.1200 (0.8359, 11.6455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0904

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0213 (-0.0022, 0.0448)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0754

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	6 (2.11)
Relative Risk (RR) (95% CI)		2.0352 (0.5140, 8.0590)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3115
Odds Ratio (OR) (95% CI)		2.0576 (0.5096, 8.3080)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3110
Risk Difference (RD) (95% CI)		0.0107 (-0.0097, 0.0311)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3019
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Insomnia	14 (4.84)	11 (3.87)
Relative Risk (RR) (95% CI)		0.7995 (0.3693, 1.7312)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5703
Odds Ratio (OR) (95% CI)		0.7915 (0.3531, 1.7743)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5702
Risk Difference (RD) (95% CI)		-0.0097 (-0.0431, 0.0237)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5689
Grade 1/Mild	7 (2.42)	6 (2.11)
Relative Risk (RR) (95% CI)		0.8722 (0.2968, 2.5635)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8037
Odds Ratio (OR) (95% CI)		0.8695 (0.2886, 2.6197)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8037

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0031 (-0.0275, 0.0213)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8034

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	7 (2.42)	4 (1.41)
Relative Risk (RR) (95% CI)		0.5815 (0.1721, 1.9647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3828
Odds Ratio (OR) (95% CI)		0.5755 (0.1666, 1.9878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3823
Risk Difference (RD) (95% CI)		-0.0101 (-0.0325, 0.0123)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3752
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Depression	3 (1.04)	10 (3.52)
Relative Risk (RR) (95% CI)		3.3920 (0.9433, 12.1971)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0614
Odds Ratio (OR) (95% CI)		3.4793 (0.9475, 12.7769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0603
Risk Difference (RD) (95% CI)		0.0248 (0.0004, 0.0492)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0462
Grade 1/Mild	1 (0.35)	6 (2.11)
Relative Risk (RR) (95% CI)		6.1056 (0.7397, 50.3940)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0929
Odds Ratio (OR) (95% CI)		6.2158 (0.7436, 51.9617)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0917

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0177 (-0.0004, 0.0357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0550

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	2 (0.70)
Relative Risk (RR) (95% CI)		1.0176 (0.1443, 7.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9860
Odds Ratio (OR) (95% CI)		1.0177 (0.1424, 7.2748)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9860
Risk Difference (RD) (95% CI)		0.0001 (-0.0135, 0.0138)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9860
Grade 3/Severe	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Metabolism and nutrition disorders	25 (8.65)	25 (8.80)
Relative Risk (RR) (95% CI)		1.0176 (0.5992, 1.7282)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9485
Odds Ratio (OR) (95% CI)		1.0193 (0.5706, 1.8210)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9485
Risk Difference (RD) (95% CI)		0.0015 (-0.0447, 0.0477)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9485
Grade 1/Mild	18 (6.23)	18 (6.34)
Relative Risk (RR) (95% CI)		1.0176 (0.5406, 1.9154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9569
Odds Ratio (OR) (95% CI)		1.0188 (0.5188, 2.0007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9569

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0011 (-0.0386, 0.0408)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9569

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	6 (2.08)	7 (2.46)
Relative Risk (RR) (95% CI)		1.1872 (0.4040, 3.4892)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7551
Odds Ratio (OR) (95% CI)		1.1919 (0.3956, 3.5913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7550
Risk Difference (RD) (95% CI)		0.0039 (-0.0205, 0.0283)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7549
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Decreased appetite	8 (2.77)	3 (1.06)
Relative Risk (RR) (95% CI)		0.3816 (0.1023, 1.4239)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1516
Odds Ratio (OR) (95% CI)		0.3750 (0.0985, 1.4281)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1505
Risk Difference (RD) (95% CI)		-0.0171 (-0.0395, 0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1332
Grade 1/Mild	8 (2.77)	3 (1.06)
Relative Risk (RR) (95% CI)		0.3816 (0.1023, 1.4239)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1516
Odds Ratio (OR) (95% CI)		0.3750 (0.0985, 1.4281)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1505

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0171 (-0.0395, 0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1332

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Eye disorders	18 (6.23)	17 (5.99)
Relative Risk (RR) (95% CI)		0.9611 (0.5056, 1.8269)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9036
Odds Ratio (OR) (95% CI)		0.9586 (0.4837, 1.8999)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9036
Risk Difference (RD) (95% CI)		-0.0024 (-0.0416, 0.0368)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9035
Grade 1/Mild	15 (5.19)	12 (4.23)
Relative Risk (RR) (95% CI)		0.8141 (0.3879, 1.7083)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5865
Odds Ratio (OR) (95% CI)		0.8059 (0.3704, 1.7535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5864

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0096 (-0.0443, 0.0250)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5853

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	5 (1.76)
Relative Risk (RR) (95% CI)		1.6960 (0.4091, 7.0303)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4665
Odds Ratio (OR) (95% CI)		1.7085 (0.4045, 7.2169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4663
Risk Difference (RD) (95% CI)		0.0072 (-0.0120, 0.0265)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4619
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Renal and urinary disorders	15 (5.19)	10 (3.52)
Relative Risk (RR) (95% CI)		0.6784 (0.3100, 1.4847)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3316
Odds Ratio (OR) (95% CI)		0.6667 (0.2944, 1.5099)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3310
Risk Difference (RD) (95% CI)		-0.0167 (-0.0501, 0.0167)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3269
Grade 1/Mild	7 (2.42)	5 (1.76)
Relative Risk (RR) (95% CI)		0.7269 (0.2334, 2.2634)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5820
Odds Ratio (OR) (95% CI)		0.7220 (0.2264, 2.3019)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5819

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0066 (-0.0300, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5797

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	7 (2.42)	4 (1.41)
Relative Risk (RR) (95% CI)		0.5815 (0.1721, 1.9647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3828
Odds Ratio (OR) (95% CI)		0.5755 (0.1666, 1.9878)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3823
Risk Difference (RD) (95% CI)		-0.0101 (-0.0325, 0.0123)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3752
Grade 3/Severe	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nephrolithiasis	6 (2.08)	4 (1.41)
Relative Risk (RR) (95% CI)		0.6784 (0.1935, 2.3786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5444
Odds Ratio (OR) (95% CI)		0.6738 (0.1881, 2.4135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5442
Risk Difference (RD) (95% CI)		-0.0067 (-0.0281, 0.0147)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5409
Grade 1/Mild	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	2 (0.70)
Relative Risk (RR) (95% CI)		0.6784 (0.1142, 4.0296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6695
Odds Ratio (OR) (95% CI)		0.6761 (0.1121, 4.0770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6694
Risk Difference (RD) (95% CI)		-0.0033 (-0.0185, 0.0119)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6669
Grade 3/Severe	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Reproductive system and breast disorders	19 (6.57)	10 (3.52)
Relative Risk (RR) (95% CI)		0.5356 (0.2535, 1.1316)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1018
Odds Ratio (OR) (95% CI)		0.5186 (0.2368, 1.1359)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1007
Risk Difference (RD) (95% CI)		-0.0305 (-0.0663, 0.0052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0939
Grade 1/Mild	10 (3.46)	4 (1.41)
Relative Risk (RR) (95% CI)		0.4070 (0.1292, 1.2828)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1249
Odds Ratio (OR) (95% CI)		0.3986 (0.1235, 1.2859)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1238

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0205 (-0.0457, 0.0046)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1096

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	8 (2.77)	6 (2.11)
Relative Risk (RR) (95% CI)		0.7632 (0.2682, 2.1717)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6125
Odds Ratio (OR) (95% CI)		0.7581 (0.2597, 2.2132)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6124
Risk Difference (RD) (95% CI)		-0.0066 (-0.0318, 0.0187)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6109
Grade 3/Severe	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Ear and labyrinth disorders	11 (3.81)	9 (3.17)
Relative Risk (RR) (95% CI)		0.8326 (0.3504, 1.9786)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6782
Odds Ratio (OR) (95% CI)		0.8271 (0.3374, 2.0274)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6782
Risk Difference (RD) (95% CI)		-0.0064 (-0.0364, 0.0237)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6775
Grade 1/Mild	10 (3.46)	9 (3.17)
Relative Risk (RR) (95% CI)		0.9158 (0.3778, 2.2202)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8457
Odds Ratio (OR) (95% CI)		0.9131 (0.3654, 2.2816)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8457

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0029 (-0.0322, 0.0264)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8456

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Congenital, familial and genetic disorders	5 (1.73)	8 (2.82)
Relative Risk (RR) (95% CI)		1.6282 (0.5391, 4.9172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3874
Odds Ratio (OR) (95% CI)		1.6464 (0.5321, 5.0944)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3870
Risk Difference (RD) (95% CI)		0.0109 (-0.0136, 0.0353)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3830
Grade 1/Mild	5 (1.73)	6 (2.11)
Relative Risk (RR) (95% CI)		1.2211 (0.3769, 3.9560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7391
Odds Ratio (OR) (95% CI)		1.2259 (0.3699, 4.0631)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7390

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0038 (-0.0187, 0.0263)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7388

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- A subject with multiple events within a category is counted only once with the maximum severity in that category.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Immune system disorders	8 (2.77)	8 (2.82)
Relative Risk (RR) (95% CI)		1.0176 (0.3872, 2.6742)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9718
Odds Ratio (OR) (95% CI)		1.0181 (0.3768, 2.7509)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9718
Risk Difference (RD) (95% CI)		0.0005 (-0.0265, 0.0275)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9718
Grade 1/Mild	6 (2.08)	6 (2.11)
Relative Risk (RR) (95% CI)		1.0176 (0.3321, 3.1178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9756
Odds Ratio (OR) (95% CI)		1.0180 (0.3244, 3.1946)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9756

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0004 (-0.0231, 0.0238)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9756

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	2 (0.69)	1 (0.35)
Relative Risk (RR) (95% CI)		0.5088 (0.0464, 5.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5803
Odds Ratio (OR) (95% CI)		0.5071 (0.0457, 5.6235)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5801
Risk Difference (RD) (95% CI)		-0.0034 (-0.0152, 0.0084)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5717
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Seasonal allergy	6 (2.08)	7 (2.46)
Relative Risk (RR) (95% CI)		1.1872 (0.4040, 3.4892)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7551
Odds Ratio (OR) (95% CI)		1.1919 (0.3956, 3.5913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7550
Risk Difference (RD) (95% CI)		0.0039 (-0.0205, 0.0283)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7549
Grade 1/Mild	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901
Grade 3/Severe	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Cardiac disorders	4 (1.38)	7 (2.46)
Relative Risk (RR) (95% CI)		1.7808 (0.5271, 6.0169)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3529
Odds Ratio (OR) (95% CI)		1.8005 (0.5213, 6.2192)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3524
Risk Difference (RD) (95% CI)		0.0108 (-0.0117, 0.0333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3467
Grade 1/Mild	4 (1.38)	5 (1.76)
Relative Risk (RR) (95% CI)		1.2720 (0.3451, 4.6886)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7177
Odds Ratio (OR) (95% CI)		1.2769 (0.3394, 4.8044)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7177

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0038 (-0.0166, 0.0241)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7173

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Vascular disorders	9 (3.11)	5 (1.76)
Relative Risk (RR) (95% CI)		0.5653 (0.1918, 1.6662)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3010
Odds Ratio (OR) (95% CI)		0.5575 (0.1845, 1.6846)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3004
Risk Difference (RD) (95% CI)		-0.0135 (-0.0387, 0.0117)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2924
Grade 1/Mild	6 (2.08)	5 (1.76)
Relative Risk (RR) (95% CI)		0.8480 (0.2618, 2.7472)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7834
Odds Ratio (OR) (95% CI)		0.8453 (0.2550, 2.8016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7834

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0032 (-0.0256, 0.0193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7830

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Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	3 (1.04)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0104 (-0.0221, 0.0013)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0817
Grade 3/Severe	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

- MedDRA version 26.1.
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- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Hepatobiliary disorders	9 (3.11)	4 (1.41)
Relative Risk (RR) (95% CI)		0.4523 (0.1409, 1.4519)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1824
Odds Ratio (OR) (95% CI)		0.4444 (0.1353, 1.4600)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1814
Risk Difference (RD) (95% CI)		-0.0171 (-0.0413, 0.0072)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1683
Grade 1/Mild	4 (1.38)	2 (0.70)
Relative Risk (RR) (95% CI)		0.5088 (0.0939, 2.7560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4331
Odds Ratio (OR) (95% CI)		0.5053 (0.0918, 2.7809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4328

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0068 (-0.0234, 0.0098)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4225

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 2/Moderate	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535
Grade 3/Severe	4 (1.38)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0138 (-0.0273, -0.0004)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0440

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Grade 4/Life Threatening	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-
Grade 5/Death	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.1.1
Study VX20-121-103: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any Grade 3/4/5 TEAEs	29 (10.03)	24 (8.45)
Relative Risk (RR) (95% CI)		0.8422 (0.5030, 1.4101)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5136
Odds Ratio (OR) (95% CI)		0.8276 (0.4692, 1.4598)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5134
Risk Difference (RD) (95% CI)		-0.0158 (-0.0632, 0.0316)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5125
Infections and infestations	6 (2.08)	5 (1.76)
Relative Risk (RR) (95% CI)		0.8480 (0.2618, 2.7472)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7834
Odds Ratio (OR) (95% CI)		0.8453 (0.2550, 2.8016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7834

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- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0032 (-0.0256, 0.0193)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7830

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Investigations	5 (1.73)	5 (1.76)
Relative Risk (RR) (95% CI)		1.0176 (0.2978, 3.4770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9778
Odds Ratio (OR) (95% CI)		1.0179 (0.2915, 3.5549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9778
Risk Difference (RD) (95% CI)		0.0003 (-0.0211, 0.0218)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9778

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.3
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any serious TEAEs	33 (11.42)	23 (8.10)
Relative Risk (RR) (95% CI)		0.7092 (0.4274, 1.1770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1838
Odds Ratio (OR) (95% CI)		0.6836 (0.3906, 1.1963)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1828
Risk Difference (RD) (95% CI)		-0.0332 (-0.0817, 0.0153)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1796
Infections and infestations	12 (4.15)	9 (3.17)
Relative Risk (RR) (95% CI)		0.7632 (0.3267, 1.7831)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5325
Odds Ratio (OR) (95% CI)		0.7555 (0.3133, 1.8217)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5323

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.3
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		-0.0098 (-0.0406, 0.0209)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5305

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.3
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gastrointestinal disorders	7 (2.42)	3 (1.06)
Relative Risk (RR) (95% CI)		0.4361 (0.1139, 1.6698)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2257
Odds Ratio (OR) (95% CI)		0.4301 (0.1101, 1.6800)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2249
Risk Difference (RD) (95% CI)		-0.0137 (-0.0350, 0.0077)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2098

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any TEAEs leading to treatment discontinuation	9 (3.11)	14 (4.93)
Relative Risk (RR) (95% CI)		1.5829 (0.6963, 3.5985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2730
Odds Ratio (OR) (95% CI)		1.6132 (0.6868, 3.7890)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2724
Risk Difference (RD) (95% CI)		0.0182 (-0.0140, 0.0503)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2687
Investigations	3 (1.04)	7 (2.46)
Relative Risk (RR) (95% CI)		2.3744 (0.6201, 9.0912)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2068
Odds Ratio (OR) (95% CI)		2.4091 (0.6168, 9.4105)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2059

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Risk Difference (RD) (95% CI)		0.0143 (-0.0072, 0.0358)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1931

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Alanine aminotransferase increased	2 (0.69)	6 (2.11)
Relative Risk (RR) (95% CI)		3.0528 (0.6214, 14.9988)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1694
Odds Ratio (OR) (95% CI)		3.0971 (0.6198, 15.4754)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1684
Risk Difference (RD) (95% CI)		0.0142 (-0.0051, 0.0335)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1483
Aspartate aminotransferase increased	2 (0.69)	5 (1.76)
Relative Risk (RR) (95% CI)		2.5440 (0.4976, 13.0055)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2620
Odds Ratio (OR) (95% CI)		2.5717 (0.4948, 13.3651)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2613
Risk Difference (RD) (95% CI)		0.0107 (-0.0074, 0.0287)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2456

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood bilirubin increased	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558
Blood bilirubin unconjugated increased	0	2 (0.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0070 (-0.0027, 0.0168)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1558

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Blood alkaline phosphatase increased	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901
Blood creatine phosphokinase increased	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Gamma-glutamyltransferase increased	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901
Sputum abnormal	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

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- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Pulmonary function test decreased	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
General disorders and administration site conditions	1 (0.35)	3 (1.06)
Relative Risk (RR) (95% CI)		3.0528 (0.3194, 29.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3325
Odds Ratio (OR) (95% CI)		3.0747 (0.3179, 29.7357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3320
Risk Difference (RD) (95% CI)		0.0071 (-0.0066, 0.0208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3089

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

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- A subject with multiple events within a category is counted only once in that category.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Fatigue	1 (0.35)	3 (1.06)
Relative Risk (RR) (95% CI)		3.0528 (0.3194, 29.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3325
Odds Ratio (OR) (95% CI)		3.0747 (0.3179, 29.7357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3320
Risk Difference (RD) (95% CI)		0.0071 (-0.0066, 0.0208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3089
Respiratory, thoracic and mediastinal disorders	1 (0.35)	3 (1.06)
Relative Risk (RR) (95% CI)		3.0528 (0.3194, 29.1747)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3325
Odds Ratio (OR) (95% CI)		3.0747 (0.3179, 29.7357)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3320
Risk Difference (RD) (95% CI)		0.0071 (-0.0066, 0.0208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3089

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Cough	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535
Dysphonia	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Sputum discoloured	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Sputum increased	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Nervous system disorders	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535
Amnesia	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

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- A subject with multiple events within a category is counted only once in that category.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

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- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Lethargy	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Hyperresponsive to stimuli	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Psychiatric disorders	1 (0.35)	2 (0.70)
Relative Risk (RR) (95% CI)		2.0352 (0.1856, 22.3195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5609
Odds Ratio (OR) (95% CI)		2.0426 (0.1842, 22.6524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5607
Risk Difference (RD) (95% CI)		0.0036 (-0.0083, 0.0154)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5535
Agitation	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Anxiety	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Depression	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Insomnia	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Mental fatigue	1 (0.35)	1 (0.35)
Relative Risk (RR) (95% CI)		1.0176 (0.0640, 16.1904)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9901
Odds Ratio (OR) (95% CI)		1.0177 (0.0633, 16.3491)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9901
Risk Difference (RD) (95% CI)		0.0001 (-0.0096, 0.0097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9901

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Stress	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Reproductive system and breast disorders	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Heavy menstrual bleeding	0	1 (0.35)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0035 (-0.0034, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Gastrointestinal disorders	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Distal intestinal obstruction syndrome	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Hepatobiliary disorders	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Cholangitis	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165
Metabolism and nutrition disorders	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.4
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Malnutrition	1 (0.35)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0035 (-0.0102, 0.0033)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3165

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.11
Study VX20-121-103: Summary of Death
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.12
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events - Total and by Severity
Safety Set

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	88 (30.45)	76 (26.76)
Relative Risk (RR) (95% CI)		0.8788 (0.6779, 1.1393)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3295
Odds Ratio (OR) (95% CI)		0.8346 (0.5805, 1.1998)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3289
Risk Difference (RD) (95% CI)		-0.0369 (-0.1108, 0.0370)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3281
Subjects with non-severe events (Maximum Grade 1/2)	80 (27.68)	63 (22.18)
Relative Risk (RR) (95% CI)		0.8014 (0.6016, 1.0674)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1300
Odds Ratio (OR) (95% CI)		0.7447 (0.5091, 1.0895)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1290
Risk Difference (RD) (95% CI)		-0.0550 (-0.1257, 0.0157)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1273

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.1.12
Study VX20-121-103: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events - Total and by Severity
Safety Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with severe events (Maximum Grade 3/4/5)	8 (2.77)	13 (4.58)
Relative Risk (RR) (95% CI)		1.6536 (0.6960, 3.9288)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2546
Odds Ratio (OR) (95% CI)		1.6850 (0.6875, 4.1294)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2540
Risk Difference (RD) (95% CI)		0.0181 (-0.0127, 0.0489)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2496
Subjects with serious events	12 (4.15)	18 (6.34)
Relative Risk (RR) (95% CI)		1.5264 (0.7491, 3.1104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2442
Odds Ratio (OR) (95% CI)		1.5620 (0.7382, 3.3054)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2435
Risk Difference (RD) (95% CI)		0.0219 (-0.0146, 0.0584)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2405

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.2497
Age at screening (<18 years vs. ≥18 years)	0.9229
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.4758
Sex (Male vs. Female)	0.2889
Region (North America vs. Rest of the World)	0.1362

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Infections and infestations	
Influenza	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.1042
Age at screening (<18 years vs. ≥18 years)	0.3127
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0666
Sex (Male vs. Female)	0.9306
Region (North America vs. Rest of the World)	0.6355
Sinusitis	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.8788
Age at screening (<18 years vs. ≥18 years)	0.4140
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0240

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Sex (Male vs. Female)	0.9805
Region (North America vs. Rest of the World)	0.0923

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Skin and subcutaneous tissue disorders	
Rash	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.0419
Age at screening (<18 years vs. ≥18 years)	0.7391
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.0084
Sex (Male vs. Female)	0.9622
Region (North America vs. Rest of the World)	0.5578

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Psychiatric disorders	
Anxiety	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.8901
Age at screening (<18 years vs. ≥18 years)	0.0874
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.1645
Sex (Male vs. Female)	0.1645
Region (North America vs. Rest of the World)	0.1909

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs	
Prior CFTR modulator use (yes vs. no)	0.1602
Genotype group (F/F, F/G, F/RF vs. TCR/non-F)	0.6881*

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Infections and infestations	
Influenza	
Prior CFTR modulator use (yes vs. no)	0.9179
Genotype group (F/F, F/G, F/RF vs. TCR/non-F)	0.7002
Sinusitis	
Prior CFTR modulator use (yes vs. no)	0.0877
Genotype group (F/F, F/G, F/RF vs. TCR/non-F)	0.1155

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Skin and subcutaneous tissue disorders	
Rash	
Prior CFTR modulator use (yes vs. no)	0.9146
Genotype group (F/F, F/G, F/RF vs. TCR/non-F)	0.2381

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs by SOC and PT for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Psychiatric disorders	
Anxiety	
Prior CFTR modulator use (yes vs. no)	0.9944
Genotype group (F/F, F/G, F/RF vs. TCR/non-F)	0.3613

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline <70 %

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any TEAEs	160 (95.81)	149 (96.75)
Relative Risk (RR) (95% CI)		1.0099 (0.9674, 1.0542)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6542
Odds Ratio (OR) (95% CI)		1.3038 (0.4050, 4.1970)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6566
Risk Difference (RD) (95% CI)		0.0094 (-0.0319, 0.0508)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6540
Infections and infestations		
Influenza	5 (2.99)	17 (11.04)
Relative Risk (RR) (95% CI)		3.6870 (1.3938, 9.7533)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0086

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline <70 %

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Odds Ratio (OR) (95% CI)		4.0204 (1.4458, 11.1801)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0077
Risk Difference (RD) (95% CI)		0.0804 (0.0246, 0.1363)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0047
Sinusitis	16 (9.58)	5 (3.25)
Relative Risk (RR) (95% CI)		0.3389 (0.1272, 0.9029)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0305
Odds Ratio (OR) (95% CI)		0.3167 (0.1131, 0.8865)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0286
Risk Difference (RD) (95% CI)		-0.0633 (-0.1160, -0.0107)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0185

- MedDRA version 26.1.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Skin and subcutaneous tissue disorders		
Rash	11 (6.59)	12 (7.79)
Relative Risk (RR) (95% CI)		1.1830 (0.5378, 2.6022)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6761
Odds Ratio (OR) (95% CI)		1.1985 (0.5127, 2.8015)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6760
Risk Difference (RD) (95% CI)		0.0121 (-0.0446, 0.0687)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6766
Psychiatric disorders		
Anxiety	3 (1.80)	8 (5.19)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Relative Risk (RR) (95% CI)		2.8918 (0.7813, 10.7036)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1118
Odds Ratio (OR) (95% CI)		2.9954 (0.7800, 11.5029)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1100
Risk Difference (RD) (95% CI)		0.0340 (-0.0064, 0.0744)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0994

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline ≥70 %

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any TEAEs	108 (90.76)	120 (96.00)
Relative Risk (RR) (95% CI)		1.0578 (0.9886, 1.1317)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1034
Odds Ratio (OR) (95% CI)		2.4444 (0.8230, 7.2604)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1076
Risk Difference (RD) (95% CI)		0.0524 (-0.0099, 0.1148)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0993
Infections and infestations		
Influenza	11 (9.24)	16 (12.80)
Relative Risk (RR) (95% CI)		1.3847 (0.6703, 2.8604)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3792

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline ≥70 %

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Odds Ratio (OR) (95% CI)		1.4412 (0.6395, 3.2477)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3780
Risk Difference (RD) (95% CI)		0.0356 (-0.0428, 0.1139)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3736
Sinusitis	10 (8.40)	4 (3.20)
Relative Risk (RR) (95% CI)		0.3808 (0.1228, 1.1812)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0946
Odds Ratio (OR) (95% CI)		0.3603 (0.1098, 1.1821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0922
Risk Difference (RD) (95% CI)		-0.0520 (-0.1107, 0.0066)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0819

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Skin and subcutaneous tissue disorders		
Rash	2 (1.68)	12 (9.60)
Relative Risk (RR) (95% CI)		5.7120 (1.3058, 24.9861)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0206
Odds Ratio (OR) (95% CI)		6.2124 (1.3599, 28.3790)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0184
Risk Difference (RD) (95% CI)		0.0792 (0.0226, 0.1358)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0061
Psychiatric disorders		
Anxiety	3 (2.52)	8 (6.40)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Relative Risk (RR) (95% CI)		2.5387 (0.6898, 9.3426)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1611
Odds Ratio (OR) (95% CI)		2.6439 (0.6844, 10.2141)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1586
Risk Difference (RD) (95% CI)		0.0388 (-0.0125, 0.0901)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1385

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening <18 years

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any TEAEs	34 (89.47)	38 (92.68)
Relative Risk (RR) (95% CI)		1.0359 (0.9015, 1.1902)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6190
Odds Ratio (OR) (95% CI)		1.4902 (0.3110, 7.1401)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6178
Risk Difference (RD) (95% CI)		0.0321 (-0.0939, 0.1581)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6176
Infections and infestations		
Influenza	4 (10.53)	5 (12.20)
Relative Risk (RR) (95% CI)		1.1585 (0.3358, 3.9974)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8159

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening <18 years

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Odds Ratio (OR) (95% CI)		1.1806 (0.2923, 4.7675)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8157
Risk Difference (RD) (95% CI)		0.0167 (-0.1231, 0.1565)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8151
Sinusitis	1 (2.63)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0263 (-0.0772, 0.0246)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3109

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Skin and subcutaneous tissue disorders		
Rash	1 (2.63)	3 (7.32)
Relative Risk (RR) (95% CI)		2.7805 (0.3021, 25.5937)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3665
Odds Ratio (OR) (95% CI)		2.9211 (0.2905, 29.3691)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3627
Risk Difference (RD) (95% CI)		0.0469 (-0.0477, 0.1414)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3315
Psychiatric disorders		
Anxiety	1 (2.63)	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0263 (-0.0772, 0.0246)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3109

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening ≥18 years

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any TEAEs	237 (94.42)	236 (97.12)
Relative Risk (RR) (95% CI)		1.0286 (0.9911, 1.0674)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1363
Odds Ratio (OR) (95% CI)		1.9916 (0.7897, 5.0225)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1444
Risk Difference (RD) (95% CI)		0.0270 (-0.0084, 0.0623)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1346
Infections and infestations		
Influenza	12 (4.78)	28 (11.52)
Relative Risk (RR) (95% CI)		2.4102 (1.2546, 4.6299)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0083

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening ≥18 years

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Odds Ratio (OR) (95% CI)		2.5938 (1.2869, 5.2280)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0077
Risk Difference (RD) (95% CI)		0.0674 (0.0194, 0.1155)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0060
Sinusitis	25 (9.96)	9 (3.70)
Relative Risk (RR) (95% CI)		0.3719 (0.1772, 0.7803)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0089
Odds Ratio (OR) (95% CI)		0.3477 (0.1588, 0.7612)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0082
Risk Difference (RD) (95% CI)		-0.0626 (-0.1066, -0.0186)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0053

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Skin and subcutaneous tissue disorders		
Rash	12 (4.78)	22 (9.05)
Relative Risk (RR) (95% CI)		1.8937 (0.9585, 3.7413)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0661
Odds Ratio (OR) (95% CI)		1.9827 (0.9586, 4.1009)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0649
Risk Difference (RD) (95% CI)		0.0427 (-0.0020, 0.0874)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0610
Psychiatric disorders		
Anxiety	5 (1.99)	16 (6.58)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Relative Risk (RR) (95% CI)		3.3053 (1.2299, 8.8828)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0178
Odds Ratio (OR) (95% CI)		3.4678 (1.2502, 9.6195)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0169
Risk Difference (RD) (95% CI)		0.0459 (0.0103, 0.0816)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0116

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline <30 mmol/L

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any TEAEs	75 (93.75)	71 (98.61)
Relative Risk (RR) (95% CI)		1.0519 (0.9878, 1.1201)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1150
Odds Ratio (OR) (95% CI)		4.7333 (0.5397, 41.5149)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1605
Risk Difference (RD) (95% CI)		0.0486 (-0.0109, 0.1081)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1095
Infections and infestations		
Influenza	2 (2.50)	11 (15.28)
Relative Risk (RR) (95% CI)		6.1111 (1.4014, 26.6481)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0160

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline <30 mmol/L

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Odds Ratio (OR) (95% CI)		7.0328 (1.5025, 32.9178)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0132
Risk Difference (RD) (95% CI)		0.1278 (0.0379, 0.2176)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0053
Sinusitis	8 (10.00)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.1000 (-0.1657, -0.0343)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0029

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- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Psychiatric disorders		
Anxiety	1 (1.25)	7 (9.72)
Relative Risk (RR) (95% CI)		7.7778 (0.9805, 61.6966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0522
Odds Ratio (OR) (95% CI)		8.5077 (1.0203, 70.9383)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0479
Risk Difference (RD) (95% CI)		0.0847 (0.0121, 0.1574)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0222
Skin and subcutaneous tissue disorders		
Rash	7 (8.75)	3 (4.17)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Relative Risk (RR) (95% CI)		0.4762 (0.1279, 1.7728)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2686
Odds Ratio (OR) (95% CI)		0.4534 (0.1127, 1.8240)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2654
Risk Difference (RD) (95% CI)		-0.0458 (-0.1231, 0.0314)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2448

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline ≥30 mmol/L

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any TEAEs	189 (93.56)	201 (95.71)
Relative Risk (RR) (95% CI)		1.0230 (0.9769, 1.0713)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3343
Odds Ratio (OR) (95% CI)		1.5362 (0.6418, 3.6769)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3350
Risk Difference (RD) (95% CI)		0.0215 (-0.0220, 0.0650)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3331
Infections and infestations		
Influenza	13 (6.44)	21 (10.00)
Relative Risk (RR) (95% CI)		1.5538 (0.7998, 3.0189)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1934

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline ≥30 mmol/L

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Odds Ratio (OR) (95% CI)		1.6154 (0.7859, 3.3203)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1920
Risk Difference (RD) (95% CI)		0.0356 (-0.0172, 0.0885)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1861
Sinusitis	18 (8.91)	9 (4.29)
Relative Risk (RR) (95% CI)		0.4810 (0.2212, 1.0455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0647
Odds Ratio (OR) (95% CI)		0.4577 (0.2006, 1.0442)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0633
Risk Difference (RD) (95% CI)		-0.0463 (-0.0941, 0.0016)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0584

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Skin and subcutaneous tissue disorders		
Rash	6 (2.97)	22 (10.48)
Relative Risk (RR) (95% CI)		3.5270 (1.4603, 8.5184)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0051
Odds Ratio (OR) (95% CI)		3.8227 (1.5164, 9.6365)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0045
Risk Difference (RD) (95% CI)		0.0751 (0.0275, 0.1226)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0020
Psychiatric disorders		
Anxiety	5 (2.48)	9 (4.29)

- MedDRA version 26.1.
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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Relative Risk (RR) (95% CI)		1.7314 (0.5903, 5.0782)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3174
Odds Ratio (OR) (95% CI)		1.7642 (0.5810, 5.3571)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3165
Risk Difference (RD) (95% CI)		0.0181 (-0.0167, 0.0529)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3076

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Male

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any TEAEs	138 (95.83)	144 (96.64)
Relative Risk (RR) (95% CI)		1.0085 (0.9638, 1.0552)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7156
Odds Ratio (OR) (95% CI)		1.2522 (0.3736, 4.1973)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7156
Risk Difference (RD) (95% CI)		0.0081 (-0.0355, 0.0517)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7155
Infections and infestations		
Influenza	9 (6.25)	19 (12.75)
Relative Risk (RR) (95% CI)		2.0403 (0.9548, 4.3597)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0657

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Male

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Odds Ratio (OR) (95% CI)		2.1923 (0.9570, 5.0220)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0634
Risk Difference (RD) (95% CI)		0.0650 (-0.0016, 0.1316)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0556
Sinusitis	11 (7.64)	4 (2.68)
Relative Risk (RR) (95% CI)		0.3514 (0.1145, 1.0784)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0675
Odds Ratio (OR) (95% CI)		0.3335 (0.1037, 1.0729)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0655
Risk Difference (RD) (95% CI)		-0.0495 (-0.1001, 0.0010)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0548

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Skin and subcutaneous tissue disorders		
Rash	6 (4.17)	12 (8.05)
Relative Risk (RR) (95% CI)		1.9329 (0.7454, 5.0121)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1752
Odds Ratio (OR) (95% CI)		2.0146 (0.7352, 5.5207)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1733
Risk Difference (RD) (95% CI)		0.0389 (-0.0157, 0.0934)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1624
Psychiatric disorders		
Anxiety	0	3 (2.01)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0201 (-0.0024, 0.0427)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0802

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Female

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any TEAEs	133 (91.72)	130 (96.30)
Relative Risk (RR) (95% CI)		1.0498 (0.9897, 1.1137)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1063
Odds Ratio (OR) (95% CI)		2.3459 (0.8039, 6.8453)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1186
Risk Difference (RD) (95% CI)		0.0457 (-0.0093, 0.1007)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1033
Infections and infestations		
Influenza	7 (4.83)	14 (10.37)
Relative Risk (RR) (95% CI)		2.1481 (0.8942, 5.1608)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0873

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- A subject with multiple events within a category is counted only once in that category.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Female

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Odds Ratio (OR) (95% CI)		2.2810 (0.8914, 5.8367)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0854
Risk Difference (RD) (95% CI)		0.0554 (-0.0067, 0.1176)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0804
Sinusitis	15 (10.34)	5 (3.70)
Relative Risk (RR) (95% CI)		0.3580 (0.1338, 0.9583)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0409
Odds Ratio (OR) (95% CI)		0.3333 (0.1177, 0.9439)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0386
Risk Difference (RD) (95% CI)		-0.0664 (-0.1253, -0.0075)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0272

- MedDRA version 26.1.
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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Skin and subcutaneous tissue disorders		
Rash	7 (4.83)	13 (9.63)
Relative Risk (RR) (95% CI)		1.9947 (0.8204, 4.8498)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1277
Odds Ratio (OR) (95% CI)		2.1007 (0.8120, 5.4350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1259
Risk Difference (RD) (95% CI)		0.0480 (-0.0128, 0.1088)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1215
Psychiatric disorders		
Anxiety	6 (4.14)	13 (9.63)

- MedDRA version 26.1.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Relative Risk (RR) (95% CI)		2.3272 (0.9104, 5.9486)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0777
Odds Ratio (OR) (95% CI)		2.4686 (0.9105, 6.6931)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0758
Risk Difference (RD) (95% CI)		0.0549 (-0.0045, 0.1143)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0699

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = North America

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any TEAEs	100 (97.09)	110 (96.49)
Relative Risk (RR) (95% CI)		0.9939 (0.9469, 1.0432)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8031
Odds Ratio (OR) (95% CI)		0.8250 (0.1802, 3.7768)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8042
Risk Difference (RD) (95% CI)		-0.0060 (-0.0528, 0.0409)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8031
Infections and infestations		
Influenza	5 (4.85)	14 (12.28)
Relative Risk (RR) (95% CI)		2.5298 (0.9440, 6.7794)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0650

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = North America

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Odds Ratio (OR) (95% CI)		2.7440 (0.9522, 7.9079)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0616
Risk Difference (RD) (95% CI)		0.0743 (0.0011, 0.1474)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0466
Sinusitis	8 (7.77)	6 (5.26)
Relative Risk (RR) (95% CI)		0.6776 (0.2433, 1.8875)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4565
Odds Ratio (OR) (95% CI)		0.6597 (0.2210, 1.9697)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4561
Risk Difference (RD) (95% CI)		-0.0250 (-0.0910, 0.0409)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4569

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Skin and subcutaneous tissue disorders		
Rash	3 (2.91)	9 (7.89)
Relative Risk (RR) (95% CI)		2.7105 (0.7542, 9.7409)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1266
Odds Ratio (OR) (95% CI)		2.8571 (0.7519, 10.8575)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1233
Risk Difference (RD) (95% CI)		0.0498 (-0.0094, 0.1090)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0991
Psychiatric disorders		
Anxiety	3 (2.91)	4 (3.51)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Relative Risk (RR) (95% CI)		1.2047 (0.2761, 5.2554)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8043
Odds Ratio (OR) (95% CI)		1.2121 (0.2648, 5.5490)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8042
Risk Difference (RD) (95% CI)		0.0060 (-0.0409, 0.0528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8031

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = Rest of World

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any TEAEs	171 (91.94)	164 (96.47)
Relative Risk (RR) (95% CI)		1.0493 (0.9968, 1.1046)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0662
Odds Ratio (OR) (95% CI)		2.3977 (0.9083, 6.3292)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0774
Risk Difference (RD) (95% CI)		0.0454 (-0.0026, 0.0933)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0639
Infections and infestations		
Influenza	11 (5.91)	19 (11.18)
Relative Risk (RR) (95% CI)		1.8898 (0.9265, 3.8549)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0801

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = Rest of World

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Odds Ratio (OR) (95% CI)		2.0018 (0.9233, 4.3400)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0788
Risk Difference (RD) (95% CI)		0.0526 (-0.0056, 0.1109)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0766
Sinusitis	18 (9.68)	3 (1.76)
Relative Risk (RR) (95% CI)		0.1824 (0.0547, 0.6081)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0056
Odds Ratio (OR) (95% CI)		0.1677 (0.0485, 0.5799)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0048
Risk Difference (RD) (95% CI)		-0.0791 (-0.1260, -0.0323)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0009

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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Skin and subcutaneous tissue disorders		
Rash	10 (5.38)	16 (9.41)
Relative Risk (RR) (95% CI)		1.7506 (0.8169, 3.7516)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1499
Odds Ratio (OR) (95% CI)		1.8286 (0.8060, 4.1482)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1487
Risk Difference (RD) (95% CI)		0.0404 (-0.0142, 0.0949)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1472
Psychiatric disorders		
Anxiety	3 (1.61)	12 (7.06)

- MedDRA version 26.1.
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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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Table 2.3.2.1.2
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Relative Risk (RR) (95% CI)		4.3765 (1.2565, 15.2440)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0204
Odds Ratio (OR) (95% CI)		4.6329 (1.2844, 16.7118)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0192
Risk Difference (RD) (95% CI)		0.0545 (0.0119, 0.0970)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0121

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Subjects with any TEAEs	238 (95.20)	233 (96.68)
Relative Risk (RR) (95% CI)		1.0156 (0.9793, 1.0532)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4055
Odds Ratio (OR) (95% CI)		1.4685 (0.5895, 3.6579)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4093
Risk Difference (RD) (95% CI)		0.0148 (-0.0200, 0.0496)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4049
Infections and infestations		
Influenza	14 (5.60)	28 (11.62)
Relative Risk (RR) (95% CI)		2.0747 (1.1198, 3.8439)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0204

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Odds Ratio (OR) (95% CI)		2.2160 (1.1365, 4.3208)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0195
Risk Difference (RD) (95% CI)		0.0602 (0.0107, 0.1097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0171
Sinusitis	22 (8.80)	9 (3.73)
Relative Risk (RR) (95% CI)		0.4244 (0.1994, 0.9030)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0261
Odds Ratio (OR) (95% CI)		0.4020 (0.1812, 0.8919)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0250
Risk Difference (RD) (95% CI)		-0.0507 (-0.0932, -0.0082)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0195

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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

System Organ Class Preferred Term	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Skin and subcutaneous tissue disorders		
Rash	10 (4.00)	19 (7.88)
Relative Risk (RR) (95% CI)		1.9710 (0.9357, 4.1517)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0743
Odds Ratio (OR) (95% CI)		2.0541 (0.9349, 4.5131)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0731
Risk Difference (RD) (95% CI)		0.0388 (-0.0030, 0.0806)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0686
Psychiatric disorders		
Anxiety	5 (2.00)	13 (5.39)

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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

System Organ Class Preferred Term	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Relative Risk (RR) (95% CI)		2.6971 (0.9763, 7.4505)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0556
Odds Ratio (OR) (95% CI)		2.7939 (0.9806, 7.9604)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0545
Risk Difference (RD) (95% CI)		0.0339 (0.0006, 0.0673)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0463

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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Subjects with any TEAEs	33 (84.62)	41 (95.35)
Relative Risk (RR) (95% CI)		1.1268 (0.9706, 1.3082)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1167
Odds Ratio (OR) (95% CI)		3.7273 (0.7054, 19.6943)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1214
Risk Difference (RD) (95% CI)		0.1073 (-0.0222, 0.2369)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1044
Infections and infestations		
Influenza	2 (5.13)	5 (11.63)
Relative Risk (RR) (95% CI)		2.2674 (0.4663, 11.0250)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3103

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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Odds Ratio (OR) (95% CI)		2.4342 (0.4442, 13.3402)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3054
Risk Difference (RD) (95% CI)		0.0650 (-0.0532, 0.1832)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2812
Sinusitis	4 (10.26)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.1026 (-0.1978, -0.0073)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0348

- MedDRA version 26.1.
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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

System Organ Class Preferred Term	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Psychiatric disorders		
Anxiety	1 (2.56)	3 (6.98)
Relative Risk (RR) (95% CI)		2.7209 (0.2951, 25.0847)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3771
Odds Ratio (OR) (95% CI)		2.8500 (0.2839, 28.6064)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3734
Risk Difference (RD) (95% CI)		0.0441 (-0.0468, 0.1350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3413
Skin and subcutaneous tissue disorders		
Rash	3 (7.69)	6 (13.95)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

System Organ Class Preferred Term	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Relative Risk (RR) (95% CI)		1.8140 (0.4863, 6.7660)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3753
Odds Ratio (OR) (95% CI)		1.9459 (0.4520, 8.3782)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3714
Risk Difference (RD) (95% CI)		0.0626 (-0.0705, 0.1957)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3566

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/F

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Subjects with any TEAEs	210 (93.75)	212 (95.50)
Relative Risk (RR) (95% CI)		1.0186 (0.9745, 1.0647)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4140
Odds Ratio (OR) (95% CI)		1.4133 (0.6140, 3.2530)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4160
Risk Difference (RD) (95% CI)		0.0175 (-0.0244, 0.0593)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4134
Infections and infestations		
Influenza	13 (5.80)	28 (12.61)
Relative Risk (RR) (95% CI)		2.1733 (1.1562, 4.0849)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0159

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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/F

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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Odds Ratio (OR) (95% CI)		2.3426 (1.1796, 4.6522)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0150
Risk Difference (RD) (95% CI)		0.0681 (0.0148, 0.1214)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0123
Sinusitis	17 (7.59)	8 (3.60)
Relative Risk (RR) (95% CI)		0.4748 (0.2092, 1.0776)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0749
Odds Ratio (OR) (95% CI)		0.4552 (0.1923, 1.0776)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0735
Risk Difference (RD) (95% CI)		-0.0399 (-0.0823, 0.0026)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0659

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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/F

System Organ Class Preferred Term	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Skin and subcutaneous tissue disorders		
Rash	7 (3.13)	19 (8.56)
Relative Risk (RR) (95% CI)		2.7387 (1.1747, 6.3851)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0197
Odds Ratio (OR) (95% CI)		2.9015 (1.1945, 7.0476)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0186
Risk Difference (RD) (95% CI)		0.0543 (0.0111, 0.0976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0139
Psychiatric disorders		
Anxiety	5 (2.23)	9 (4.05)

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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/F

System Organ Class Preferred Term	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Relative Risk (RR) (95% CI)		1.8162 (0.6184, 5.3340)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2776
Odds Ratio (OR) (95% CI)		1.8507 (0.6103, 5.6121)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2768
Risk Difference (RD) (95% CI)		0.0182 (-0.0141, 0.0506)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2699

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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/G

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- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Subjects with any TEAEs	19 (95.00)	19 (100.00)
Relative Risk (RR) (95% CI)		1.0526 (0.9519, 1.1640)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3174
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0500 (-0.0455, 0.1455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3049
Infections and infestations		
Influenza	0	1 (5.26)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-

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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/G

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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0526 (-0.0478, 0.1530)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3042
Sinusitis	1 (5.00)	1 (5.26)
Relative Risk (RR) (95% CI)		1.0526 (0.0708, 15.6590)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9703
Odds Ratio (OR) (95% CI)		1.0556 (0.0613, 18.1715)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9703
Risk Difference (RD) (95% CI)		0.0026 (-0.1359, 0.1412)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9703

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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/G

System Organ Class Preferred Term	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Psychiatric disorders		
Anxiety	1 (5.00)	3 (15.79)
Relative Risk (RR) (95% CI)		3.1579 (0.3590, 27.7776)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3000
Odds Ratio (OR) (95% CI)		3.5625 (0.3368, 37.6873)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2911
Risk Difference (RD) (95% CI)		0.1079 (-0.0819, 0.2976)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2651
Skin and subcutaneous tissue disorders		
Rash	1 (5.00)	0

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Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/G

System Organ Class Preferred Term	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0500 (-0.1455, 0.0455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3049

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Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
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Safety Set

Genotype group: F/RF

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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Subjects with any TEAEs	21 (91.30)	23 (100.00)
Relative Risk (RR) (95% CI)		1.0952 (0.9655, 1.2425)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1574
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0870 (-0.0282, 0.2021)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1389
Infections and infestations		
Influenza	2 (8.70)	2 (8.70)
Relative Risk (RR) (95% CI)		1.0000 (0.1537, 6.5066)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		>0.9999

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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
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Safety Set

Genotype group: F/RF

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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Odds Ratio (OR) (95% CI)		1.0000 (0.1286, 7.7770)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		>0.9999
Risk Difference (RD) (95% CI)		0.0000 (-0.1629, 0.1629)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		>0.9999
Sinusitis	4 (17.39)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.1739 (-0.3288, -0.0190)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0278

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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/RF

System Organ Class Preferred Term	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Psychiatric disorders		
Anxiety	0	2 (8.70)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0870 (-0.0282, 0.2021)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1389
Skin and subcutaneous tissue disorders		
Rash	2 (8.70)	1 (4.35)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/RF

System Organ Class Preferred Term	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Relative Risk (RR) (95% CI)		0.5000 (0.0487, 5.1381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5598
Odds Ratio (OR) (95% CI)		0.4773 (0.0402, 5.6641)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5579
Risk Difference (RD) (95% CI)		-0.0435 (-0.1856, 0.0987)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5489

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: TCR/non-F

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Subjects with any TEAEs	21 (95.45)	20 (100.00)
Relative Risk (RR) (95% CI)		1.0476 (0.9563, 1.1476)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3174
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0455 (-0.0416, 0.1325)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3061
Infections and infestations		
Influenza	1 (4.55)	2 (10.00)
Relative Risk (RR) (95% CI)		2.2000 (0.2156, 22.4498)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5059

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: TCR/non-F

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

System Organ Class Preferred Term	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Odds Ratio (OR) (95% CI)		2.3333 (0.1951, 27.9086)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5034
Risk Difference (RD) (95% CI)		0.0545 (-0.1031, 0.2122)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4978
Sinusitis	4 (18.18)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.1818 (-0.3430, -0.0206)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0270

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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: TCR/non-F

System Organ Class Preferred Term	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Psychiatric disorders		
Anxiety	0	2 (10.00)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.1000 (-0.0315, 0.2315)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1360
Skin and subcutaneous tissue disorders		
Rash	3 (13.64)	5 (25.00)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
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Table 2.3.2.1.2.1
Study VX20-121-103: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: TCR/non-F

System Organ Class Preferred Term	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Relative Risk (RR) (95% CI)		1.8333 (0.5012, 6.7066)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3597
Odds Ratio (OR) (95% CI)		2.1111 (0.4334, 10.2839)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3550
Risk Difference (RD) (95% CI)		0.1136 (-0.1242, 0.3515)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3491

- MedDRA version 26.1.
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Table 2.3.2.2.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Grade 3/4/5 TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any Grade 3/4/5 TEAEs	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.0671
Age at screening (<18 years vs. ≥18 years)	0.5119
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.8152
Sex (Male vs. Female)	0.2189
Region (North America vs. Rest of the World)	0.6222

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by "*".
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.2.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Grade 3/4/5 TEAEs by SOC and PT for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any Grade 3/4/5 TEAEs	
Prior CFTR modulator use (yes vs. no)	0.8825
Genotype group (F/F, F/G, F/RF vs. TCR/non-F)	0.1438

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by "*".
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any Grade 3/4/5 TEAEs	21 (12.57)	11 (7.14)
Relative Risk (RR) (95% CI)		0.5680 (0.2832, 1.1391)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1111
Odds Ratio (OR) (95% CI)		0.5348 (0.2488, 1.1494)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1089
Risk Difference (RD) (95% CI)		-0.0543 (-0.1190, 0.0104)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0998

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any Grade 3/4/5 TEAEs	8 (6.72)	13 (10.40)
Relative Risk (RR) (95% CI)		1.5470 (0.6651, 3.5985)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3111
Odds Ratio (OR) (95% CI)		1.6105 (0.6424, 4.0372)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3095
Risk Difference (RD) (95% CI)		0.0368 (-0.0331, 0.1067)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3026

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any Grade 3/4/5 TEAEs	5 (13.16)	3 (7.32)
Relative Risk (RR) (95% CI)		0.5561 (0.1425, 2.1702)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3983
Odds Ratio (OR) (95% CI)		0.5211 (0.1156, 2.3479)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3960
Risk Difference (RD) (95% CI)		-0.0584 (-0.1922, 0.0754)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3923

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any Grade 3/4/5 TEAEs	24 (9.56)	21 (8.64)
Relative Risk (RR) (95% CI)		0.9038 (0.5171, 1.5798)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7226
Odds Ratio (OR) (95% CI)		0.8947 (0.4841, 1.6535)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7226
Risk Difference (RD) (95% CI)		-0.0092 (-0.0599, 0.0415)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7222

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
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- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any Grade 3/4/5 TEAEs	6 (7.50)	5 (6.94)
Relative Risk (RR) (95% CI)		0.9259 (0.2951, 2.9048)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8950
Odds Ratio (OR) (95% CI)		0.9204 (0.2685, 3.1551)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8950
Risk Difference (RD) (95% CI)		-0.0056 (-0.0879, 0.0768)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8948

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
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- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any Grade 3/4/5 TEAEs	23 (11.39)	19 (9.05)
Relative Risk (RR) (95% CI)		0.7946 (0.4466, 1.4137)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4341
Odds Ratio (OR) (95% CI)		0.7742 (0.4078, 1.4696)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4338
Risk Difference (RD) (95% CI)		-0.0234 (-0.0819, 0.0351)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4335

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any Grade 3/4/5 TEAEs	16 (11.11)	10 (6.71)
Relative Risk (RR) (95% CI)		0.6040 (0.2836, 1.2866)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1913
Odds Ratio (OR) (95% CI)		0.5755 (0.2520, 1.3143)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1898
Risk Difference (RD) (95% CI)		-0.0440 (-0.1092, 0.0212)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1859

- MedDRA version 26.1.
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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any Grade 3/4/5 TEAEs	13 (8.97)	14 (10.37)
Relative Risk (RR) (95% CI)		1.1567 (0.5644, 2.3706)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6909
Odds Ratio (OR) (95% CI)		1.1748 (0.5310, 2.5995)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6909
Risk Difference (RD) (95% CI)		0.0140 (-0.0553, 0.0834)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6913

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any Grade 3/4/5 TEAEs	9 (8.74)	10 (8.77)
Relative Risk (RR) (95% CI)		1.0039 (0.4247, 2.3729)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9929
Odds Ratio (OR) (95% CI)		1.0043 (0.3912, 2.5780)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9929
Risk Difference (RD) (95% CI)		0.0003 (-0.0750, 0.0756)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9929

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any Grade 3/4/5 TEAEs	20 (10.75)	14 (8.24)
Relative Risk (RR) (95% CI)		0.7659 (0.3996, 1.4679)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4216
Odds Ratio (OR) (95% CI)		0.7449 (0.3636, 1.5259)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4208
Risk Difference (RD) (95% CI)		-0.0252 (-0.0859, 0.0356)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4166

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2.1
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

System Organ Class Preferred Term	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Subjects with any Grade 3/4/5 TEAEs	22 (8.80)	18 (7.47)
Relative Risk (RR) (95% CI)		0.8487 (0.4671, 1.5423)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5904
Odds Ratio (OR) (95% CI)		0.8365 (0.4368, 1.6019)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5902
Risk Difference (RD) (95% CI)		-0.0133 (-0.0616, 0.0350)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5892

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.2.2.1
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

System Organ Class Preferred Term	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Subjects with any Grade 3/4/5 TEAEs	7 (17.95)	6 (13.95)
Relative Risk (RR) (95% CI)		0.7774 (0.2858, 2.1145)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6219
Odds Ratio (OR) (95% CI)		0.7413 (0.2258, 2.4335)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6216
Risk Difference (RD) (95% CI)		-0.0400 (-0.1988, 0.1189)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6220

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2.1
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group F/F

System Organ Class Preferred Term	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Subjects with any Grade 3/4/5 TEAEs	21 (9.38)	21 (9.46)
Relative Risk (RR) (95% CI)		1.0090 (0.5674, 1.7943)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9756
Odds Ratio (OR) (95% CI)		1.0100 (0.5349, 1.9068)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9756
Risk Difference (RD) (95% CI)		0.0008 (-0.0534, 0.0551)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9756

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2.1
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group F/G

System Organ Class Preferred Term	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Subjects with any Grade 3/4/5 TEAEs	1 (5.00)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.0500 (-0.1455, 0.0455)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3049

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.2.2.1
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group F/RF

System Organ Class Preferred Term	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Subjects with any Grade 3/4/5 TEAEs	3 (13.04)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.1304 (-0.2681, 0.0072)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0633

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
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Table 2.3.2.2.2.1
Study VX20-121-103: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group TCR/non-F

System Organ Class Preferred Term	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Subjects with any Grade 3/4/5 TEAEs	4 (18.18)	3 (15.00)
Relative Risk (RR) (95% CI)		0.8250 (0.2098, 3.2434)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7830
Odds Ratio (OR) (95% CI)		0.7941 (0.1545, 4.0821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7826
Risk Difference (RD) (95% CI)		-0.0318 (-0.2565, 0.1928)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7813

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Zusatzanalysen zur Studie VX20-121-103

Table 2.3.2.3.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Serious TEAEs by SOC and PT
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.7126
Age at screening (<18 years vs. ≥18 years)	0.0336
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.4743
Sex (Male vs. Female)	0.3740
Region (North America vs. Rest of the World)	0.2542

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by "*".
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX20-121-103

Table 2.3.2.3.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Serious TEAEs by SOC and PT for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs	
Prior CFTR modulator use (yes vs. no)	0.5559
Genotype group (F/F, F/G, F/RF vs. TCR/non-F)	0.2775

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by "*".
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- N/C: model does not converge.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline <70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any serious TEAEs	21 (12.57)	15 (9.74)
Relative Risk (RR) (95% CI)		0.7746 (0.4145, 1.4476)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.4234
Odds Ratio (OR) (95% CI)		0.7503 (0.3718, 1.5140)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.4225
Risk Difference (RD) (95% CI)		-0.0283 (-0.0971, 0.0404)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.4188

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

$ppFEV_1$ at baseline ≥70 %

System Organ Class Preferred Term	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any serious TEAEs	12 (10.08)	8 (6.40)
Relative Risk (RR) (95% CI)		0.6347 (0.2689, 1.4978)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2994
Odds Ratio (OR) (95% CI)		0.6097 (0.2400, 1.5487)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2982
Risk Difference (RD) (95% CI)		-0.0368 (-0.1059, 0.0322)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2957

- MedDRA version 26.1.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening <18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any serious TEAEs	7 (18.42)	1 (2.44)
Relative Risk (RR) (95% CI)		0.1324 (0.0171, 1.0267)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0530
Odds Ratio (OR) (95% CI)		0.1107 (0.0129, 0.9477)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0445
Risk Difference (RD) (95% CI)		-0.1598 (-0.2918, -0.0278)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0176

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Age at screening ≥18 years

System Organ Class Preferred Term	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any serious TEAEs	26 (10.36)	22 (9.05)
Relative Risk (RR) (95% CI)		0.8740 (0.5095, 1.4993)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6248
Odds Ratio (OR) (95% CI)		0.8615 (0.4740, 1.5655)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6246
Risk Difference (RD) (95% CI)		-0.0131 (-0.0652, 0.0391)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6240

- MedDRA version 26.1.
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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline <30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any serious TEAEs	8 (10.00)	7 (9.72)
Relative Risk (RR) (95% CI)		0.9722 (0.3711, 2.5471)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9543
Odds Ratio (OR) (95% CI)		0.9692 (0.3330, 2.8211)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9543
Risk Difference (RD) (95% CI)		-0.0028 (-0.0977, 0.0921)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9542

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

SwCl at baseline ≥30 mmol/L

System Organ Class Preferred Term	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any serious TEAEs	24 (11.88)	16 (7.62)
Relative Risk (RR) (95% CI)		0.6413 (0.3511, 1.1712)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1483
Odds Ratio (OR) (95% CI)		0.6117 (0.3147, 1.1888)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1471
Risk Difference (RD) (95% CI)		-0.0426 (-0.0999, 0.0146)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1446

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- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Male

System Organ Class Preferred Term	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any serious TEAEs	14 (9.72)	13 (8.72)
Relative Risk (RR) (95% CI)		0.8974 (0.4371, 1.8424)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7680
Odds Ratio (OR) (95% CI)		0.8876 (0.4019, 1.9602)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7680
Risk Difference (RD) (95% CI)		-0.0100 (-0.0763, 0.0563)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7681

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Sex = Female

System Organ Class Preferred Term	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any serious TEAEs	19 (13.10)	10 (7.41)
Relative Risk (RR) (95% CI)		0.5653 (0.2727, 1.1718)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1251
Odds Ratio (OR) (95% CI)		0.5305 (0.2373, 1.1863)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1226
Risk Difference (RD) (95% CI)		-0.0570 (-0.1274, 0.0135)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1132

- MedDRA version 26.1.
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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = North America

System Organ Class Preferred Term	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any serious TEAEs	6 (5.83)	8 (7.02)
Relative Risk (RR) (95% CI)		1.2047 (0.4325, 3.3556)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.7216
Odds Ratio (OR) (95% CI)		1.2201 (0.4087, 3.6426)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.7214
Risk Difference (RD) (95% CI)		0.0119 (-0.0532, 0.0771)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.7198

- MedDRA version 26.1.
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- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
Safety Set

Region = Rest of World

System Organ Class Preferred Term	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any serious TEAEs	27 (14.52)	15 (8.82)
Relative Risk (RR) (95% CI)		0.6078 (0.3350, 1.1031)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1016
Odds Ratio (OR) (95% CI)		0.5699 (0.2920, 1.1124)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0994
Risk Difference (RD) (95% CI)		-0.0569 (-0.1231, 0.0093)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0918

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2.1
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

System Organ Class Preferred Term	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Subjects with any serious TEAEs	26 (10.40)	19 (7.88)
Relative Risk (RR) (95% CI)		0.7581 (0.4311, 1.3331)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3362
Odds Ratio (OR) (95% CI)		0.7374 (0.3967, 1.3707)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3354
Risk Difference (RD) (95% CI)		-0.0252 (-0.0760, 0.0257)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3325

- MedDRA version 26.1.
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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
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- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2.1
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

System Organ Class Preferred Term	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Subjects with any serious TEAEs	7 (17.95)	4 (9.30)
Relative Risk (RR) (95% CI)		0.5183 (0.1642, 1.6360)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2624
Odds Ratio (OR) (95% CI)		0.4689 (0.1260, 1.7454)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2587
Risk Difference (RD) (95% CI)		-0.0865 (-0.2349, 0.0620)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2537

- MedDRA version 26.1.
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- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2.1
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group F/F

System Organ Class Preferred Term	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Subjects with any serious TEAEs	24 (10.71)	18 (8.11)
Relative Risk (RR) (95% CI)		0.7568 (0.4228, 1.3546)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.3481
Odds Ratio (OR) (95% CI)		0.7353 (0.3871, 1.3966)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.3475
Risk Difference (RD) (95% CI)		-0.0261 (-0.0802, 0.0281)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3453

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2.1
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group F/G

System Organ Class Preferred Term	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Subjects with any serious TEAEs	3 (15.00)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-0.1500 (-0.3065, 0.0065)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0603

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2.1
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group F/RF

System Organ Class Preferred Term	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Subjects with any serious TEAEs	2 (8.70)	1 (4.35)
Relative Risk (RR) (95% CI)		0.5000 (0.0487, 5.1381)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5598
Odds Ratio (OR) (95% CI)		0.4773 (0.0402, 5.6641)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5579
Risk Difference (RD) (95% CI)		-0.0435 (-0.1856, 0.0987)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5489

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.3.2.1
Study VX20-121-103: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group TCR/non-F

System Organ Class Preferred Term	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Subjects with any serious TEAEs	4 (18.18)	4 (20.00)
Relative Risk (RR) (95% CI)		1.1000 (0.3162, 3.8264)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8809
Odds Ratio (OR) (95% CI)		1.1250 (0.2410, 5.2522)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8809
Risk Difference (RD) (95% CI)		0.0182 (-0.2200, 0.2563)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8810

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done and relative risk of respective treatment effect at study level is statistically significant (p-value <0.05); 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- "-" indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs Leading to Treatment Discontinuation
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs leading to treatment discontinuation	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %)	0.0573
Age at screening (<18 years vs. ≥18 years)	0.2529
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L)	0.1237
Sex (Male vs. Female)	0.2039
Region (North America vs. Rest of the World)	0.5161

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.4.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for TEAEs Leading to Treatment Discontinuation for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

	P-value for Interaction Based on Relative Risk
Subjects with any TEAEs leading to treatment discontinuation	
Prior CFTR modulator use (yes vs. no)	0.5355
Genotype group (F/F, F/G, F/RF vs. TCR/non-F)	N/C

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- P-values are for Relative Risk obtained from Generalized Linear Model for Outcome = treatment, subgroup (one factor at a time), treatment*subgroup; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- N/C: model does not converge.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with any TEAEs leading to treatment discontinuation	8 (4.79)	7 (4.55)
Relative Risk (RR) (95% CI)		0.9489 (0.3524, 2.5548)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9173
Odds Ratio (OR) (95% CI)		0.9464 (0.3349, 2.6746)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9173
Risk Difference (RD) (95% CI)		-0.0024 (-0.0486, 0.0437)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9172

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

$ppFEV_1$ at baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with any TEAEs leading to treatment discontinuation	1 (0.84)	7 (5.60)
Relative Risk (RR) (95% CI)		6.6640 (0.8324, 53.3524)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.0739
Odds Ratio (OR) (95% CI)		7.0000 (0.8480, 57.7821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.0708
Risk Difference (RD) (95% CI)		0.0476 (0.0041, 0.0911)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0321

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with any TEAEs leading to treatment discontinuation	2 (5.26)	1 (2.44)
Relative Risk (RR) (95% CI)		0.4634 (0.0438, 4.9057)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.5229
Odds Ratio (OR) (95% CI)		0.4500 (0.0391, 5.1749)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.5217
Risk Difference (RD) (95% CI)		-0.0282 (-0.1135, 0.0570)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.5162

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with any TEAEs leading to treatment discontinuation	7 (2.79)	13 (5.35)
Relative Risk (RR) (95% CI)		1.9183 (0.7785, 4.7265)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1568
Odds Ratio (OR) (95% CI)		1.9702 (0.7724, 5.0252)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1558
Risk Difference (RD) (95% CI)		0.0256 (-0.0093, 0.0605)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1499

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with any TEAEs leading to treatment discontinuation	1 (1.25)	5 (6.94)
Relative Risk (RR) (95% CI)		5.5556 (0.6646, 46.4368)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1134
Odds Ratio (OR) (95% CI)		5.8955 (0.6721, 51.7157)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1093
Risk Difference (RD) (95% CI)		0.0569 (-0.0066, 0.1205)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.0791

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

SwCl at baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with any TEAEs leading to treatment discontinuation	8 (3.96)	9 (4.29)
Relative Risk (RR) (95% CI)		1.0821 (0.4259, 2.7498)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8682
Odds Ratio (OR) (95% CI)		1.0858 (0.4106, 2.8718)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8682
Risk Difference (RD) (95% CI)		0.0033 (-0.0351, 0.0416)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8681

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with any TEAEs leading to treatment discontinuation	6 (4.17)	6 (4.03)
Relative Risk (RR) (95% CI)		0.9664 (0.3191, 2.9272)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9519
Odds Ratio (OR) (95% CI)		0.9650 (0.3039, 3.0646)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9519
Risk Difference (RD) (95% CI)		-0.0014 (-0.0468, 0.0440)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9519

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with any TEAEs leading to treatment discontinuation	3 (2.07)	8 (5.93)
Relative Risk (RR) (95% CI)		2.8642 (0.7759, 10.5732)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.1143
Odds Ratio (OR) (95% CI)		2.9816 (0.7743, 11.4821)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.1123
Risk Difference (RD) (95% CI)		0.0386 (-0.0075, 0.0846)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.1009

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with any TEAEs leading to treatment discontinuation	4 (3.88)	5 (4.39)
Relative Risk (RR) (95% CI)		1.1294 (0.3117, 4.0926)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.8531
Odds Ratio (OR) (95% CI)		1.1353 (0.2965, 4.3473)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.8530
Risk Difference (RD) (95% CI)		0.0050 (-0.0479, 0.0580)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.8525

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Region = Rest of World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with any TEAEs leading to treatment discontinuation	5 (2.69)	9 (5.29)
Relative Risk (RR) (95% CI)		1.9694 (0.6733, 5.7603)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2158
Odds Ratio (OR) (95% CI)		2.0236 (0.6645, 6.1628)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2148
Risk Difference (RD) (95% CI)		0.0261 (-0.0148, 0.0670)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2118

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2.1
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: Yes

	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Subjects with any TEAEs leading to treatment discontinuation	7 (2.80)	12 (4.98)
Relative Risk (RR) (95% CI)		1.7783 (0.7121, 4.4409)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2176
Odds Ratio (OR) (95% CI)		1.8191 (0.7039, 4.7011)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2168
Risk Difference (RD) (95% CI)		0.0218 (-0.0124, 0.0560)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2122

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2.1
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Subjects with any TEAEs leading to treatment discontinuation	2 (5.13)	2 (4.65)
Relative Risk (RR) (95% CI)		0.9070 (0.1341, 6.1338)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.9203
Odds Ratio (OR) (95% CI)		0.9024 (0.1210, 6.7333)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.9203
Risk Difference (RD) (95% CI)		-0.0048 (-0.0983, 0.0888)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.9204

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2.1
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Subjects with any TEAEs leading to treatment discontinuation	7 (3.13)	12 (5.41)
Relative Risk (RR) (95% CI)		1.7297 (0.6938, 4.3122)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.2397
Odds Ratio (OR) (95% CI)		1.7714 (0.6842, 4.5862)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.2388
Risk Difference (RD) (95% CI)		0.0228 (-0.0147, 0.0603)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.2329

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2.1
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Subjects with any TEAEs leading to treatment discontinuation	0	1 (5.26)
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		0.0526 (-0.0478, 0.1530)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.3042

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2.1
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Subjects with any TEAEs leading to treatment discontinuation	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.3.2.4.2.1
Study VX20-121-103: Summary of TEAEs Leading to Treatment Discontinuation by Each Applicable Subgroup Factor for Additional Subgroups
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Subjects with any TEAEs leading to treatment discontinuation	2 (9.09)	1 (5.00)
Relative Risk (RR) (95% CI)		0.5500 (0.0539, 5.6124)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]		0.6139
Odds Ratio (OR) (95% CI)		0.5263 (0.0440, 6.2925)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]		0.6121
Risk Difference (RD) (95% CI)		-0.0409 (-0.1944, 0.1126)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]		0.6014

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).
- [1] Relative risk from 2x2 table.
- [2] Odds ratio from 2x2 table.
- [3] Risk difference estimate from 2x2 table.
- '-' indicates that point estimate, CI or p-value is not estimable.

Table 2.4.1.1
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with at least one Pulmonary Exacerbation	59 (20.4)	61 (21.5)
Relative Risk (RR) (95% CI)		1.0421 (0.7576, 1.4335)
P-value vs. ELX/TEZ/IVA [1]	-	0.7997
Odds Ratio (OR) (95% CI)		1.0729 (0.7123, 1.6160)
P-value vs. ELX/TEZ/IVA [2]	-	0.7364
Risk Difference (RD) (95% CI)		0.0200 (-0.0476, 0.0875)
P-value vs. ELX/TEZ/IVA [3]	-	0.5629
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	9 (3.1)	14 (4.9)
Relative Risk (RR) (95% CI)		1.4298 (0.6225, 3.2840)
P-value vs. ELX/TEZ/IVA [1]	-	0.3994
Odds Ratio (OR) (95% CI)		1.4430 (0.6047, 3.4435)
P-value vs. ELX/TEZ/IVA [2]	-	0.4085
Risk Difference (RD) (95% CI)		0.0090 (-0.0284, 0.0463)
P-value vs. ELX/TEZ/IVA [3]	-	0.6381

- A subject is considered to have at least one Pulmonary Exacerbation (PEx) requiring IV antibiotics or hospitalization, if they had at least one PEx requiring IV antibiotics, or at least one PEx requiring hospitalization or at least one PEx requiring both IV antibiotics and hospitalization.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	17 (5.9)	19 (6.7)
Relative Risk (RR) (95% CI)		1.0957 (0.5714, 2.1011)
P-value vs. ELX/TEZ/IVA [1]	-	0.7833
Odds Ratio (OR) (95% CI)		1.1063 (0.5495, 2.2272)
P-value vs. ELX/TEZ/IVA [2]	-	0.7772
Risk Difference (RD) (95% CI)		N/C
P-value vs. ELX/TEZ/IVA [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	17 (5.9)	19 (6.7)
Relative Risk (RR) (95% CI)		1.0957 (0.5714, 2.1011)
P-value vs. ELX/TEZ/IVA [1]	-	0.7833
Odds Ratio (OR) (95% CI)		1.1063 (0.5495, 2.2272)
P-value vs. ELX/TEZ/IVA [2]	-	0.7772
Risk Difference (RD) (95% CI)		N/C
P-value vs. ELX/TEZ/IVA [3]	-	N/C

- A subject is considered to have at least one Pulmonary Exacerbation (PEx) requiring IV antibiotics or hospitalization, if they had at least one PEx requiring IV antibiotics, or at least one PEx requiring hospitalization or at least one PEx requiring both IV antibiotics and hospitalization.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

	ELX/TEZ/IVA N = 289 n (%)	VNZ/TEZ/D-IVA N = 284 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	9 (3.1)	6 (2.1)
Relative Risk (RR) (95% CI)		0.7244 (0.2550, 2.0582)
P-value vs. ELX/TEZ/IVA [1]	-	0.5451
Odds Ratio (OR) (95% CI)		0.6917 (0.2334, 2.0497)
P-value vs. ELX/TEZ/IVA [2]	-	0.5061
Risk Difference (RD) (95% CI)		N/C
P-value vs. ELX/TEZ/IVA [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization but not IV Antibiotics	0	0
Relative Risk (RR) (95% CI)		- (-, -)
P-value vs. ELX/TEZ/IVA [1]	-	-
Odds Ratio (OR) (95% CI)		- (-, -)
P-value vs. ELX/TEZ/IVA [2]	-	-
Risk Difference (RD) (95% CI)		- (-, -)
P-value vs. ELX/TEZ/IVA [3]	-	-

- A subject is considered to have at least one Pulmonary Exacerbation (PEx) requiring IV antibiotics or hospitalization, if they had at least one PEx requiring IV antibiotics, or at least one PEx requiring hospitalization or at least one PEx requiring both IV antibiotics and hospitalization.
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- N/C: model does not converge.

Table 2.4.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
Subjects with at least one Pulmonary Exacerbation	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3812
Age at screening (<18 years vs. ≥18 years) [2]	0.4488
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.4100
Sex (Male vs. Female) [1]	0.7623
Region (North America vs. Rest of the World) [1]	0.9533
Prior CFTR modulator use (yes vs. no) [1]	0.0493
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [3]	0.2872

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, age at screening (<18 vs ≥18 years), and &geno. as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride and &geno. as covariates; Distribution: binomial with log link.
- [3] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.4.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	
ppFEV$_1$ at baseline (<70 % vs. ≥70 %) [1]	0.4064
Age at screening (<18 years vs. ≥18 years) [2]	0.2533
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1719
Sex (Male vs. Female) [1]	0.4874
Region (North America vs. Rest of the World) [1]	0.4995
Prior CFTR modulator use (yes vs. no) [1]	0.9453
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [3]	0.0426*

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline ppFEV$_1$, baseline sweat chloride, age at screening (<18 vs ≥18 years), and &geno. as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline ppFEV$_1$, baseline sweat chloride and &geno. as covariates; Distribution: binomial with log link.
- [3] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline ppFEV$_1$, baseline sweat chloride and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.4.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1630
Age at screening (<18 years vs. ≥18 years) [2]	0.1456
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.7572
Sex (Male vs. Female) [1]	0.8599
Region (North America vs. Rest of the World) [1]	0.2377
Prior CFTR modulator use (yes vs. no) [1]	0.7225
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [3]	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, age at screening (<18 vs ≥18 years), and &geno. as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride and &geno. as covariates; Distribution: binomial with log link.
- [3] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.4.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.1630
Age at screening (<18 years vs. ≥18 years) [2]	0.1456
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.7572
Sex (Male vs. Female) [1]	0.8599
Region (North America vs. Rest of the World) [1]	0.2377
Prior CFTR modulator use (yes vs. no) [1]	0.7225
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [3]	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, age at screening (<18 vs ≥18 years), and &geno. as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride and &geno. as covariates; Distribution: binomial with log link.
- [3] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.4.1.1.1
Study VX20-121-103: Treatment by Subgroup Factor Interactions for Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52
Full Analysis Set

Subgroup	P-value for Interaction
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	
$ppFEV_1$ at baseline (<70 % vs. ≥70 %) [1]	0.3941*
Age at screening (<18 years vs. ≥18 years) [2]	N/C
SwCl at baseline (<30 mmol/L vs. ≥30 mmol/L) [1]	0.1340*
Sex (Male vs. Female) [1]	0.0711*
Region (North America vs. Rest of the World) [1]	0.8456*
Prior CFTR modulator use (yes vs. no) [1]	N/C
Genotype group (F/F, F/G, F/RF vs. TCR/non-F) [3]	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride, age at screening (<18 vs ≥18 years), and &geno. as covariates; Distribution: binomial with log link.
- [2] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride and &geno. as covariates; Distribution: binomial with log link.
- [3] P-values are for relative risk obtained from Generalized Linear Model: treatment, subgroup, treatment*subgroup, with adjustment for continuous baseline $ppFEV_1$, baseline sweat chloride and age at screening (<18 vs ≥18 years) as covariates; Distribution: binomial with log link.
-If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
-N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with at least one Pulmonary Exacerbation	41 (24.6)	36 (23.4)
Relative Risk (RR) (95% CI)		0.9396 (0.6345, 1.3915)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7559
Odds Ratio (OR) (95% CI)		0.9239 (0.5497, 1.5528)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7651
Risk Difference (RD) (95% CI)		-0.0131 (-0.1085, 0.0823)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.7885
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	6 (3.6)	6 (3.9)
Relative Risk (RR) (95% CI)		1.0430 (0.3467, 3.1374)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9403
Odds Ratio (OR) (95% CI)		1.0666 (0.3307, 3.4395)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.9141
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	13 (7.8)	9 (5.8)
Relative Risk (RR) (95% CI)		0.7915 (0.3447, 1.8172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5813
Odds Ratio (OR) (95% CI)		0.7739 (0.3139, 1.9078)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5777
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	13 (7.8)	9 (5.8)
Relative Risk (RR) (95% CI)		0.7915 (0.3447, 1.8172)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5813
Odds Ratio (OR) (95% CI)		0.7739 (0.3139, 1.9078)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5777

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline <70 %

	ELX/TEZ/IVA N = 167 n (%)	VNZ/TEZ/D-IVA N = 154 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	7 (4.2)	3 (1.9)
Relative Risk (RR) (95% CI)		0.4957 (0.1267, 1.9389)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3132
Odds Ratio (OR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	N/C
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with at least one Pulmonary Exacerbation	18 (15.1)	24 (19.2)
Relative Risk (RR) (95% CI)		1.2391 (0.7112, 2.1587)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4491
Odds Ratio (OR) (95% CI)		1.3199 (0.6676, 2.6097)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4249
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	3 (2.5)	7 (5.6)
Relative Risk (RR) (95% CI)		2.0925 (0.5518, 7.9348)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2776
Odds Ratio (OR) (95% CI)		2.1341 (0.5297, 8.5988)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2864
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	4 (3.4)	9 (7.2)
Relative Risk (RR) (95% CI)		2.0261 (0.6379, 6.4355)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2311
Odds Ratio (OR) (95% CI)		2.1088 (0.6203, 7.1689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2320
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	4 (3.4)	9 (7.2)
Relative Risk (RR) (95% CI)		2.0261 (0.6379, 6.4355)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2311
Odds Ratio (OR) (95% CI)		2.1088 (0.6203, 7.1689)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2320

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

$ppFEV_1$ at Baseline ≥70 %

	ELX/TEZ/IVA N = 119 n (%)	VNZ/TEZ/D-IVA N = 125 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	2 (1.7)	3 (2.4)
Relative Risk (RR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	N/C
Odds Ratio (OR) (95% CI)		1.2969 (0.2012, 8.3594)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7845
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with at least one Pulmonary Exacerbation	4 (10.5)	8 (19.5)
Relative Risk (RR) (95% CI)		1.8208 (0.5707, 5.8093)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3114
Odds Ratio (OR) (95% CI)		1.8972 (0.4747, 7.5820)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.3650
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	1 (2.6)	5 (12.2)
Relative Risk (RR) (95% CI)		10.3008 (3.8450, 27.5958)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	<0.0001*
Odds Ratio (OR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	N/C
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	1 (2.6)	5 (12.2)
Relative Risk (RR) (95% CI)		10.3008 (3.8450, 27.5958)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	<0.0001*
Odds Ratio (OR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	N/C
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	1 (2.6)	5 (12.2)
Relative Risk (RR) (95% CI)		10.3008 (3.8450, 27.5958)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	<0.0001*
Odds Ratio (OR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening <18 years

	ELX/TEZ/IVA N = 38 n (%)	VNZ/TEZ/D-IVA N = 41 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with at least one Pulmonary Exacerbation	55 (21.9)	53 (21.8)
Relative Risk (RR) (95% CI)		1.0057 (0.7204, 1.4041)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9734
Odds Ratio (OR) (95% CI)		1.0268 (0.6660, 1.5830)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.9046
Risk Difference (RD) (95% CI)		0.0155 (-0.0607, 0.0916)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.6903
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	8 (3.2)	9 (3.7)
Relative Risk (RR) (95% CI)		1.1322 (0.4440, 2.8873)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7948
Odds Ratio (OR) (95% CI)		1.1383 (0.4299, 3.0139)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7943
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	16 (6.4)	14 (5.8)
Relative Risk (RR) (95% CI)		0.9172 (0.4525, 1.8591)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8104
Odds Ratio (OR) (95% CI)		0.9138 (0.4286, 1.9482)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8154
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	16 (6.4)	14 (5.8)
Relative Risk (RR) (95% CI)		0.9172 (0.4525, 1.8591)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8104
Odds Ratio (OR) (95% CI)		0.9138 (0.4286, 1.9482)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8154

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Age at screening ≥18 years

	ELX/TEZ/IVA N = 251 n (%)	VNZ/TEZ/D-IVA N = 243 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	9 (3.6)	6 (2.5)
Relative Risk (RR) (95% CI)		0.6917 (0.2435, 1.9646)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4888
Odds Ratio (OR) (95% CI)		0.6917 (0.2334, 2.0497)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5061
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with at least one Pulmonary Exacerbation	21 (26.3)	15 (20.8)
Relative Risk (RR) (95% CI)		0.8491 (0.4810, 1.4988)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5726
Odds Ratio (OR) (95% CI)		0.7889 (0.3613, 1.7224)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5517
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	4 (5.0)	2 (2.8)
Relative Risk (RR) (95% CI)		0.4771 (0.1001, 2.2743)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3530*
Odds Ratio (OR) (95% CI)		0.4976 (0.0819, 3.0241)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4484
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	4 (5.0)	3 (4.2)
Relative Risk (RR) (95% CI)		0.7580 (0.1787, 3.2159)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7071*
Odds Ratio (OR) (95% CI)		0.8031 (0.1593, 4.0484)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7905
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	4 (5.0)	3 (4.2)
Relative Risk (RR) (95% CI)		0.7580 (0.1787, 3.2159)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7071*
Odds Ratio (OR) (95% CI)		0.8031 (0.1593, 4.0484)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7905

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline <30 mmol/L

	ELX/TEZ/IVA N = 80 n (%)	VNZ/TEZ/D-IVA N = 72 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	0	1 (1.4)
Relative Risk (RR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	N/C
Odds Ratio (OR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	N/C
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with at least one Pulmonary Exacerbation	37 (18.3)	46 (21.9)
Relative Risk (RR) (95% CI)		1.1697 (0.7904, 1.7310)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.4332
Odds Ratio (OR) (95% CI)		1.2220 (0.7499, 1.9913)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4210
Risk Difference (RD) (95% CI)		0.0397 (-0.0392, 0.1185)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.3243
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	5 (2.5)	12 (5.7)
Relative Risk (RR) (95% CI)		2.0766 (0.7383, 5.8406)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.1661
Odds Ratio (OR) (95% CI)		2.1595 (0.7297, 6.3909)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.1643
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	12 (5.9)	16 (7.6)
Relative Risk (RR) (95% CI)		1.1588 (0.5568, 2.4117)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6936
Odds Ratio (OR) (95% CI)		1.1770 (0.5339, 2.5948)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6862
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	12 (5.9)	16 (7.6)
Relative Risk (RR) (95% CI)		1.1588 (0.5568, 2.4117)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6936
Odds Ratio (OR) (95% CI)		1.1770 (0.5339, 2.5948)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6862

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sweat Chloride at Baseline ≥30 mmol/L

	ELX/TEZ/IVA N = 202 n (%)	VNZ/TEZ/D-IVA N = 210 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	8 (4.0)	5 (2.4)
Relative Risk (RR) (95% CI)		0.5959 (0.1986, 1.7883)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.3558
Odds Ratio (OR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	N/C
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with at least one Pulmonary Exacerbation	23 (16.0)	25 (16.8)
Relative Risk (RR) (95% CI)		1.0278 (0.6040, 1.7490)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9194
Odds Ratio (OR) (95% CI)		1.0445 (0.5522, 1.9756)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8936
Risk Difference (RD) (95% CI)		0.0185 (-0.0732, 0.1103)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.6924
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	2 (1.4)	5 (3.4)
Relative Risk (RR) (95% CI)		2.3871 (0.4680, 12.1752)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2952
Odds Ratio (OR) (95% CI)		2.4196 (0.4513, 12.9732)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.3024
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	5 (3.5)	5 (3.4)
Relative Risk (RR) (95% CI)		1.1178 (0.3029, 4.1252)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8672
Odds Ratio (OR) (95% CI)		1.1097 (0.2861, 4.3040)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8804
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	5 (3.5)	5 (3.4)
Relative Risk (RR) (95% CI)		1.1178 (0.3029, 4.1252)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8672
Odds Ratio (OR) (95% CI)		1.1097 (0.2861, 4.3040)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8804

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Male

	ELX/TEZ/IVA N = 144 n (%)	VNZ/TEZ/D-IVA N = 149 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	3 (2.1)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with at least one Pulmonary Exacerbation	36 (24.8)	36 (26.7)
Relative Risk (RR) (95% CI)		1.1186 (0.7487, 1.6714)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5843
Odds Ratio (OR) (95% CI)		1.1929 (0.6843, 2.0794)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.5339
Risk Difference (RD) (95% CI)		0.0297 (-0.0710, 0.1304)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.5629
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	7 (4.8)	9 (6.7)
Relative Risk (RR) (95% CI)		1.1792 (0.4349, 3.1972)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.7460
Odds Ratio (OR) (95% CI)		1.2104 (0.4180, 3.5052)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7249
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

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- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	12 (8.3)	14 (10.4)
Relative Risk (RR) (95% CI)		1.2072 (0.5556, 2.6234)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6344*
Odds Ratio (OR) (95% CI)		1.2452 (0.5356, 2.8951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6105
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	12 (8.3)	14 (10.4)
Relative Risk (RR) (95% CI)		1.2072 (0.5556, 2.6234)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6344*
Odds Ratio (OR) (95% CI)		1.2452 (0.5356, 2.8951)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6105

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Sex = Female

	ELX/TEZ/IVA N = 145 n (%)	VNZ/TEZ/D-IVA N = 135 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	6 (4.1)	6 (4.4)
Relative Risk (RR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	N/C
Odds Ratio (OR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	N/C
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with at least one Pulmonary Exacerbation	21 (20.4)	26 (22.8)
Relative Risk (RR) (95% CI)		1.0113 (0.6059, 1.6880)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9656
Odds Ratio (OR) (95% CI)		1.0219 (0.5271, 1.9809)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.9489
Risk Difference (RD) (95% CI)		0.0137 (-0.0993, 0.1267)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.8120
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	3 (2.9)	8 (7.0)
Relative Risk (RR) (95% CI)		2.1088 (0.5607, 7.9310)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2696
Odds Ratio (OR) (95% CI)		2.1331 (0.5226, 8.7061)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2911
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	4 (3.9)	10 (8.8)
Relative Risk (RR) (95% CI)		1.9601 (0.6268, 6.1296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2473
Odds Ratio (OR) (95% CI)		2.0108 (0.5866, 6.8932)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2665
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	4 (3.9)	10 (8.8)
Relative Risk (RR) (95% CI)		1.9601 (0.6268, 6.1296)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2473
Odds Ratio (OR) (95% CI)		2.0108 (0.5866, 6.8932)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2665

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = North America

	ELX/TEZ/IVA N = 103 n (%)	VNZ/TEZ/D-IVA N = 114 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	2 (1.9)	2 (1.8)
Relative Risk (RR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	N/C
Odds Ratio (OR) (95% CI)		0.9285 (0.1213, 7.1078)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.9430
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with at least one Pulmonary Exacerbation	38 (20.4)	35 (20.6)
Relative Risk (RR) (95% CI)		1.0500 (0.6981, 1.5793)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8147
Odds Ratio (OR) (95% CI)		1.0809 (0.6387, 1.8292)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7720
Risk Difference (RD) (95% CI)		0.0220 (-0.0638, 0.1077)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.6155
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	6 (3.2)	6 (3.5)
Relative Risk (RR) (95% CI)		1.1019 (0.3640, 3.3358)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.8637
Odds Ratio (OR) (95% CI)		1.1295 (0.3537, 3.6062)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8372
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	13 (7.0)	9 (5.3)
Relative Risk (RR) (95% CI)		0.8131 (0.3520, 1.8781)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6281
Odds Ratio (OR) (95% CI)		0.8166 (0.3317, 2.0103)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6593
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	13 (7.0)	9 (5.3)
Relative Risk (RR) (95% CI)		0.8131 (0.3520, 1.8781)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6281
Odds Ratio (OR) (95% CI)		0.8166 (0.3317, 2.0103)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6593

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Region = Rest of the World

	ELX/TEZ/IVA N = 186 n (%)	VNZ/TEZ/D-IVA N = 170 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	7 (3.8)	4 (2.4)
Relative Risk (RR) (95% CI)		0.7269 (0.2089, 2.5297)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6162
Odds Ratio (OR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	N/C
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Prior CFTR modulator use: yes

	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Subjects with at least one Pulmonary Exacerbation	54 (21.6)	49 (20.3)
Relative Risk (RR) (95% CI)		0.9167 (0.6493, 1.2943)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6213
Odds Ratio (OR) (95% CI)		0.9105 (0.5850, 1.4171)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6779
Risk Difference (RD) (95% CI)		-0.0048 (-0.0783, 0.0688)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.8990
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	8 (3.2)	12 (5.0)
Relative Risk (RR) (95% CI)		1.3559 (0.5546, 3.3151)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.5045
Odds Ratio (OR) (95% CI)		1.4131 (0.5543, 3.6027)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.4690
Risk Difference (RD) (95% CI)		0.0149 (-0.0249, 0.0548)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.4623

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Prior CFTR modulator use: yes

	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	16 (6.4)	17 (7.1)
Relative Risk (RR) (95% CI)		1.0326 (0.5235, 2.0367)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9263
Odds Ratio (OR) (95% CI)		1.0625 (0.5090, 2.2175)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8718
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	16 (6.4)	17 (7.1)
Relative Risk (RR) (95% CI)		1.0326 (0.5235, 2.0367)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9263
Odds Ratio (OR) (95% CI)		1.0625 (0.5090, 2.2175)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.8718

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Prior CFTR modulator use: yes

	ELX/TEZ/IVA N = 250 n (%)	VNZ/TEZ/D-IVA N = 241 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	9 (3.6)	6 (2.5)
Relative Risk (RR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	N/C
Odds Ratio (OR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	N/C
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Subjects with at least one Pulmonary Exacerbation	5 (12.8)	12 (27.9)
Relative Risk (RR) (95% CI)		2.4200 (0.9264, 6.3216)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0712
Odds Ratio (OR) (95% CI)		3.0319 (0.8864, 10.3705)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0771
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	1 (2.6)	2 (4.7)
Relative Risk (RR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	N/C
Odds Ratio (OR) (95% CI)		1.5603 (0.0699, 34.8305)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7789
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	1 (2.6)	2 (4.7)
Relative Risk (RR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	N/C
Odds Ratio (OR) (95% CI)		1.5603 (0.0699, 34.8305)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7789
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	1 (2.6)	2 (4.7)
Relative Risk (RR) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	N/C
Odds Ratio (OR) (95% CI)		1.5603 (0.0699, 34.8305)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.7789

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Prior CFTR modulator use: No

	ELX/TEZ/IVA N = 39 n (%)	VNZ/TEZ/D-IVA N = 43 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Subjects with at least one Pulmonary Exacerbation	50 (22.3)	46 (20.7)
Relative Risk (RR) (95% CI)		0.9168 (0.6425, 1.3082)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6320
Odds Ratio (OR) (95% CI)		0.9118 (0.5751, 1.4457)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6947
Risk Difference (RD) (95% CI)		-0.0043 (-0.0821, 0.0735)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.9138
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	5 (2.2)	14 (6.3)
Relative Risk (RR) (95% CI)		2.5751 (0.9341, 7.0992)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.0675
Odds Ratio (OR) (95% CI)		2.6604 (0.9296, 7.6139)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.0682
Risk Difference (RD) (95% CI)		0.0344 (-0.0076, 0.0765)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.1085

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	12 (5.4)	19 (8.6)
Relative Risk (RR) (95% CI)		1.5881 (0.7671, 3.2877)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2128
Odds Ratio (OR) (95% CI)		1.6472 (0.7571, 3.5839)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2083
Risk Difference (RD) (95% CI)		0.0378 (-0.0153, 0.0908)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.1629
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	12 (5.4)	19 (8.6)
Relative Risk (RR) (95% CI)		1.5881 (0.7671, 3.2877)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2128
Odds Ratio (OR) (95% CI)		1.6472 (0.7571, 3.5839)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2083

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Genotype group: F/F

	ELX/TEZ/IVA N = 224 n (%)	VNZ/TEZ/D-IVA N = 222 n (%)
Risk Difference (RD) (95% CI)		0.0378 (-0.0153, 0.0908)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	0.1629
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	7 (3.1)	6 (2.7)
Relative Risk (RR) (95% CI)		0.9551 (0.3123, 2.9211)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.9358
Odds Ratio (OR) (95% CI)		0.9598 (0.3016, 3.0546)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.9447
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Subjects with at least one Pulmonary Exacerbation	2 (10.0)	4 (21.1)
Relative Risk (RR) (95% CI)		2.7190 (0.5777, 12.7974)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2056
Odds Ratio (OR) (95% CI)		2.9746 (0.4223, 20.9544)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.2738
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	1 (5.0)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	1 (5.0)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	1 (5.0)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Genotype group: F/G

	ELX/TEZ/IVA N = 20 n (%)	VNZ/TEZ/D-IVA N = 19 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Subjects with at least one Pulmonary Exacerbation	5 (21.7)	6 (26.1)
Relative Risk (RR) (95% CI)		1.2779 (0.4437, 3.6807)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.6496
Odds Ratio (OR) (95% CI)		1.3457 (0.3339, 5.4237)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.6763
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	2 (8.7)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	3 (13.0)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	3 (13.0)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Genotype group: F/RF

	ELX/TEZ/IVA N = 23 n (%)	VNZ/TEZ/D-IVA N = 23 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	2 (8.7)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Subjects with at least one Pulmonary Exacerbation	2 (9.1)	5 (25.0)
Relative Risk (RR) (95% CI)		2.8863 (0.5453, 15.2774)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	0.2125*
Odds Ratio (OR) (95% CI)		3.9386 (0.6035, 25.7053)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	0.1521
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring Hospitalization	1 (4.5)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics	1 (4.5)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics or Hospitalization	1 (4.5)	0
Relative Risk (RR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		0.0000 (-, -)
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline ppFEV$_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 2.4.1.1.2
Study VX20-121-103: Summary of Number (%) of Patients with at least one Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Genotype group: TCR/non-F

	ELX/TEZ/IVA N = 22 n (%)	VNZ/TEZ/D-IVA N = 20 n (%)
Risk Difference (RD) (95% CI)		N/C
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	N/C
Subjects with at least one Pulmonary Exacerbation Requiring IV Antibiotics but not Hospitalization	0	0
Relative Risk (RR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [1]	-	-
Odds Ratio (OR) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [2]	-	-
Risk Difference (RD) (95% CI)		-
Two-sided P-value (VNZ/TEZ/D-IVA vs ELX/TEZ/IVA), superiority [3]	-	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- [1] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with log link. If the log-binomial model does not converge, modified Poisson regression model with log link is used and indicated by '*'.
- [2] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with logit link.
- [3] Generalized Linear Model: treatment group, age at screening (<18 vs ≥18 years), genotype, and baseline $ppFEV_1$ and baseline sweat chloride as covariates; Distribution: binomial with identity link.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.
- N/C: model does not converge.

Table 14.2.8.1.1
Summary of CFQ-R Respiratory Domain Score and Change from Baseline at Each Visit
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline	n	282	280
	Mean (SD)	85.6 (13.2)	85.7 (13.2)
	Median	88.9	88.9
	Min, max	27.8, 100.0	33.3, 100.0
Week 8	n	287	280
	Mean (SD)	85.0 (15.9)	84.8 (16.3)
	Median	88.9	88.9
	Min, max	16.7, 100.0	16.7, 100.0
Change at Week 8	n	280	277
	Mean (SD)	-0.6 (16.7)	-1.0 (15.5)
	Median	0.0	0.0
	Min, max	-77.8, 58.3	-66.7, 44.4
Week 16	n	282	274
	Mean (SD)	85.2 (16.5)	85.4 (16.1)
	Median	88.9	88.9
	Min, max	0.0, 100.0	16.7, 100.0
Change at Week 16	n	275	271
	Mean (SD)	-0.4 (15.3)	-0.3 (15.8)
	Median	0.0	0.0
	Min, max	-100.0, 58.3	-72.2, 38.9

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.1.1
Summary of CFQ-R Respiratory Domain Score and Change from Baseline at Each Visit
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 24	n	283	271
	Mean (SD)	83.5 (16.8)	83.9 (15.2)
	Median	88.9	88.9
	Min, max	11.1, 100.0	33.3, 100.0
Change at Week 24	n	276	268
	Mean (SD)	-2.2 (16.1)	-1.6 (13.7)
	Median	0.0	0.0
	Min, max	-61.1, 55.6	-50.0, 55.6
Week 52	n	277	264
	Mean (SD)	84.9 (16.9)	87.2 (13.2)
	Median	88.9	88.9
	Min, max	16.7, 100.0	38.9, 100.0
Change at Week 52	n	270	260
	Mean (SD)	-0.8 (17.3)	1.6 (13.4)
	Median	0.0	0.0
	Min, max	-72.2, 58.3	-44.4, 55.6

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Physical

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline	n	282	280
	Mean (SD)	80.7 (20.3)	82.8 (18.6)
	Median	87.5	87.5
	Min, max	8.3, 100.0	4.2, 100.0
Week 8	n	286	280
	Mean (SD)	79.9 (21.5)	82.4 (20.2)
	Median	87.5	87.5
	Min, max	0.0, 100.0	8.3, 100.0
Change at Week 8	n	280	277
	Mean (SD)	-0.7 (16.2)	-0.8 (15.0)
	Median	0.0	0.0
	Min, max	-70.8, 57.1	-87.5, 54.2
Week 16	n	283	274
	Mean (SD)	81.4 (21.1)	82.7 (20.1)
	Median	87.5	87.5
	Min, max	4.2, 100.0	8.3, 100.0
Change at Week 16	n	276	271
	Mean (SD)	1.0 (15.4)	-0.3 (14.4)
	Median	0.0	0.0
	Min, max	-66.7, 57.1	-79.2, 54.2

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Physical

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 24	n	282	271
	Mean (SD)	80.2 (22.5)	82.3 (19.8)
	Median	87.5	87.5
	Min, max	0.0, 100.0	8.3, 100.0
Change at Week 24	n	275	268
	Mean (SD)	-0.5 (16.9)	-0.5 (13.3)
	Median	0.0	0.0
	Min, max	-83.3, 57.1	-70.8, 45.8
Week 52	n	277	265
	Mean (SD)	81.4 (20.4)	84.4 (18.2)
	Median	87.5	91.7
	Min, max	4.2, 100.0	12.5, 100.0
Change at Week 52	n	270	261
	Mean (SD)	1.0 (16.4)	1.4 (12.4)
	Median	0.0	0.0
	Min, max	-58.3, 66.7	-50.0, 50.0

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Vitality

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline	n	269	266
	Mean (SD)	66.8 (19.0)	66.8 (18.9)
	Median	66.7	66.7
	Min, max	8.3, 100.0	8.3, 100.0
Week 8	n	274	267
	Mean (SD)	64.2 (20.8)	66.7 (20.6)
	Median	66.7	66.7
	Min, max	8.3, 100.0	0.0, 100.0
Change at Week 8	n	269	264
	Mean (SD)	-2.4 (16.5)	-0.3 (15.8)
	Median	0.0	0.0
	Min, max	-66.7, 50.0	-58.3, 50.0
Week 16	n	271	261
	Mean (SD)	64.3 (20.2)	65.7 (21.0)
	Median	66.7	66.7
	Min, max	0.0, 100.0	8.3, 100.0
Change at Week 16	n	265	258
	Mean (SD)	-2.1 (14.7)	-1.2 (16.4)
	Median	0.0	0.0
	Min, max	-66.7, 41.7	-50.0, 50.0

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Vitality

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 24	n	268	257
	Mean (SD)	63.0 (21.3)	65.2 (20.6)
	Median	66.7	66.7
	Min, max	0.0, 100.0	8.3, 100.0
Change at Week 24	n	262	255
	Mean (SD)	-3.7 (17.4)	-1.9 (16.8)
	Median	0.0	0.0
	Min, max	-100.0, 41.7	-58.3, 41.7
Week 52	n	266	251
	Mean (SD)	64.9 (19.9)	67.7 (18.4)
	Median	66.7	66.7
	Min, max	8.3, 100.0	0.0, 100.0
Change at Week 52	n	260	248
	Mean (SD)	-1.5 (16.3)	0.5 (15.1)
	Median	0.0	0.0
	Min, max	-41.7, 41.7	-33.3, 50.0

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Emotion

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline	n	282	280
	Mean (SD)	81.8 (16.3)	81.8 (17.8)
	Median	86.7	86.7
	Min, max	26.7, 100.0	6.7, 100.0
Week 8	n	286	280
	Mean (SD)	82.3 (16.4)	82.9 (17.4)
	Median	86.7	86.7
	Min, max	13.3, 100.0	13.3, 100.0
Change at Week 8	n	280	277
	Mean (SD)	0.5 (10.7)	1.0 (11.6)
	Median	0.0	0.0
	Min, max	-60.0, 33.3	-60.0, 40.0
Week 16	n	283	274
	Mean (SD)	82.9 (15.8)	81.3 (18.1)
	Median	86.7	86.7
	Min, max	20.0, 100.0	26.7, 100.0
Change at Week 16	n	276	271
	Mean (SD)	1.0 (11.2)	-0.5 (12.3)
	Median	0.0	0.0
	Min, max	-53.3, 33.3	-40.0, 46.7

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Emotion

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 24	n	282	271
	Mean (SD)	81.9 (16.5)	81.3 (18.4)
	Median	86.7	86.7
	Min, max	20.0, 100.0	26.7, 100.0
Change at Week 24	n	275	268
	Mean (SD)	0.0 (13.2)	-0.6 (11.8)
	Median	0.0	0.0
	Min, max	-66.7, 40.0	-46.7, 46.7
Week 52	n	277	265
	Mean (SD)	81.7 (17.0)	81.9 (18.3)
	Median	86.7	86.7
	Min, max	20.0, 100.0	0.0, 100.0
Change at Week 52	n	270	261
	Mean (SD)	-0.4 (14.0)	0.3 (14.6)
	Median	0.0	0.0
	Min, max	-53.3, 46.7	-58.3, 62.5

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Body

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline	n	282	280
	Mean (SD)	75.8 (23.7)	78.6 (21.4)
	Median	77.8	77.8
	Min, max	0.0, 100.0	0.0, 100.0
Week 8	n	287	279
	Mean (SD)	78.0 (22.9)	79.3 (22.3)
	Median	77.8	88.9
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 8	n	280	276
	Mean (SD)	2.1 (15.0)	0.6 (14.7)
	Median	0.0	0.0
	Min, max	-88.9, 55.6	-66.7, 66.7
Week 16	n	283	273
	Mean (SD)	78.4 (20.7)	79.5 (21.2)
	Median	77.8	88.9
	Min, max	11.1, 100.0	11.1, 100.0
Change at Week 16	n	276	270
	Mean (SD)	2.2 (14.8)	0.7 (13.3)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-55.6, 44.4

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Body

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 24	n	283	271
	Mean (SD)	79.1 (21.4)	79.3 (22.3)
	Median	88.9	88.9
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 24	n	276	268
	Mean (SD)	3.0 (14.8)	0.9 (15.9)
	Median	0.0	0.0
	Min, max	-33.3, 55.6	-88.9, 44.4
Week 52	n	277	265
	Mean (SD)	78.6 (21.1)	79.6 (21.8)
	Median	77.8	88.9
	Min, max	0.0, 100.0	11.1, 100.0
Change at Week 52	n	270	261
	Mean (SD)	2.5 (17.1)	1.3 (16.5)
	Median	0.0	0.0
	Min, max	-55.6, 66.7	-77.8, 55.6

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Eat

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline	n	282	280
	Mean (SD)	92.8 (14.5)	94.2 (11.9)
	Median	100.0	100.0
	Min, max	22.2, 100.0	44.4, 100.0
Week 8	n	287	280
	Mean (SD)	92.5 (14.3)	94.0 (13.1)
	Median	100.0	100.0
	Min, max	33.3, 100.0	0.0, 100.0
Change at Week 8	n	280	277
	Mean (SD)	0.0 (11.5)	-0.2 (10.3)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-44.4, 44.4
Week 16	n	283	274
	Mean (SD)	92.6 (13.8)	93.1 (15.1)
	Median	100.0	100.0
	Min, max	44.4, 100.0	0.0, 100.0
Change at Week 16	n	276	271
	Mean (SD)	0.1 (11.6)	-1.2 (12.2)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-100.0, 44.4

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Eat

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 24	n	283	271
	Mean (SD)	92.5 (14.9)	92.4 (15.8)
	Median	100.0	100.0
	Min, max	22.2, 100.0	0.0, 100.0
Change at Week 24	n	276	268
	Mean (SD)	0.0 (12.8)	-1.8 (11.5)
	Median	0.0	0.0
	Min, max	-66.7, 66.7	-77.8, 33.3
Week 52	n	277	265
	Mean (SD)	92.9 (14.9)	93.4 (13.5)
	Median	100.0	100.0
	Min, max	33.3, 100.0	11.1, 100.0
Change at Week 52	n	270	261
	Mean (SD)	0.5 (13.3)	-1.0 (11.4)
	Median	0.0	0.0
	Min, max	-66.7, 44.4	-44.4, 55.6

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Treatment Burden

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline	n	282	280
	Mean (SD)	70.3 (19.7)	71.7 (19.1)
	Median	66.7	66.7
	Min, max	22.2, 100.0	22.2, 100.0
Week 8	n	287	279
	Mean (SD)	71.1 (20.6)	73.4 (19.6)
	Median	66.7	77.8
	Min, max	0.0, 100.0	11.1, 100.0
Change at Week 8	n	280	276
	Mean (SD)	0.6 (14.5)	1.9 (12.8)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-55.6, 44.4
Week 16	n	283	274
	Mean (SD)	72.1 (20.0)	73.7 (19.6)
	Median	66.7	77.8
	Min, max	22.2, 100.0	11.1, 100.0
Change at Week 16	n	276	271
	Mean (SD)	1.9 (14.9)	2.1 (13.5)
	Median	0.0	0.0
	Min, max	-66.7, 44.4	-44.4, 55.6

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Treatment Burden

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 24	n	283	271
	Mean (SD)	70.9 (20.7)	73.6 (19.9)
	Median	66.7	77.8
	Min, max	11.1, 100.0	22.2, 100.0
Change at Week 24	n	276	268
	Mean (SD)	0.8 (15.5)	2.2 (13.6)
	Median	0.0	0.0
	Min, max	-66.7, 55.6	-55.6, 44.4
Week 52	n	277	265
	Mean (SD)	73.5 (19.9)	75.9 (19.3)
	Median	77.8	77.8
	Min, max	22.2, 100.0	11.1, 100.0
Change at Week 52	n	270	261
	Mean (SD)	3.4 (16.6)	4.4 (15.3)
	Median	0.0	0.0
	Min, max	-55.6, 55.6	-44.4, 55.6

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Health Perceptions

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline	n	269	266
	Mean (SD)	71.5 (19.6)	72.8 (20.1)
	Median	66.7	77.8
	Min, max	11.1, 100.0	0.0, 100.0
Week 8	n	275	266
	Mean (SD)	71.4 (20.1)	71.9 (20.0)
	Median	66.7	66.7
	Min, max	0.0, 100.0	11.1, 100.0
Change at Week 8	n	269	263
	Mean (SD)	-0.1 (15.8)	-0.9 (13.1)
	Median	0.0	0.0
	Min, max	-77.8, 44.4	-44.4, 44.4
Week 16	n	271	260
	Mean (SD)	71.5 (19.6)	72.0 (20.2)
	Median	66.7	66.7
	Min, max	11.1, 100.0	22.2, 100.0
Change at Week 16	n	265	257
	Mean (SD)	0.2 (15.4)	-1.0 (14.6)
	Median	0.0	0.0
	Min, max	-66.7, 44.4	-66.7, 33.3

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Health Perceptions

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 24	n	269	257
	Mean (SD)	70.0 (21.4)	72.4 (20.8)
	Median	66.7	66.7
	Min, max	0.0, 100.0	11.1, 100.0
Change at Week 24	n	263	255
	Mean (SD)	-1.4 (16.9)	-0.7 (15.3)
	Median	0.0	0.0
	Min, max	-100.0, 44.4	-66.7, 33.3
Week 52	n	266	251
	Mean (SD)	74.0 (19.4)	73.4 (19.7)
	Median	77.8	66.7
	Min, max	0.0, 100.0	11.1, 100.0
Change at Week 52	n	260	248
	Mean (SD)	2.4 (15.8)	0.5 (14.8)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-66.7, 44.4

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Weight

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline	n	266	266
	Mean (SD)	88.5 (24.1)	84.3 (27.0)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Week 8	n	270	266
	Mean (SD)	87.2 (25.7)	84.7 (27.3)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 8	n	266	263
	Mean (SD)	-1.4 (19.5)	0.0 (22.4)
	Median	0.0	0.0
	Min, max	-100.0, 66.7	-66.7, 100.0
Week 16	n	264	261
	Mean (SD)	86.2 (27.6)	85.7 (27.3)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 16	n	260	258
	Mean (SD)	-2.4 (21.9)	0.6 (23.4)
	Median	0.0	0.0
	Min, max	-100.0, 66.7	-100.0, 66.7

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Weight

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 24	n	264	257
	Mean (SD)	86.2 (28.0)	84.8 (28.1)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 24	n	260	255
	Mean (SD)	-2.3 (20.4)	0.7 (22.0)
	Median	0.0	0.0
	Min, max	-100.0, 66.7	-66.7, 100.0
Week 52	n	266	250
	Mean (SD)	87.1 (26.3)	84.3 (28.0)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at Week 52	n	257	247
	Mean (SD)	-1.8 (22.6)	-0.1 (22.2)
	Median	0.0	0.0
	Min, max	-100.0, 66.7	-66.7, 66.7

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Digestion

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline	n	282	280
	Mean (SD)	81.1 (17.1)	82.1 (18.4)
	Median	77.8	88.9
	Min, max	33.3, 100.0	22.2, 100.0
Week 8	n	287	279
	Mean (SD)	81.5 (18.7)	81.0 (18.7)
	Median	88.9	88.9
	Min, max	0.0, 100.0	33.3, 100.0
Change at Week 8	n	280	276
	Mean (SD)	0.4 (14.4)	-1.0 (14.9)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-55.6, 66.7
Week 16	n	282	274
	Mean (SD)	80.9 (19.4)	81.0 (18.2)
	Median	88.9	88.9
	Min, max	0.0, 100.0	22.2, 100.0
Change at Week 16	n	275	271
	Mean (SD)	-0.1 (15.2)	-1.1 (15.0)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-44.4, 66.7

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Digestion

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 24	n	282	271
	Mean (SD)	81.0 (19.6)	80.2 (19.5)
	Median	88.9	77.8
	Min, max	0.0, 100.0	22.2, 100.0
Change at Week 24	n	275	268
	Mean (SD)	0.2 (15.1)	-2.0 (15.3)
	Median	0.0	0.0
	Min, max	-66.7, 44.4	-66.7, 44.4
Week 52	n	277	264
	Mean (SD)	79.6 (20.3)	79.8 (19.1)
	Median	88.9	77.8
	Min, max	11.1, 100.0	0.0, 100.0
Change at Week 52	n	270	260
	Mean (SD)	-1.5 (15.7)	-2.4 (16.1)
	Median	0.0	0.0
	Min, max	-44.4, 44.4	-66.7, 55.6

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Role

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline	n	269	266
	Mean (SD)	86.6 (15.6)	86.7 (16.4)
	Median	91.7	91.7
	Min, max	25.0, 100.0	8.3, 100.0
Week 8	n	275	265
	Mean (SD)	86.4 (16.1)	87.4 (16.3)
	Median	91.7	91.7
	Min, max	25.0, 100.0	8.3, 100.0
Change at Week 8	n	269	262
	Mean (SD)	-0.2 (12.9)	0.3 (13.7)
	Median	0.0	0.0
	Min, max	-50.0, 41.7	-66.7, 58.3
Week 16	n	269	261
	Mean (SD)	86.9 (16.6)	86.8 (16.5)
	Median	91.7	91.7
	Min, max	25.0, 100.0	16.7, 100.0
Change at Week 16	n	263	258
	Mean (SD)	0.3 (13.6)	0.0 (14.1)
	Median	0.0	0.0
	Min, max	-66.7, 41.7	-66.7, 66.7

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Role

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 24	n	269	256
	Mean (SD)	86.0 (18.0)	86.6 (16.9)
	Median	91.7	91.7
	Min, max	0.0, 100.0	8.3, 100.0
Change at Week 24	n	263	254
	Mean (SD)	-0.4 (16.4)	-0.3 (14.4)
	Median	0.0	0.0
	Min, max	-91.7, 50.0	-66.7, 66.7
Week 52	n	266	250
	Mean (SD)	87.1 (17.1)	89.0 (14.0)
	Median	91.7	91.7
	Min, max	0.0, 100.0	33.3, 100.0
Change at Week 52	n	260	247
	Mean (SD)	0.6 (15.1)	1.7 (13.3)
	Median	0.0	0.0
	Min, max	-75.0, 41.7	-41.7, 66.7

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Baseline	n	282	280
	Mean (SD)	72.5 (17.8)	75.0 (17.8)
	Median	72.2	77.8
	Min, max	11.1, 100.0	23.8, 100.0
Week 8	n	287	279
	Mean (SD)	73.6 (17.5)	75.8 (17.7)
	Median	77.8	77.8
	Min, max	22.2, 100.0	27.8, 100.0
Change at Week 8	n	280	276
	Mean (SD)	1.0 (13.4)	0.5 (13.8)
	Median	0.0	0.0
	Min, max	-44.4, 44.4	-66.7, 44.4
Week 16	n	283	273
	Mean (SD)	74.7 (17.2)	76.3 (18.2)
	Median	77.8	77.8
	Min, max	22.2, 100.0	22.2, 100.0
Change at Week 16	n	276	270
	Mean (SD)	2.3 (13.1)	1.1 (14.7)
	Median	0.0	0.0
	Min, max	-50.0, 44.4	-66.7, 47.6

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.6
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Baseline at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

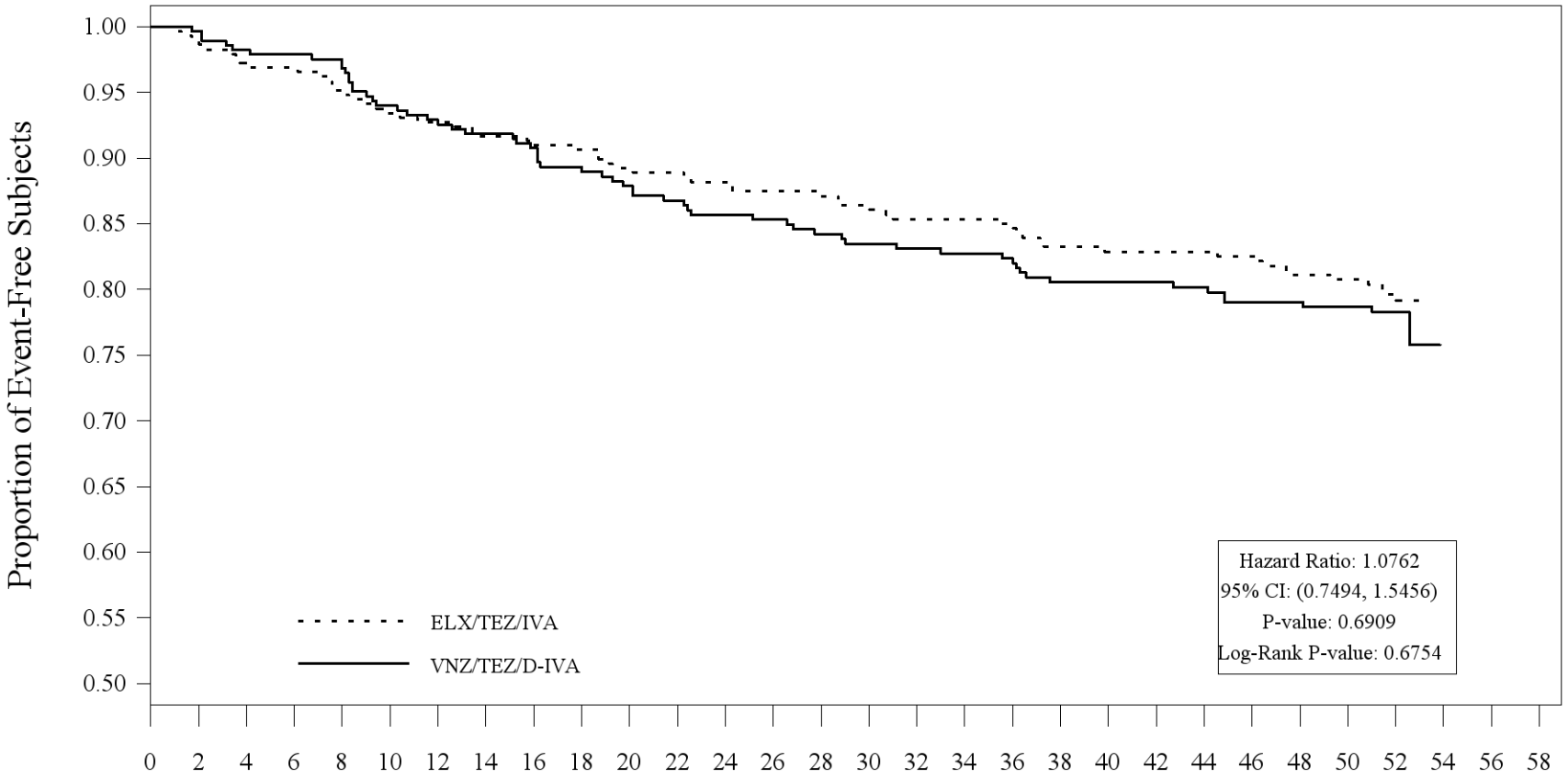
Domain: Social

Visit	Statistics	ELX/TEZ/IVA N = 289	VNZ/TEZ/D-IVA N = 284
Week 24	n	283	271
	Mean (SD)	73.3 (18.4)	77.5 (16.9)
	Median	77.8	77.8
	Min, max	5.6, 100.0	27.8, 100.0
Change at Week 24	n	276	268
	Mean (SD)	1.0 (14.3)	2.2 (13.6)
	Median	0.0	0.0
	Min, max	-44.4, 47.6	-50.0, 44.4
Week 52	n	277	265
	Mean (SD)	76.5 (18.1)	79.6 (17.5)
	Median	77.8	83.3
	Min, max	5.6, 100.0	27.8, 100.0
Change at Week 52	n	270	261
	Mean (SD)	4.1 (14.6)	4.3 (13.9)
	Median	5.6	0.0
	Min, max	-50.0, 52.4	-50.0, 76.2

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.

Figure 2.2.1.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52
Full Analysis Set

Zusatzanalysen zur Studie VX20-121-103



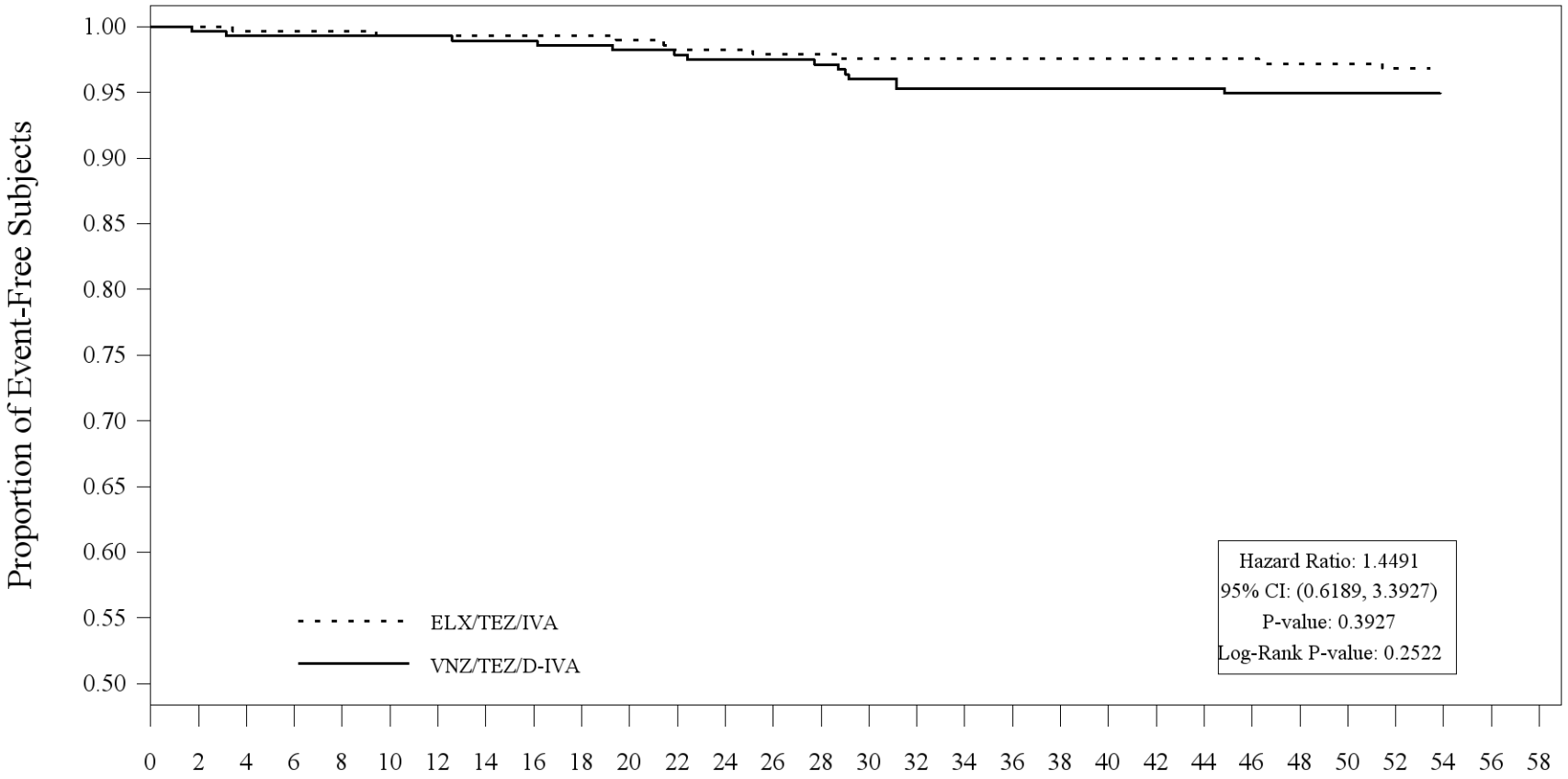
ELX/TEZ/IVA - Number of patients					
at risk	289	267	250	240	228
with event(s)	0	21	34	44	54
censored	0	1	5	5	7
VNZ/TEZ/D-IVA - Number of patients					
at risk	284	260	235	224	212
with event(s)	0	21	40	50	58
censored	0	3	9	10	14

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Zusatzanalysen zur Studie VX20-121-103

Figure 2.2.1.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52
Full Analysis Set

Zusatzanalysen zur Studie VX20-121-103

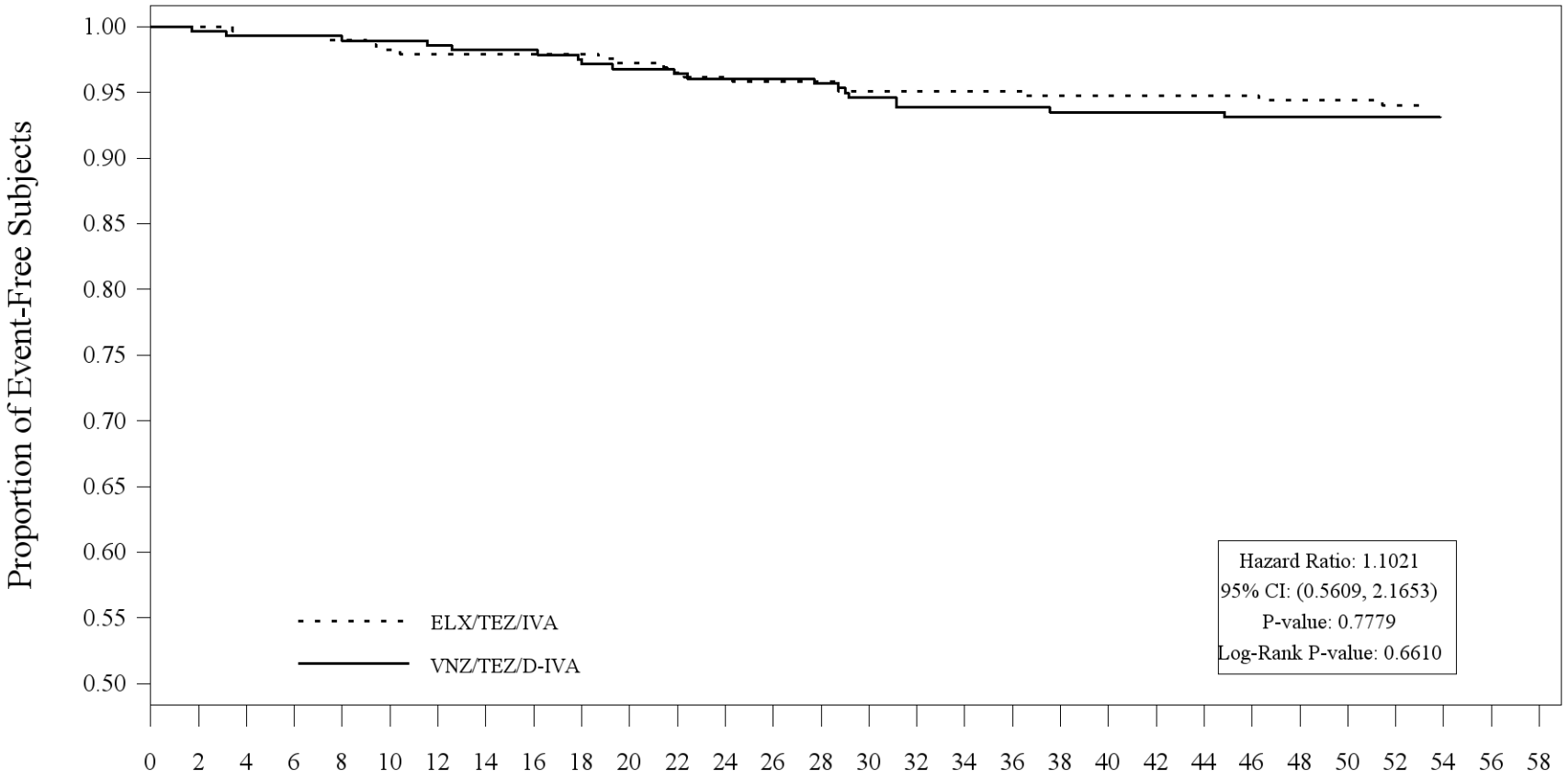


ELX/TEZ/IVA - Number of patients at risk	289	286	279	276	274
with event(s)	0	2	5	7	8
censored	0	1	5	6	7
VNZ/TEZ/D-IVA - Number of patients at risk	284	278	268	260	255
with event(s)	0	2	7	13	14
censored	0	4	9	11	15

Zusatzanalysen zur Studie VX20-121-103

Figure 2.2.1.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52
Full Analysis Set

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	289	282	273	269	266
with event(s)	0	6	11	14	16
censored	0	1	5	6	7
VNZ/TEZ/D-IVA - Number of patients					
at risk	284	276	264	256	250
with event(s)	0	4	11	17	19
censored	0	4	9	11	15

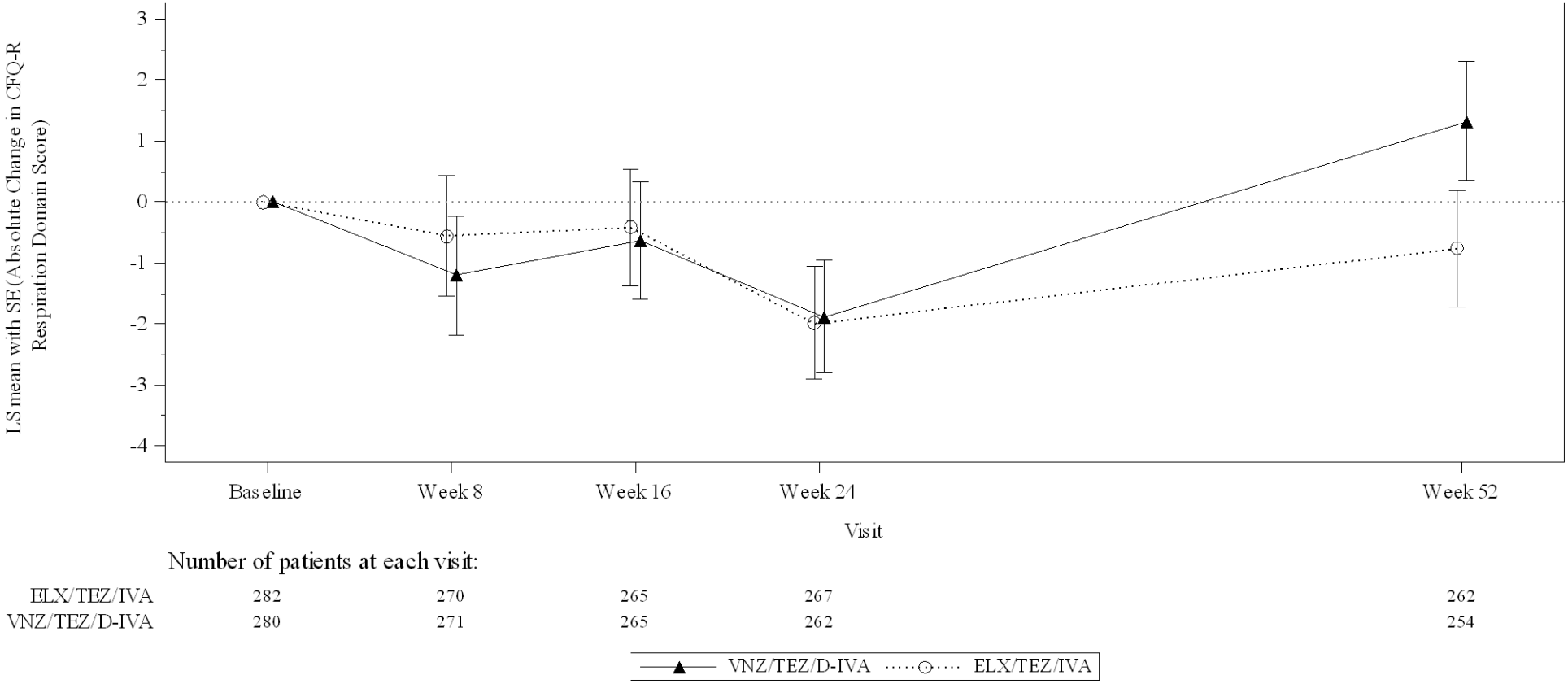
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

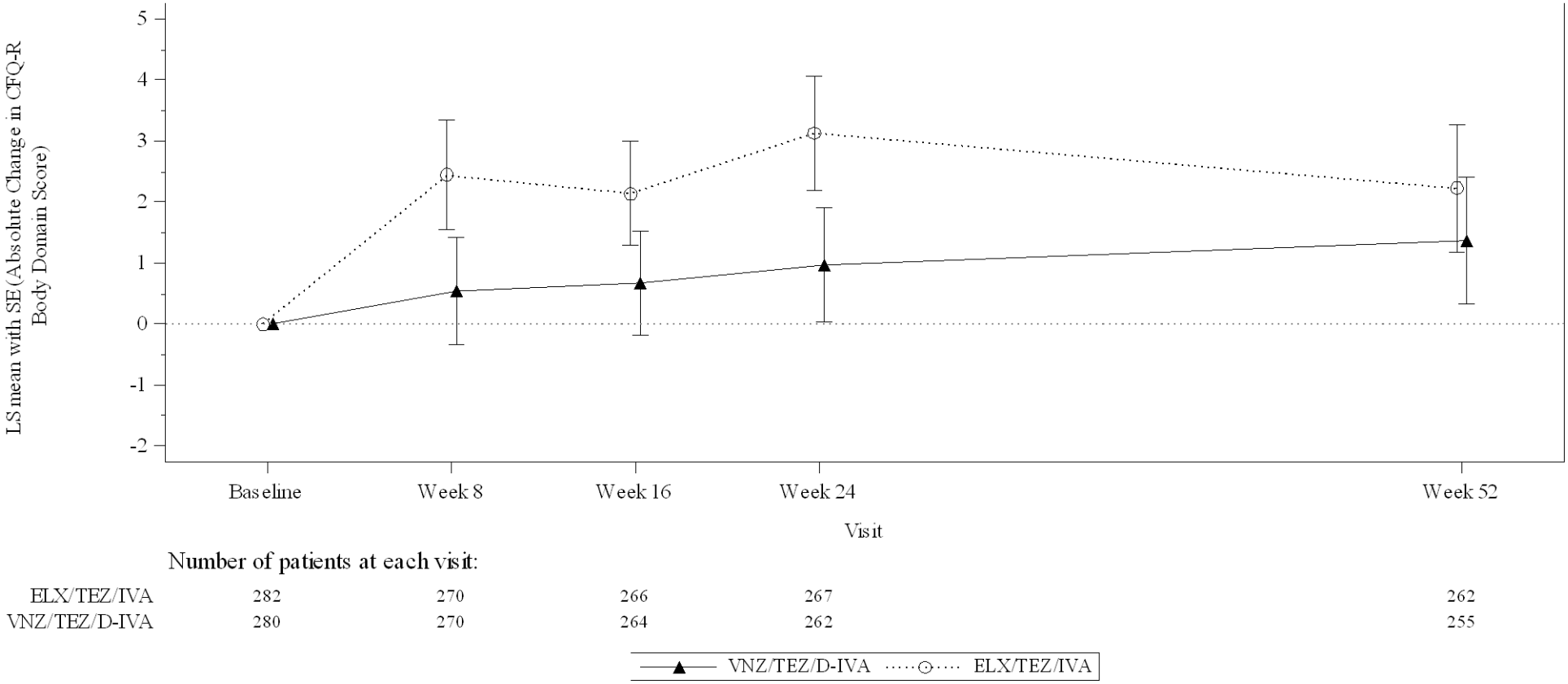
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Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

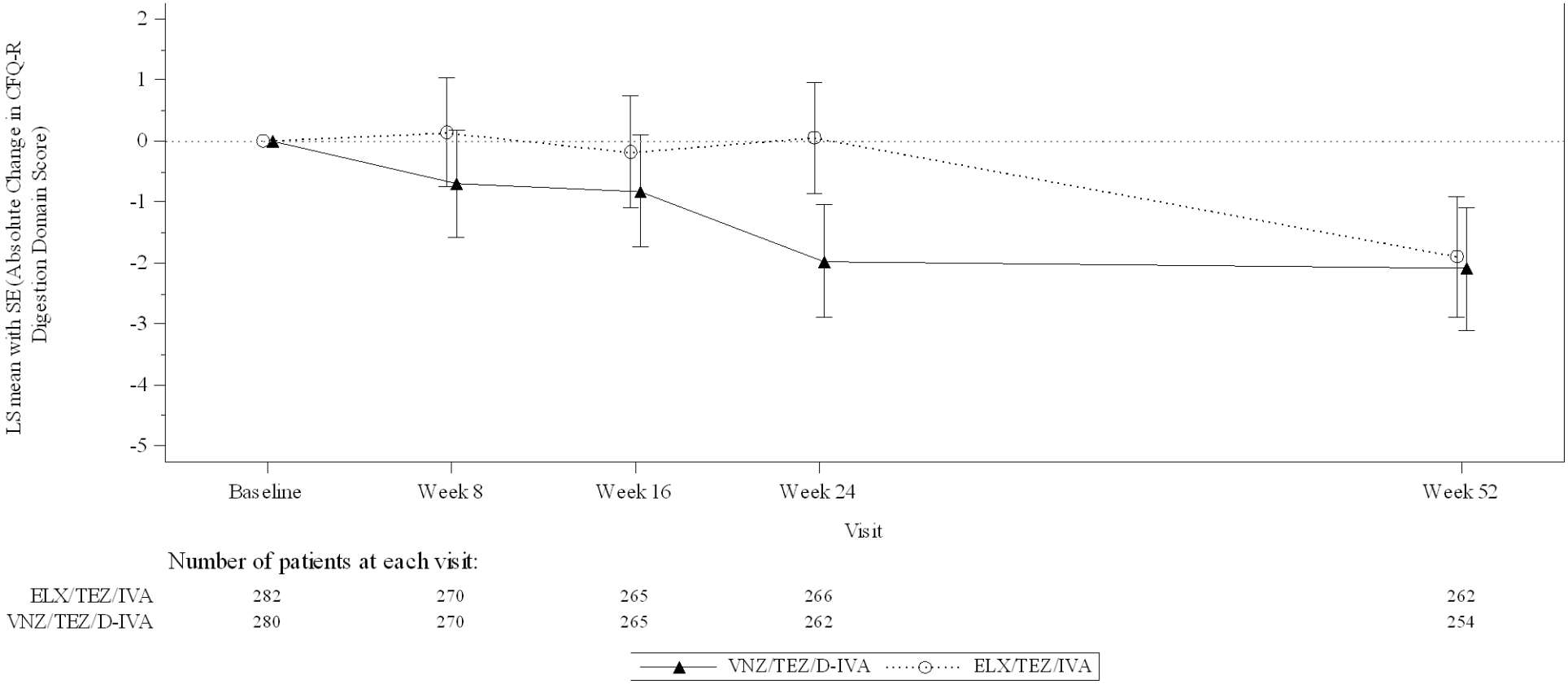
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Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

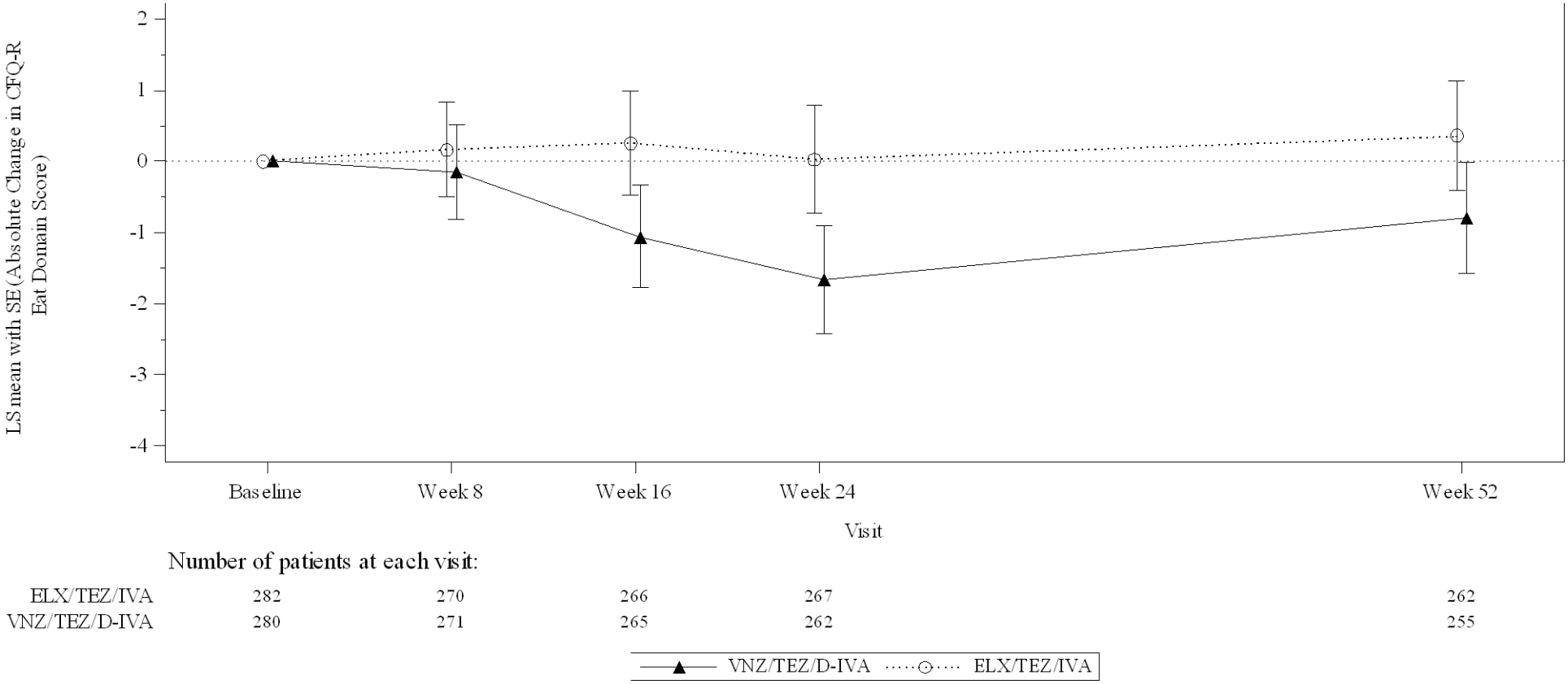
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Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



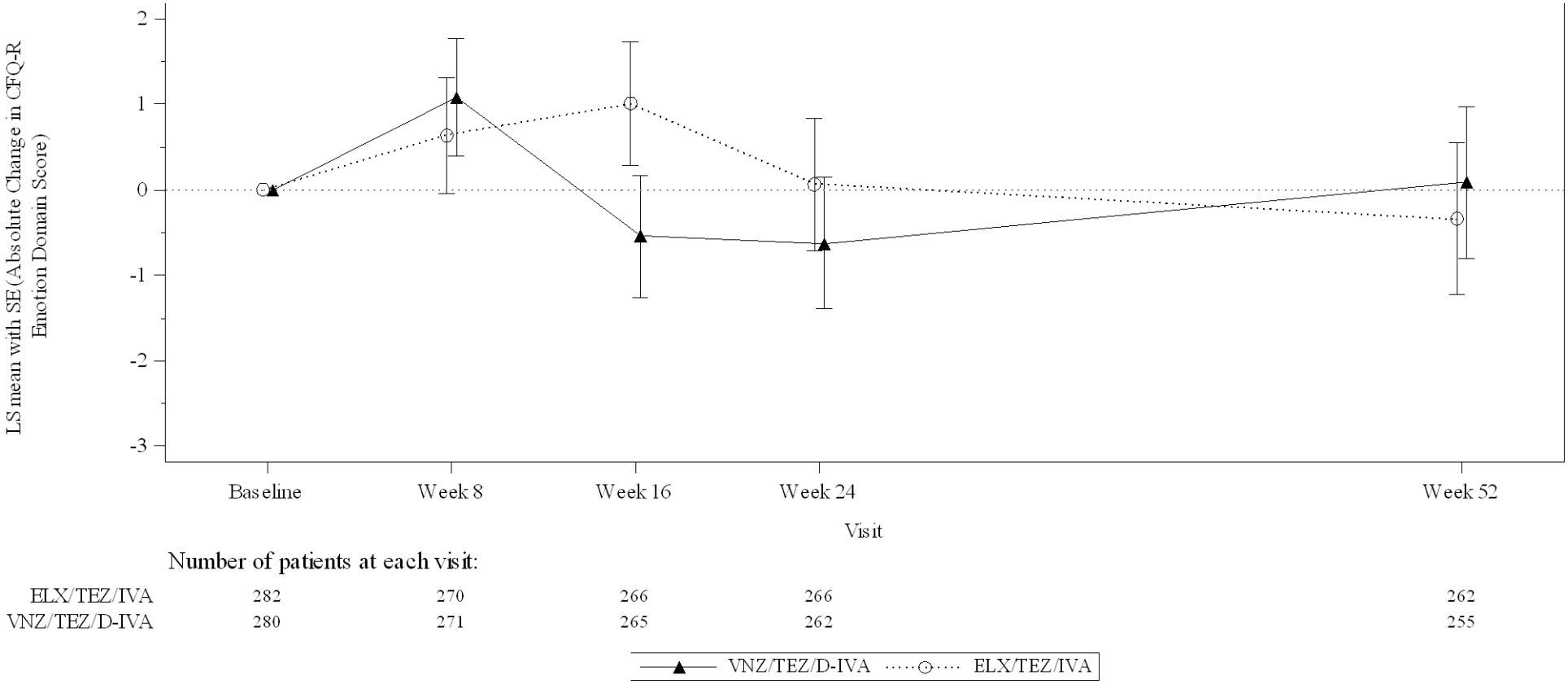
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



Number of patients at each visit:

	Baseline	Week 8	Week 16	Week 24	Week 52
ELX/TEZ/IVA	282	270	266	266	262
VNZ/TEZ/D-IVA	280	271	265	262	255

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

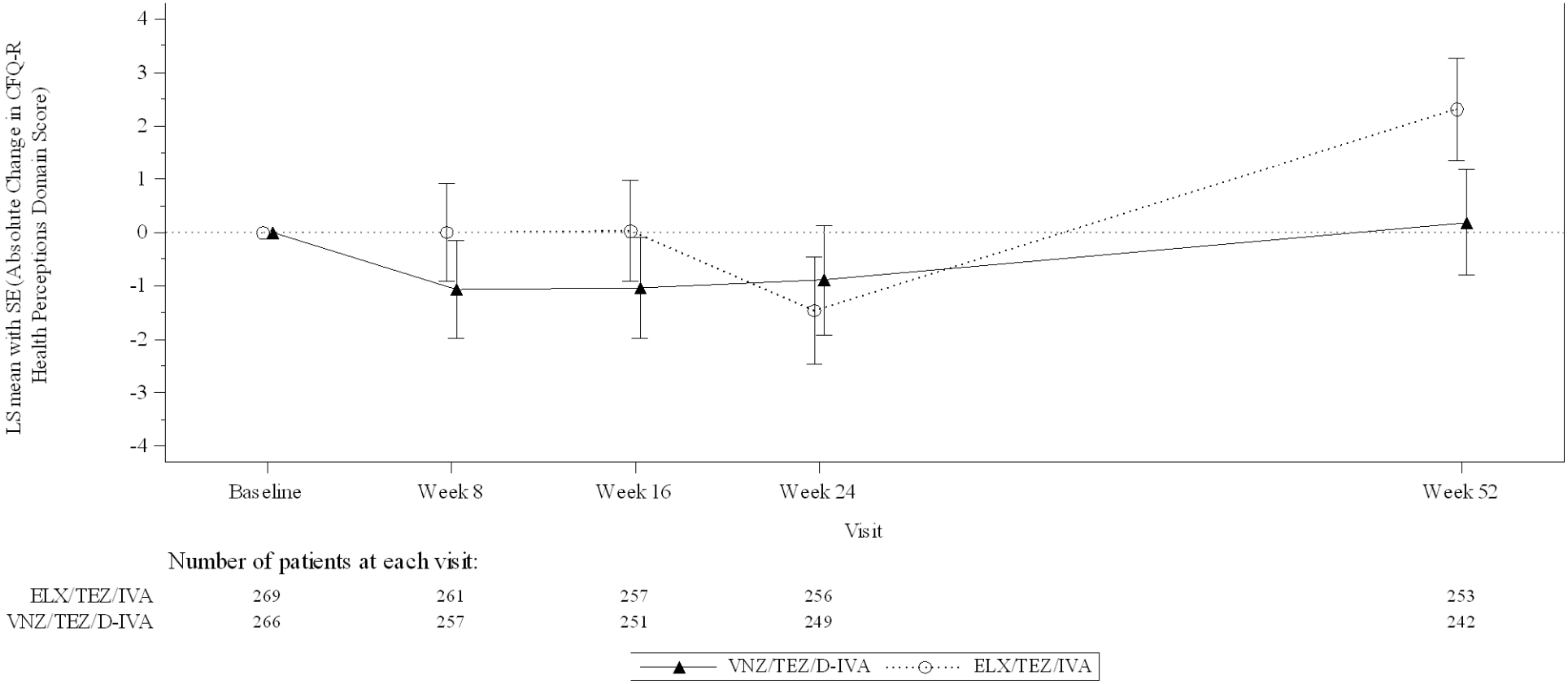
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Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

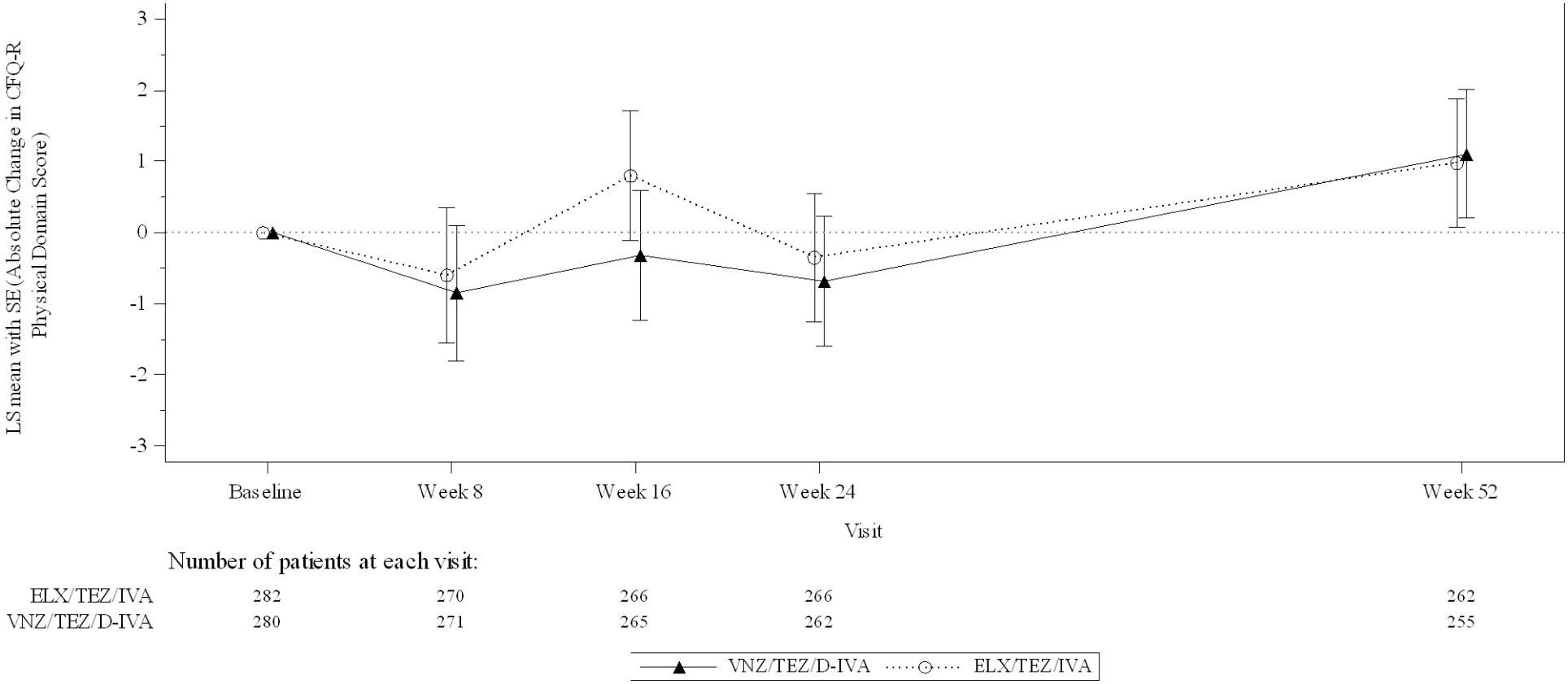
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Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

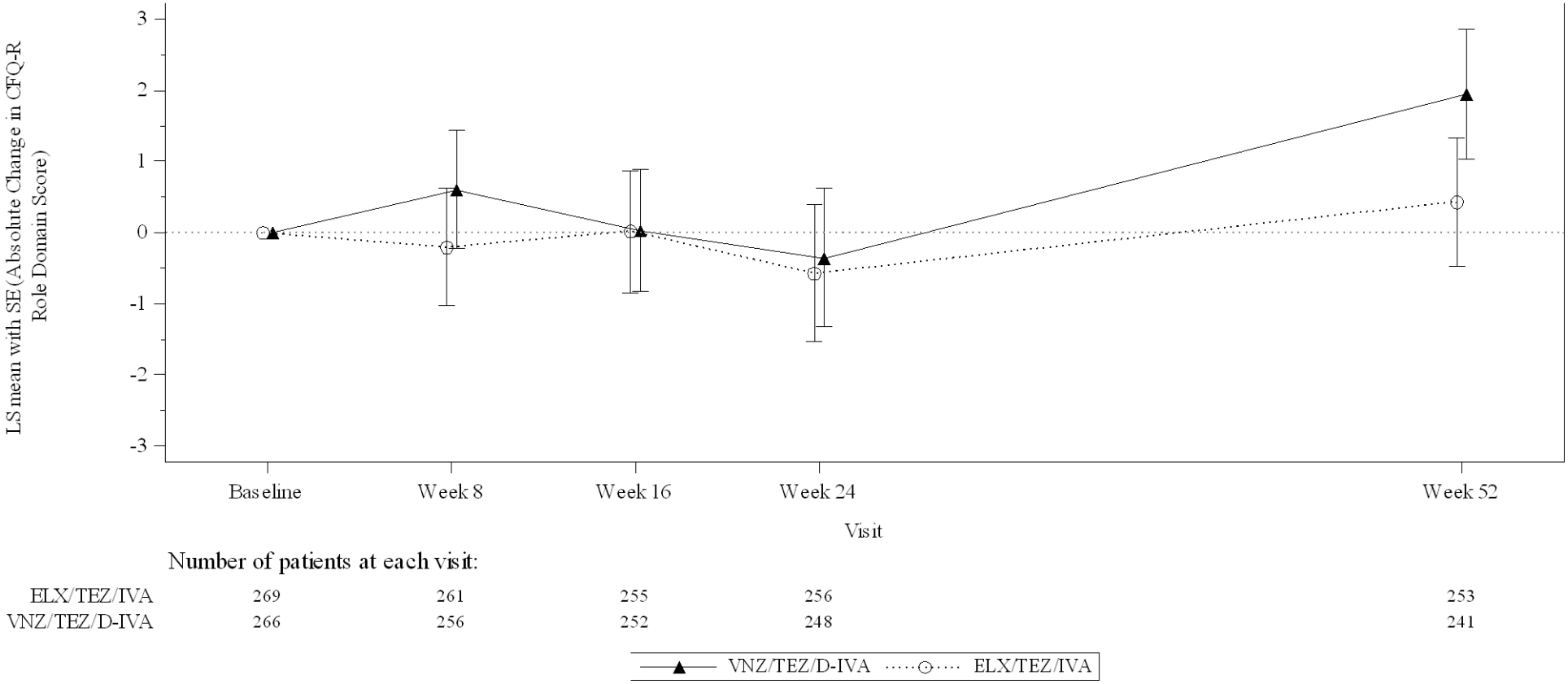
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Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

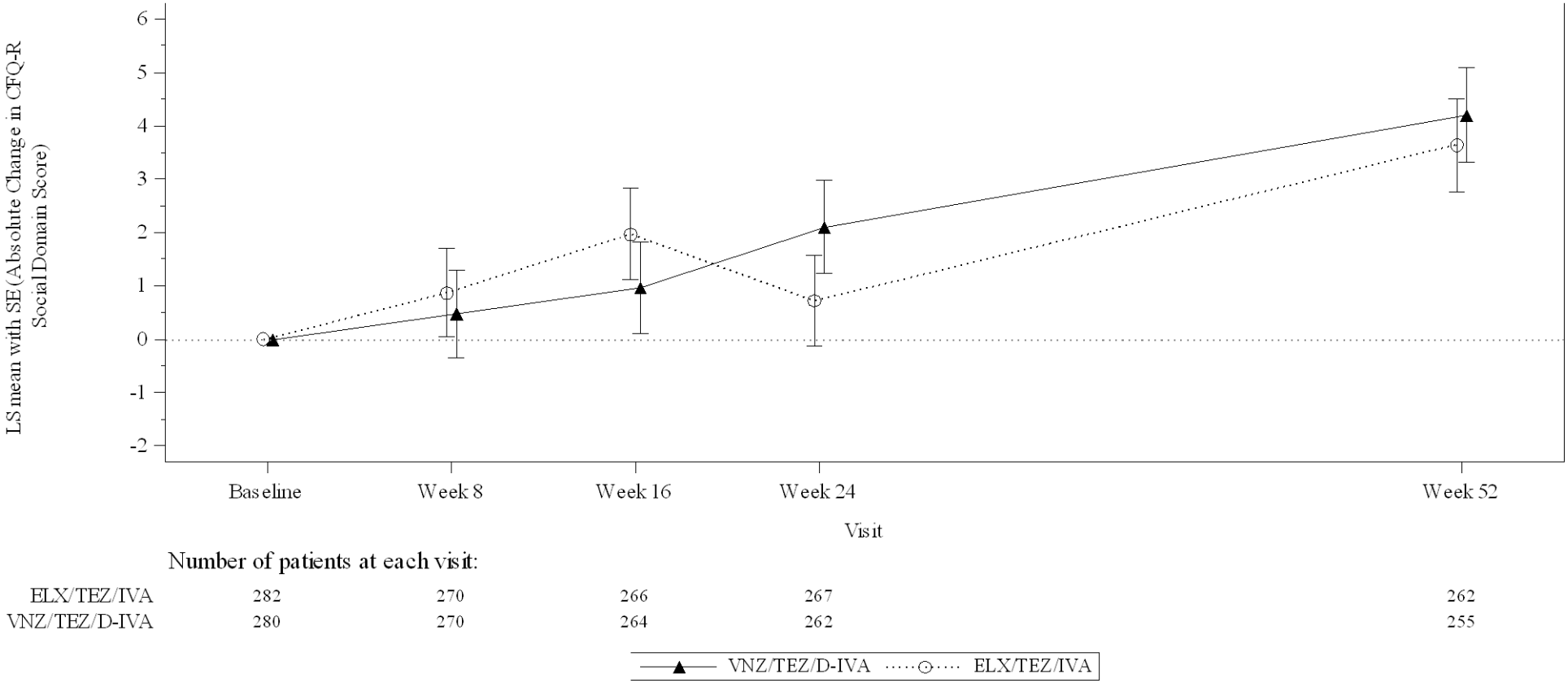
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Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

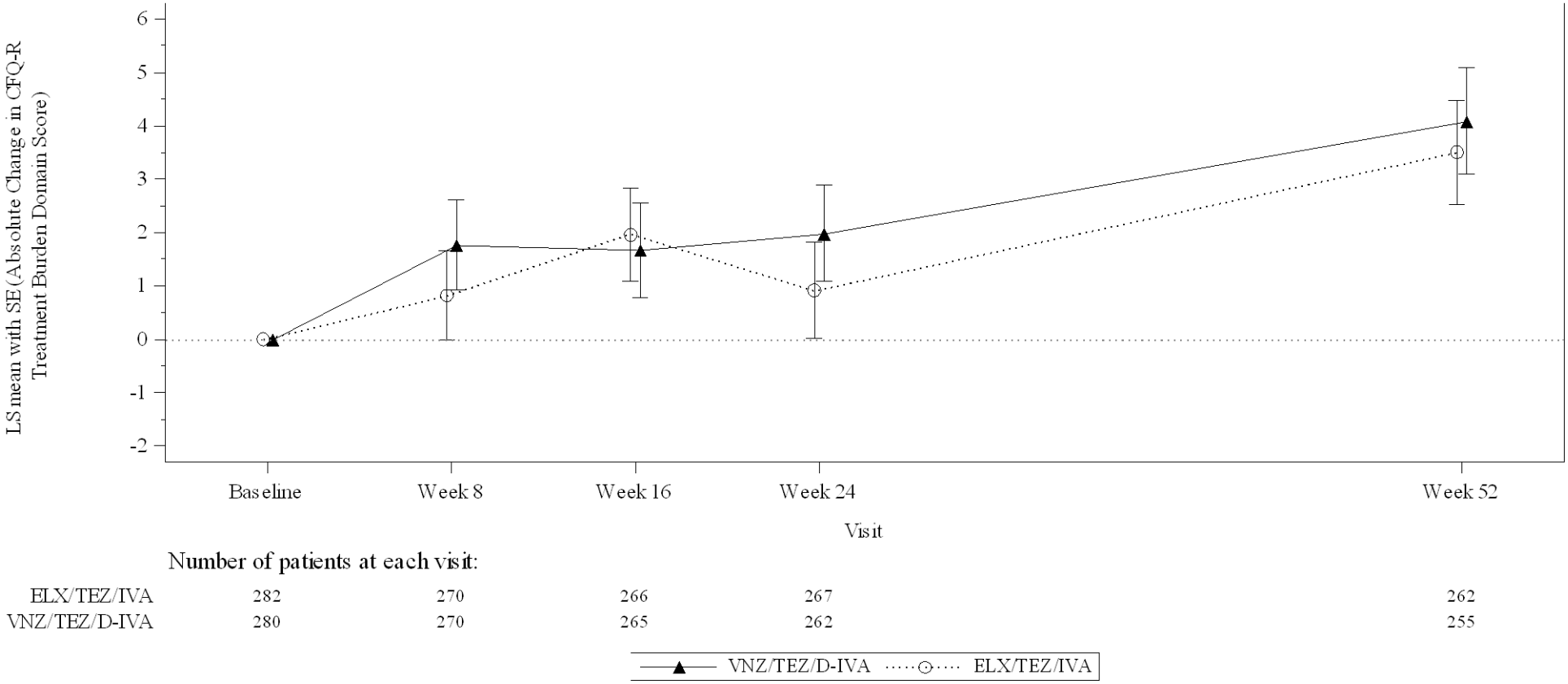
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Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

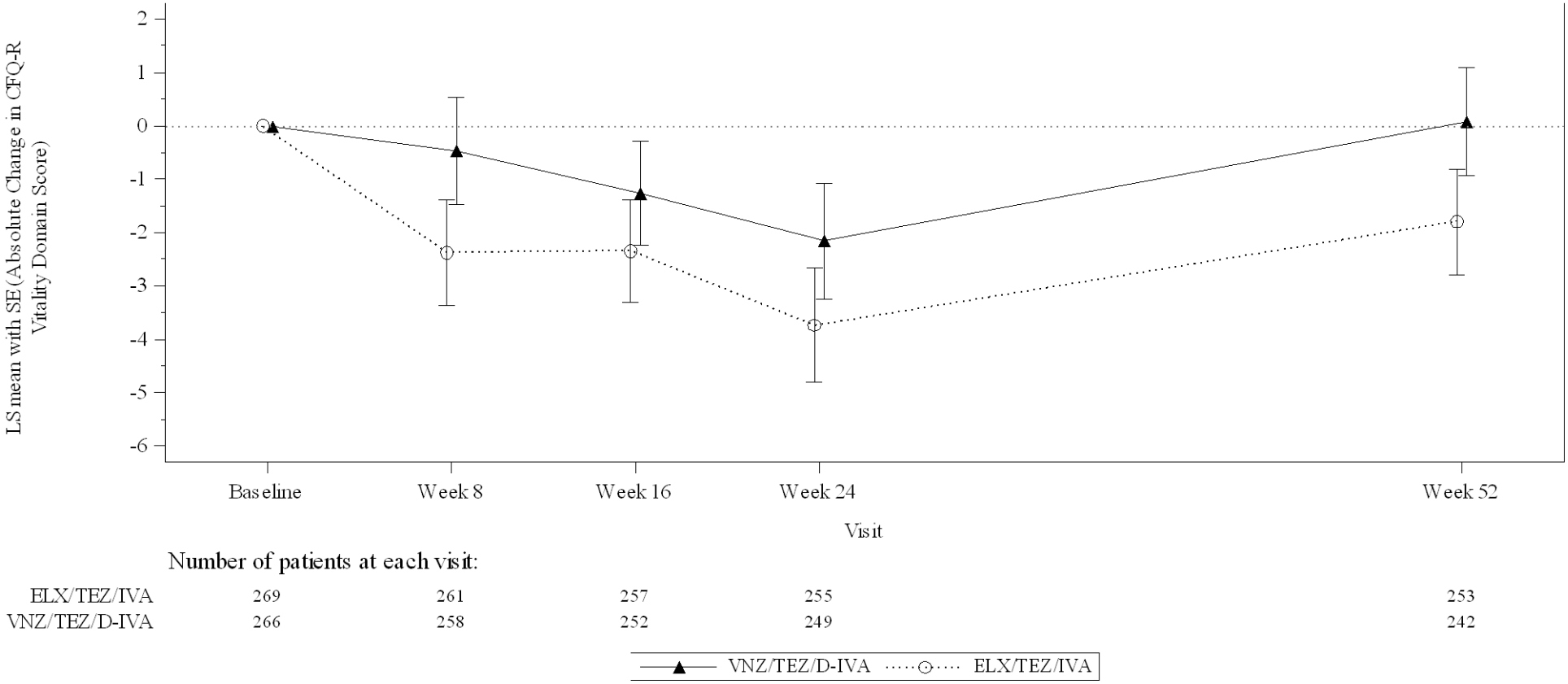
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Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

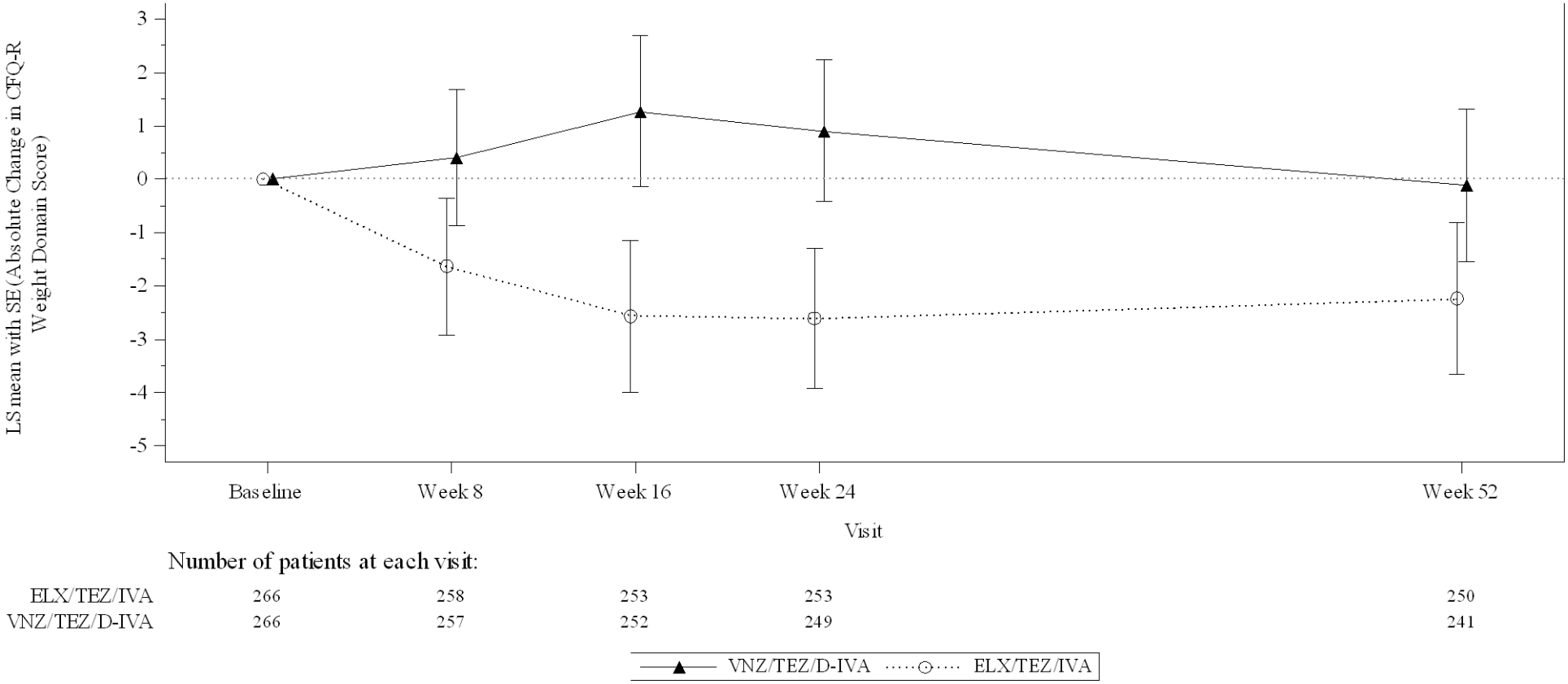
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Figure 2.2.1.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

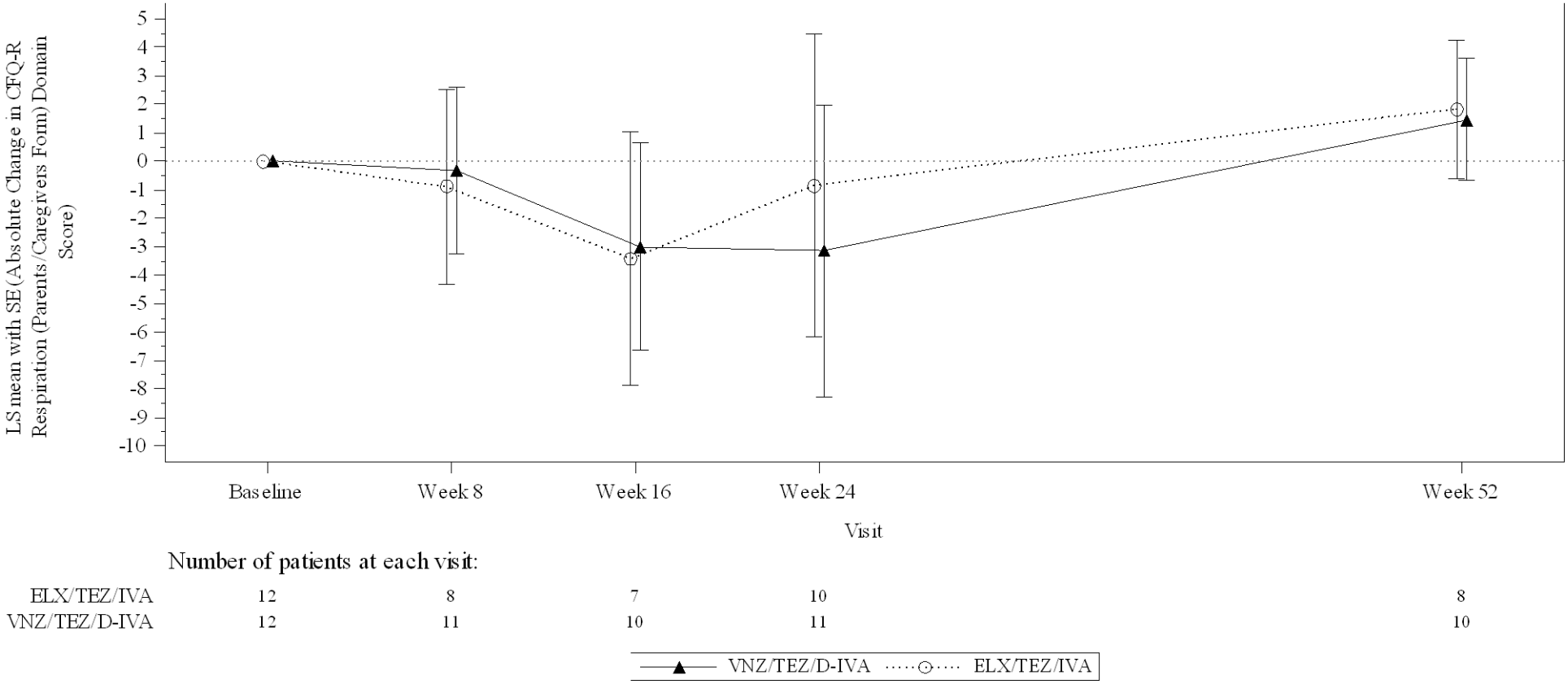
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Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

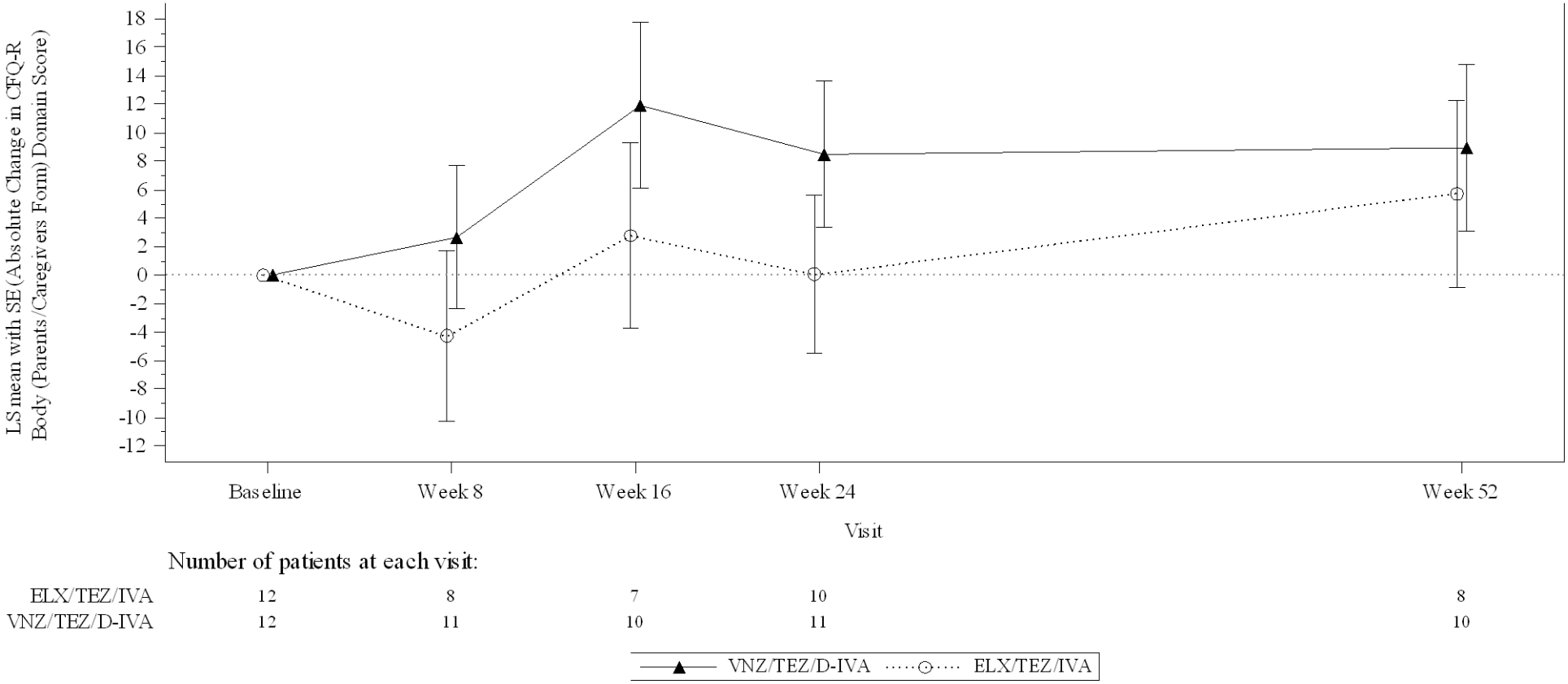
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Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

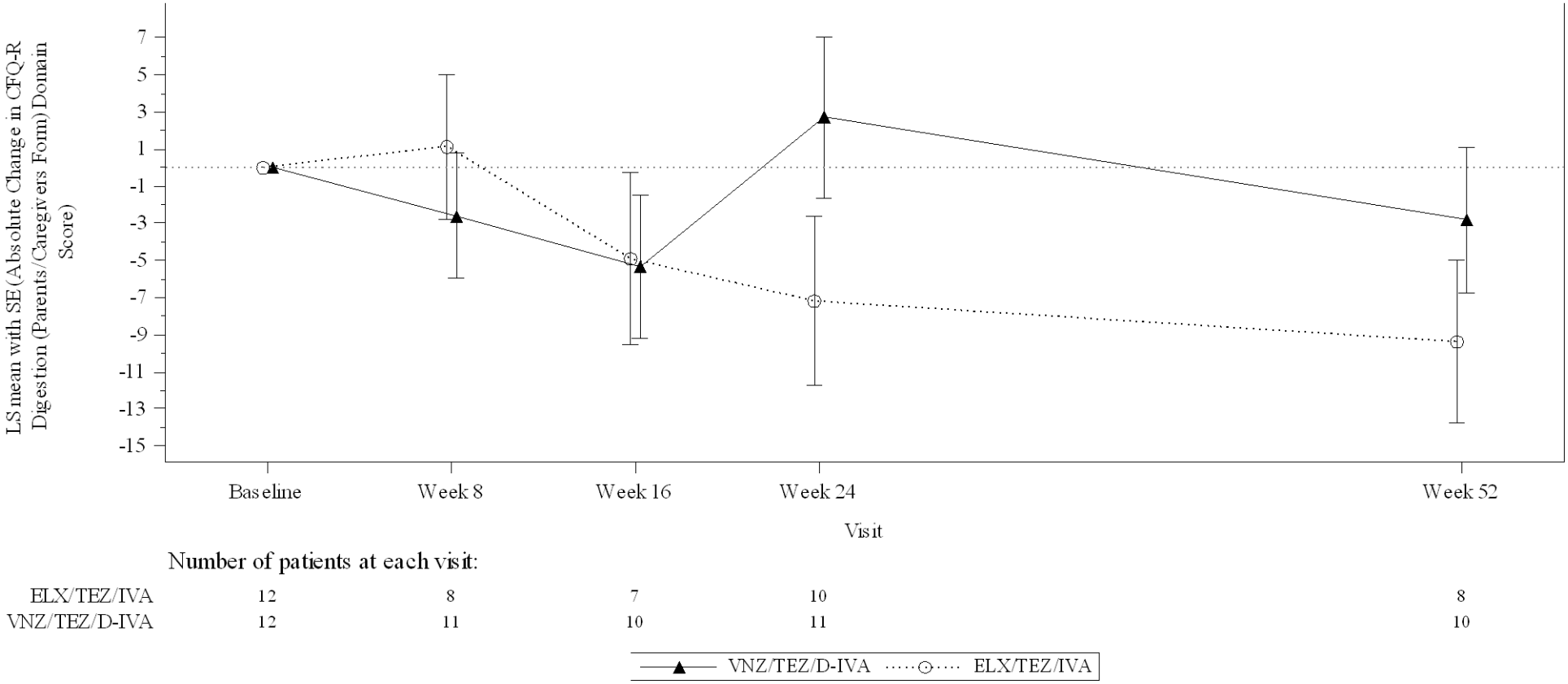
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Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

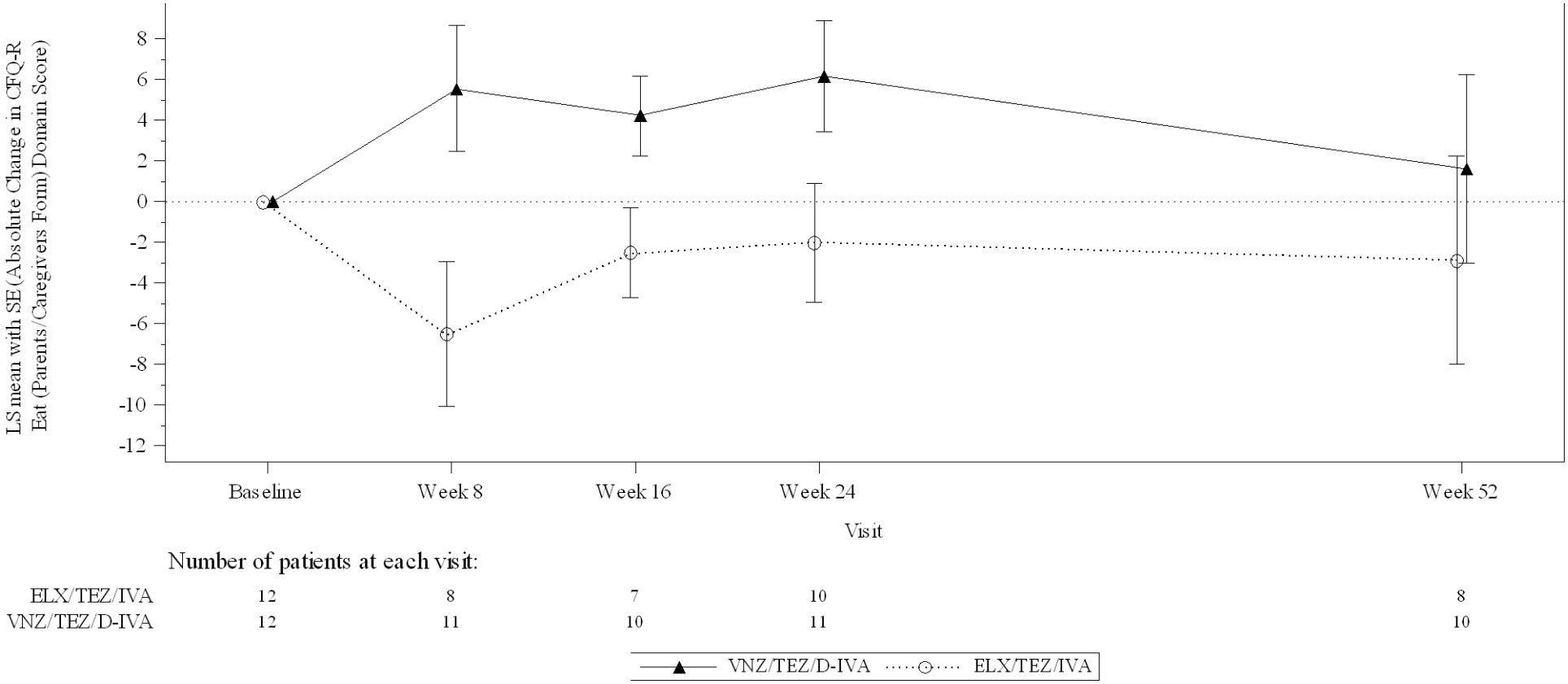
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Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

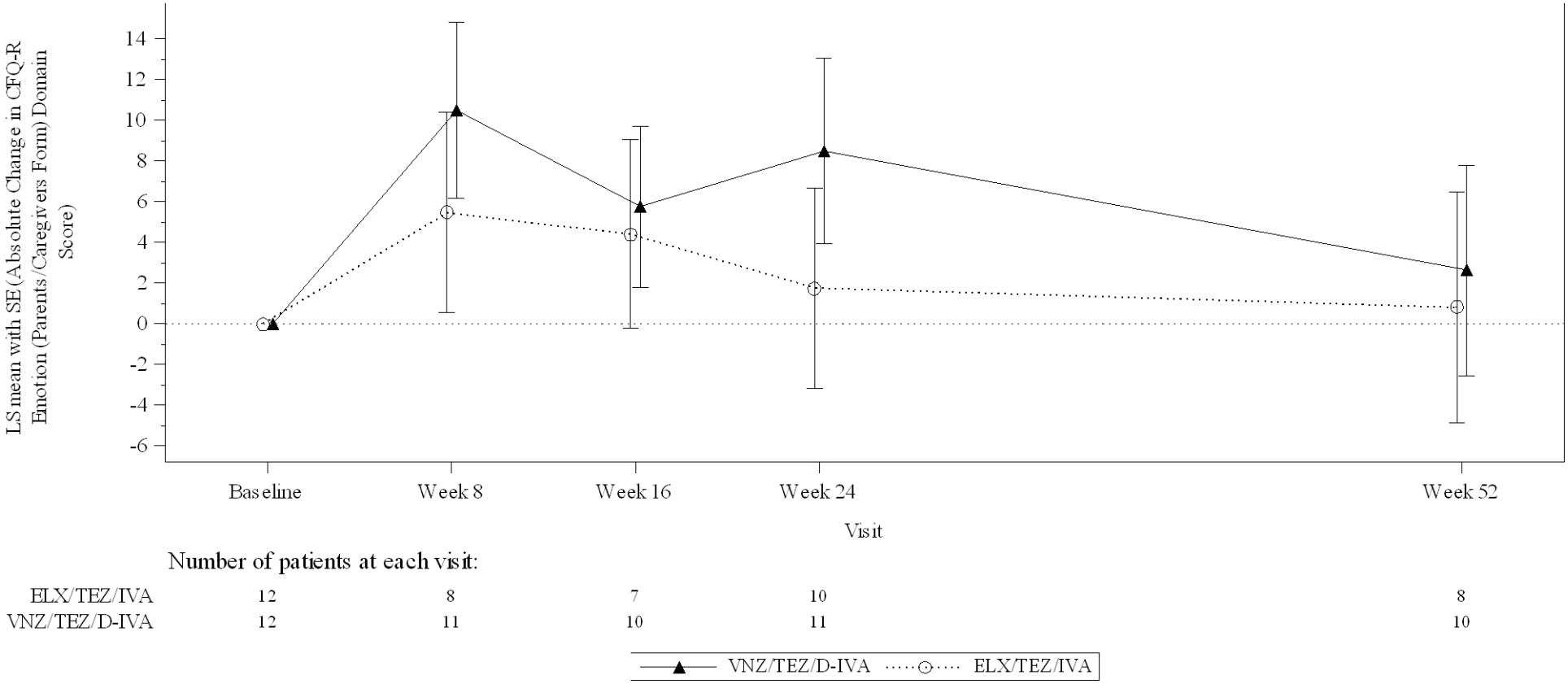
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Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

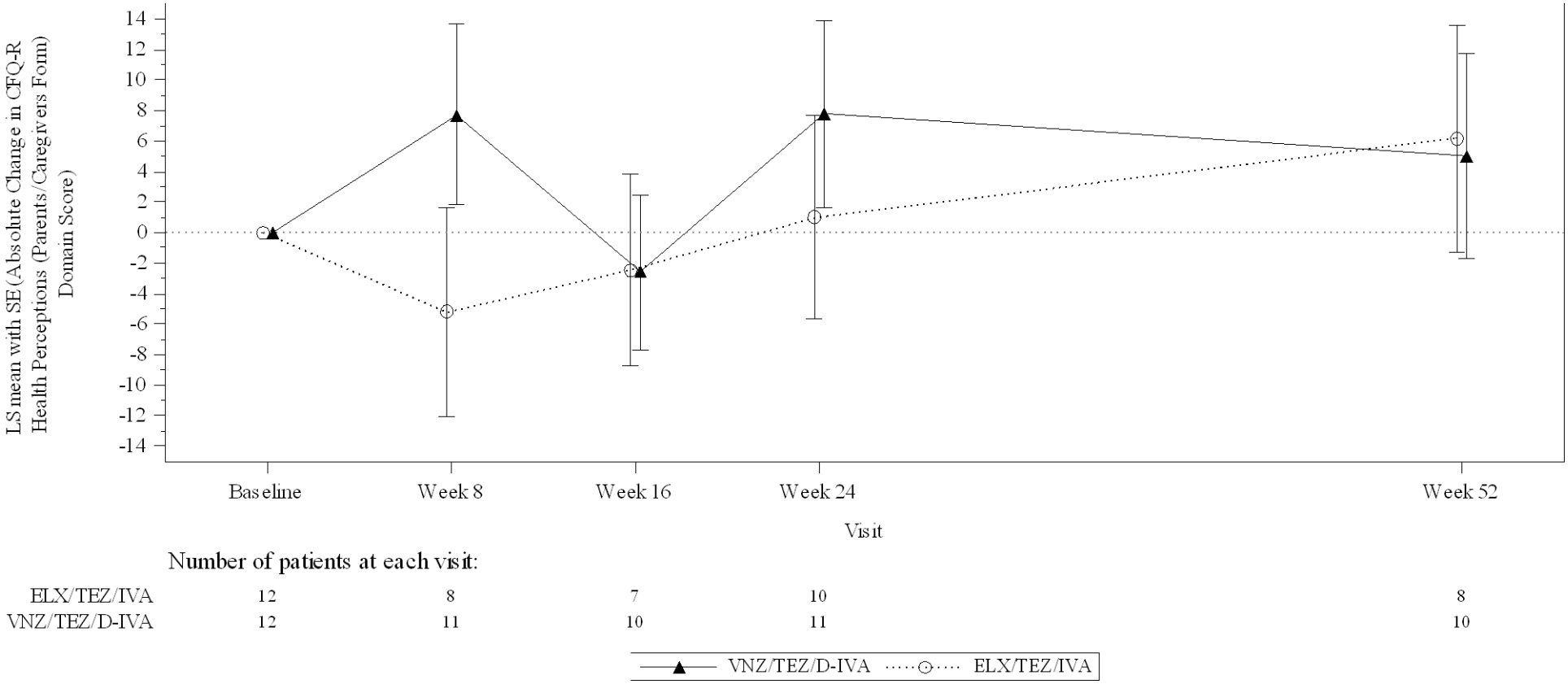
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Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



Number of patients at each visit:

ELX/TEZ/IVA	12	8	7	10	8
VNZ/TEZ/D-IVA	12	11	10	11	10

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

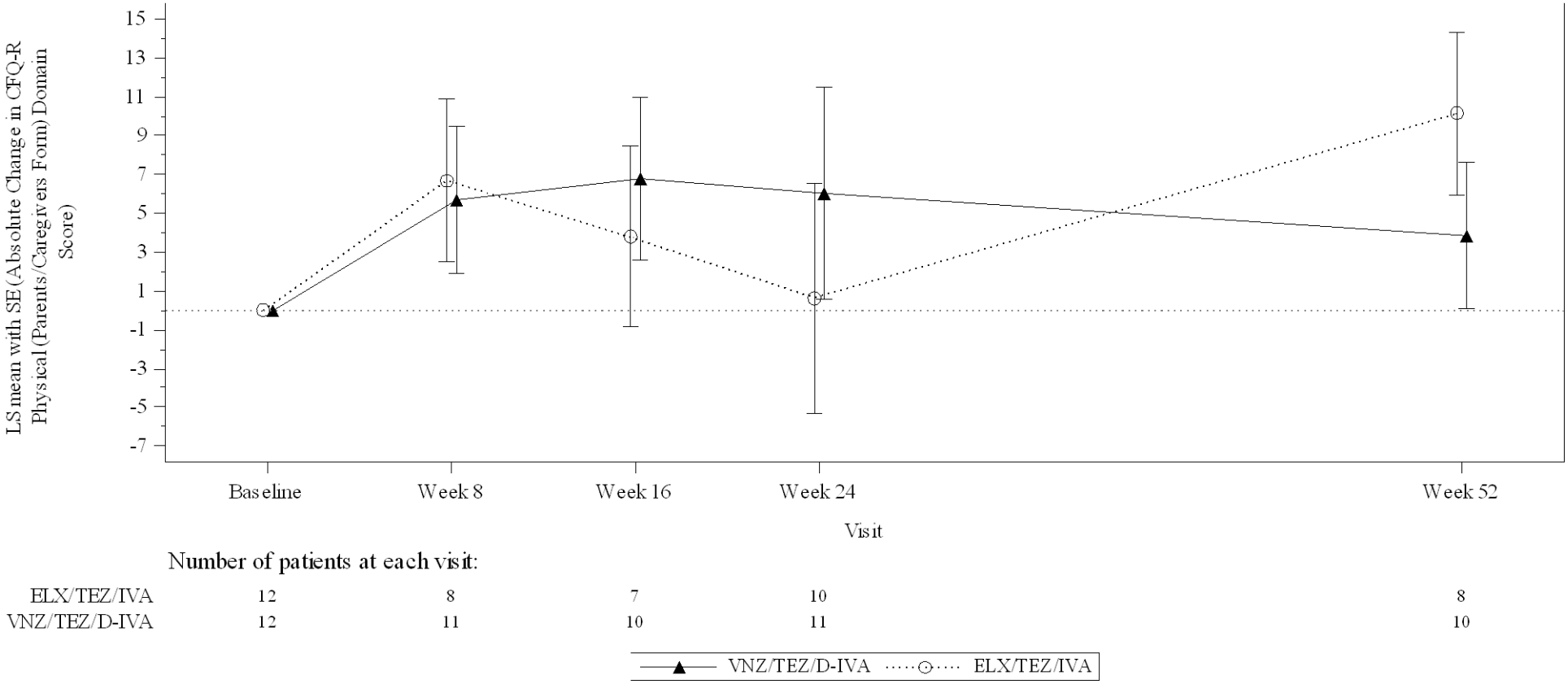
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Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

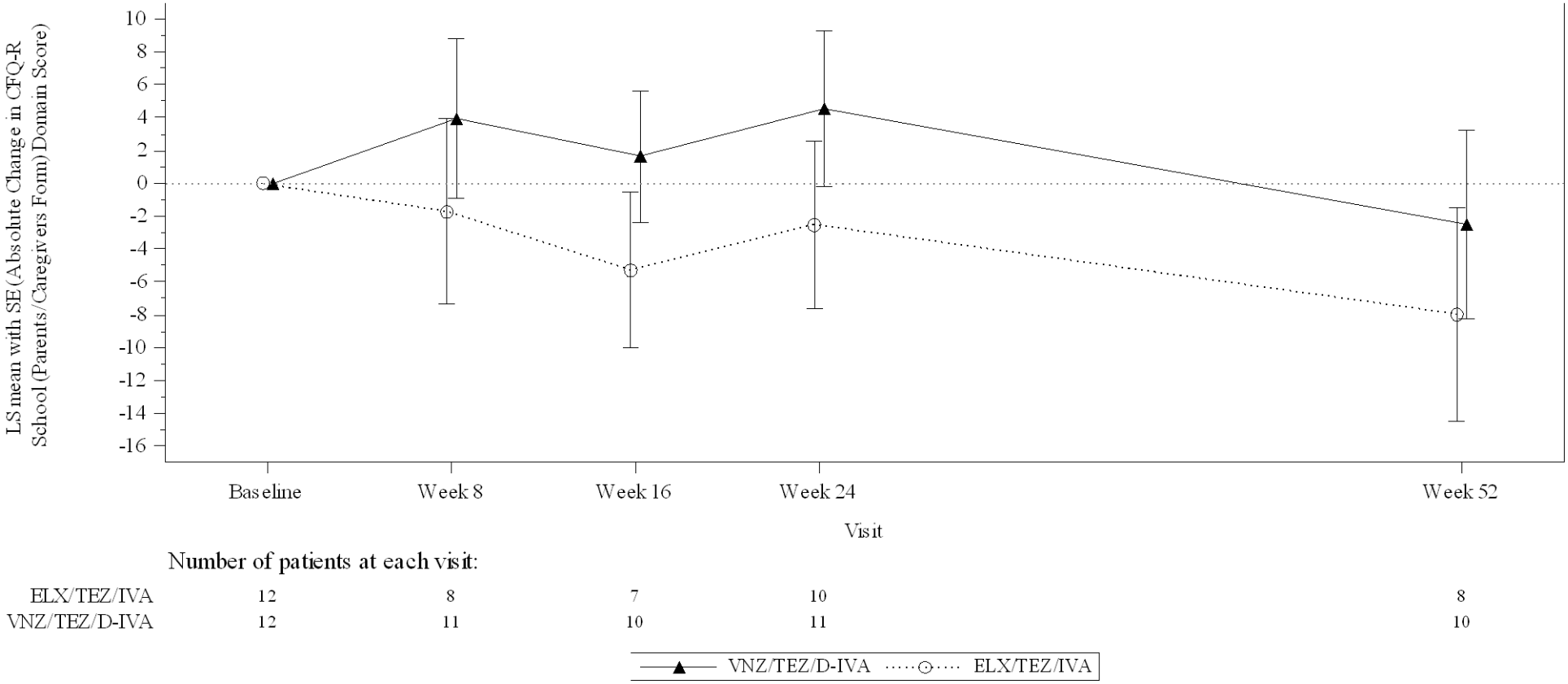
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Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

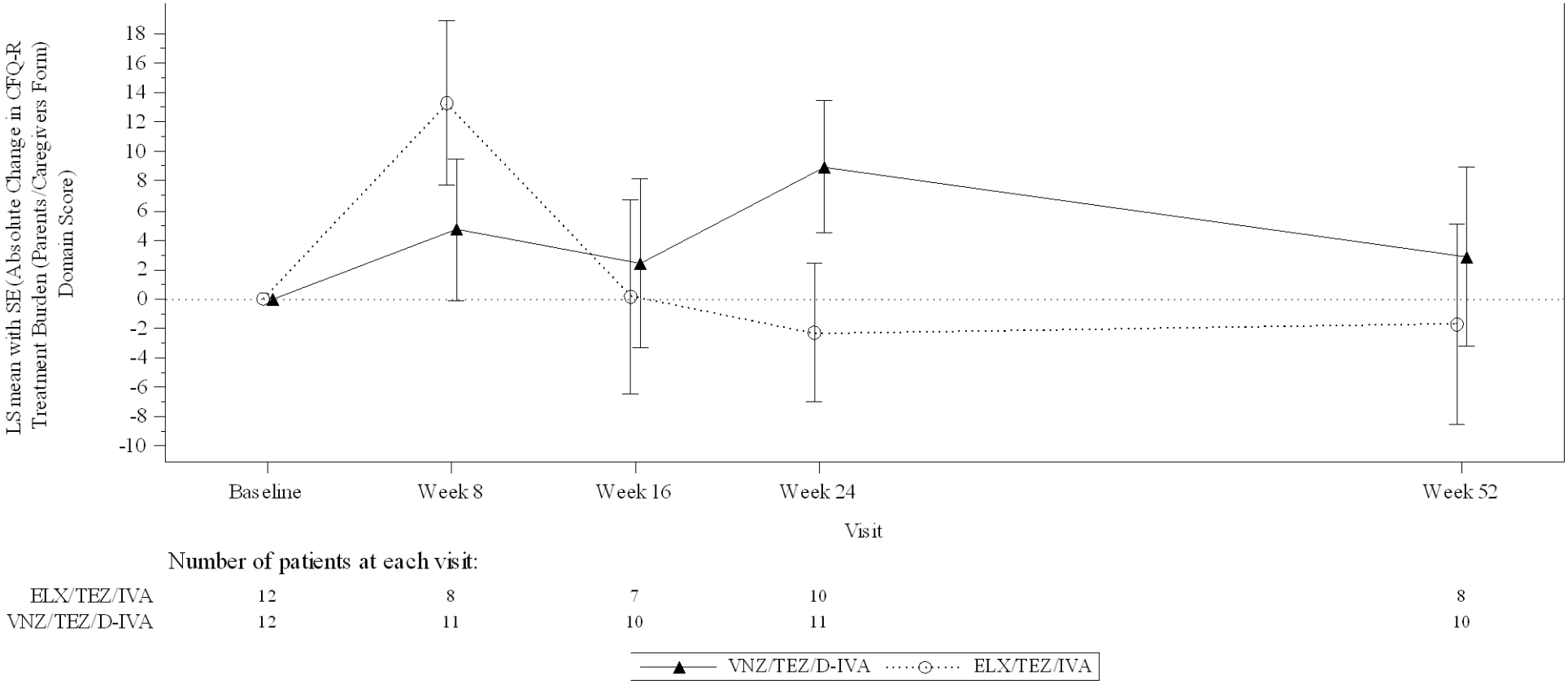
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Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

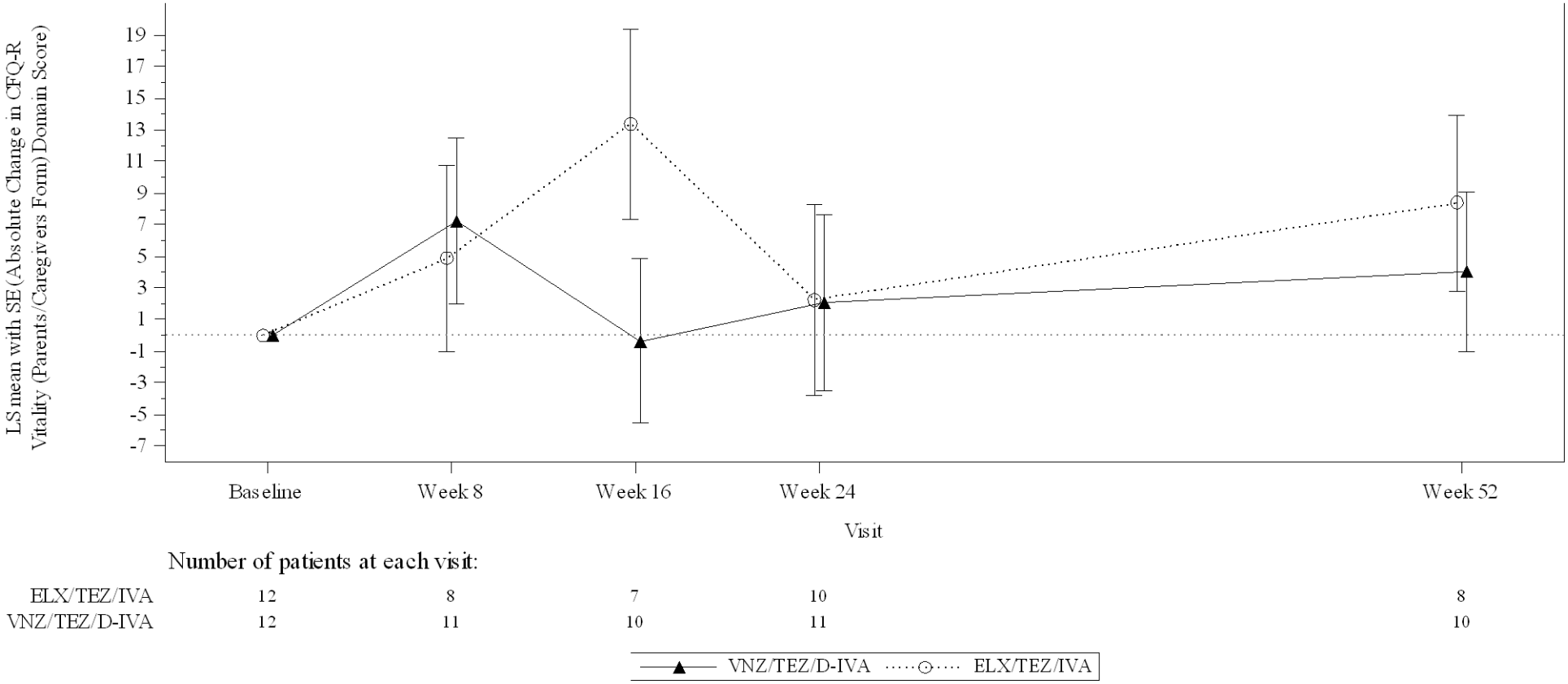
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Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

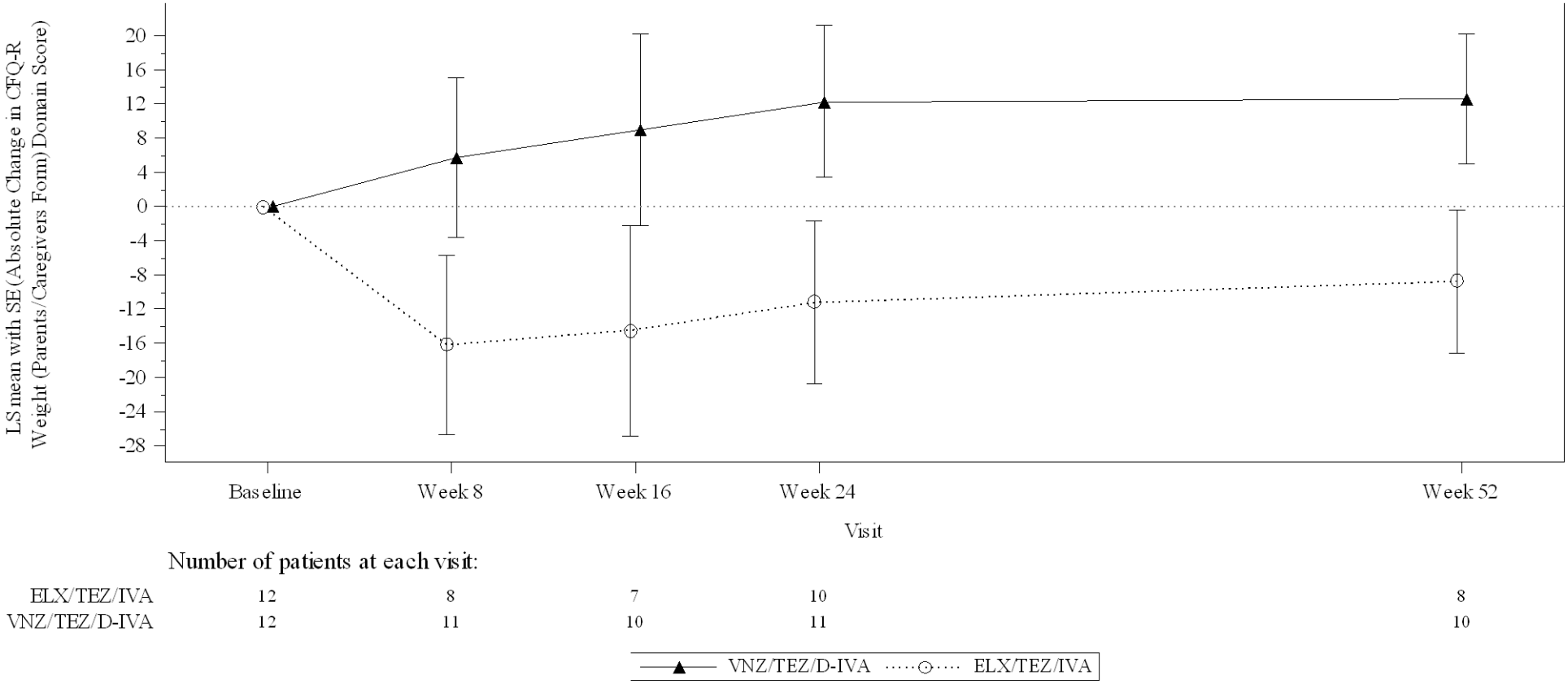
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Figure 2.2.1.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)

- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-103

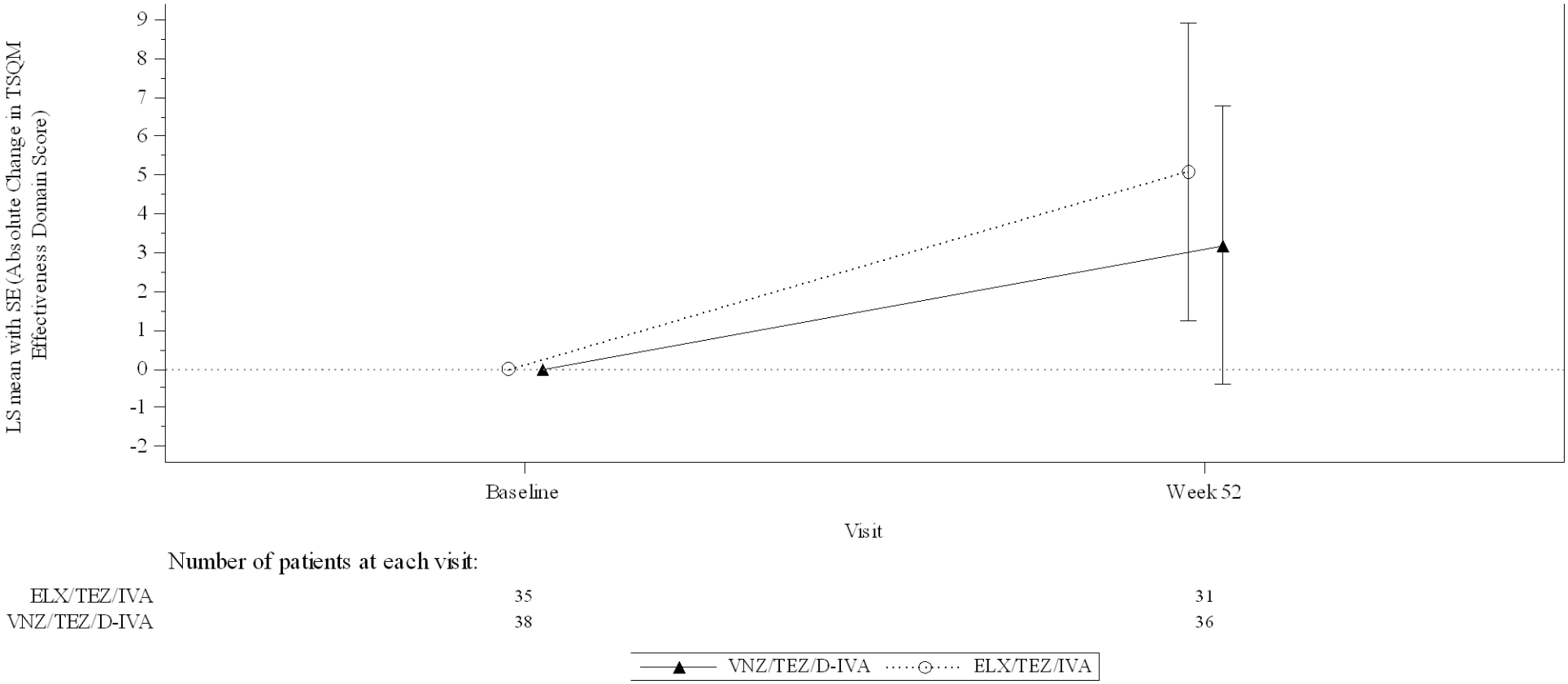


- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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Figure 2.2.1.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

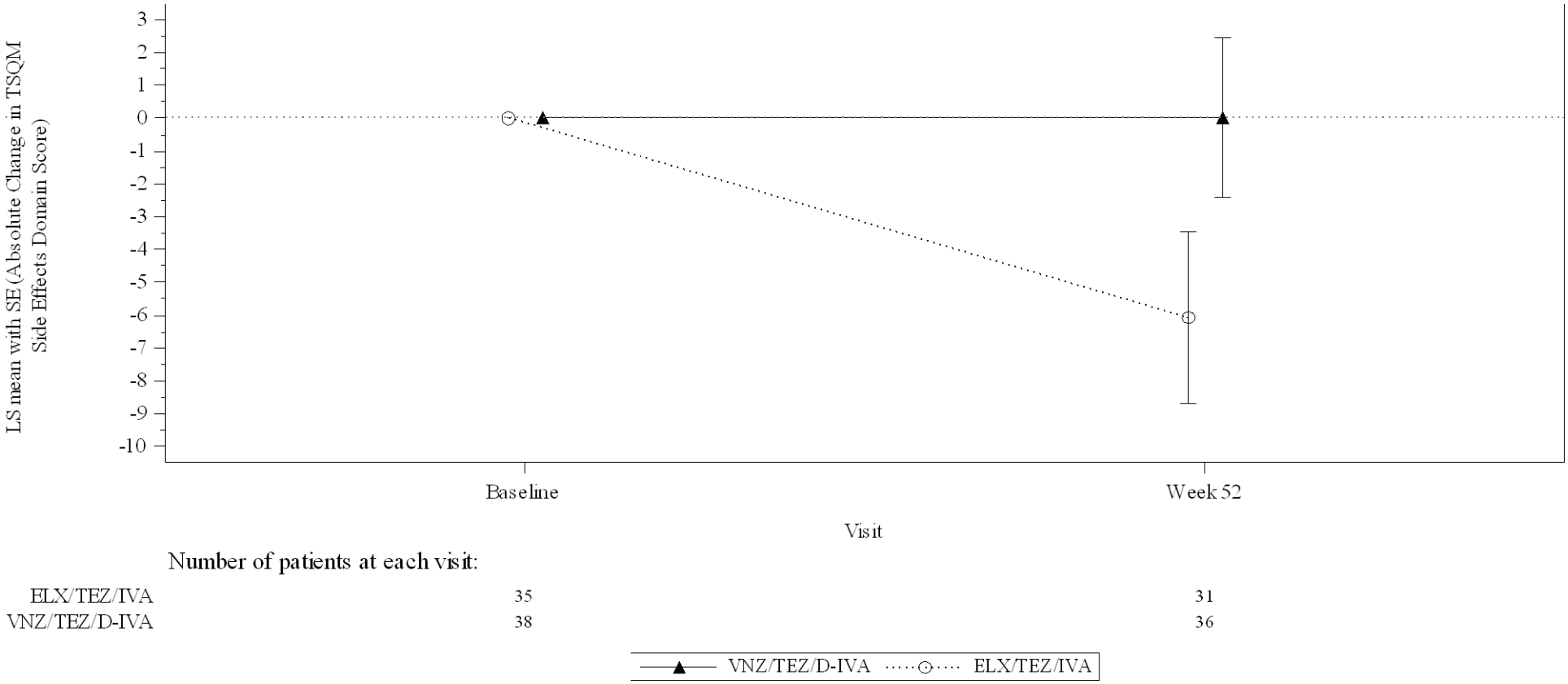
Domain: Effectiveness



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 2.2.1.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

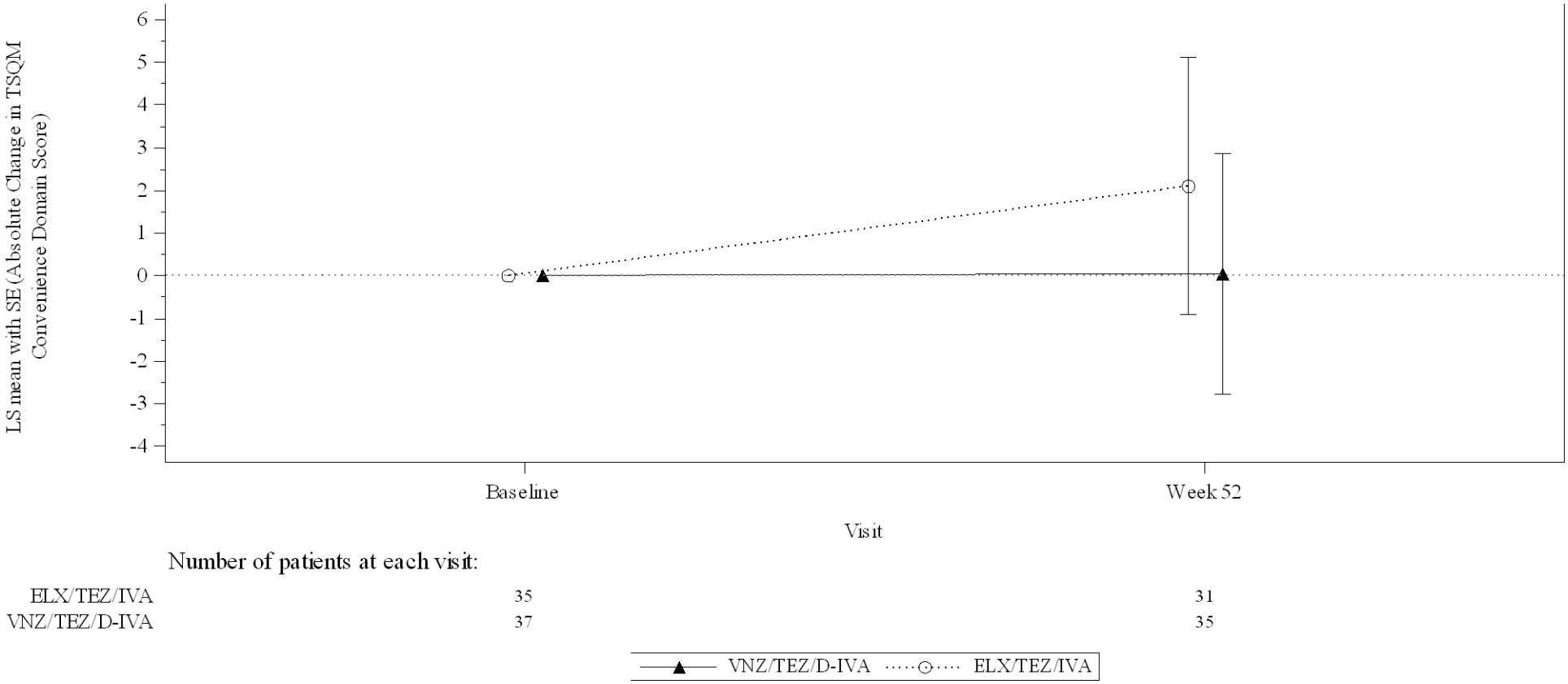
Domain: Side Effects



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 2.2.1.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

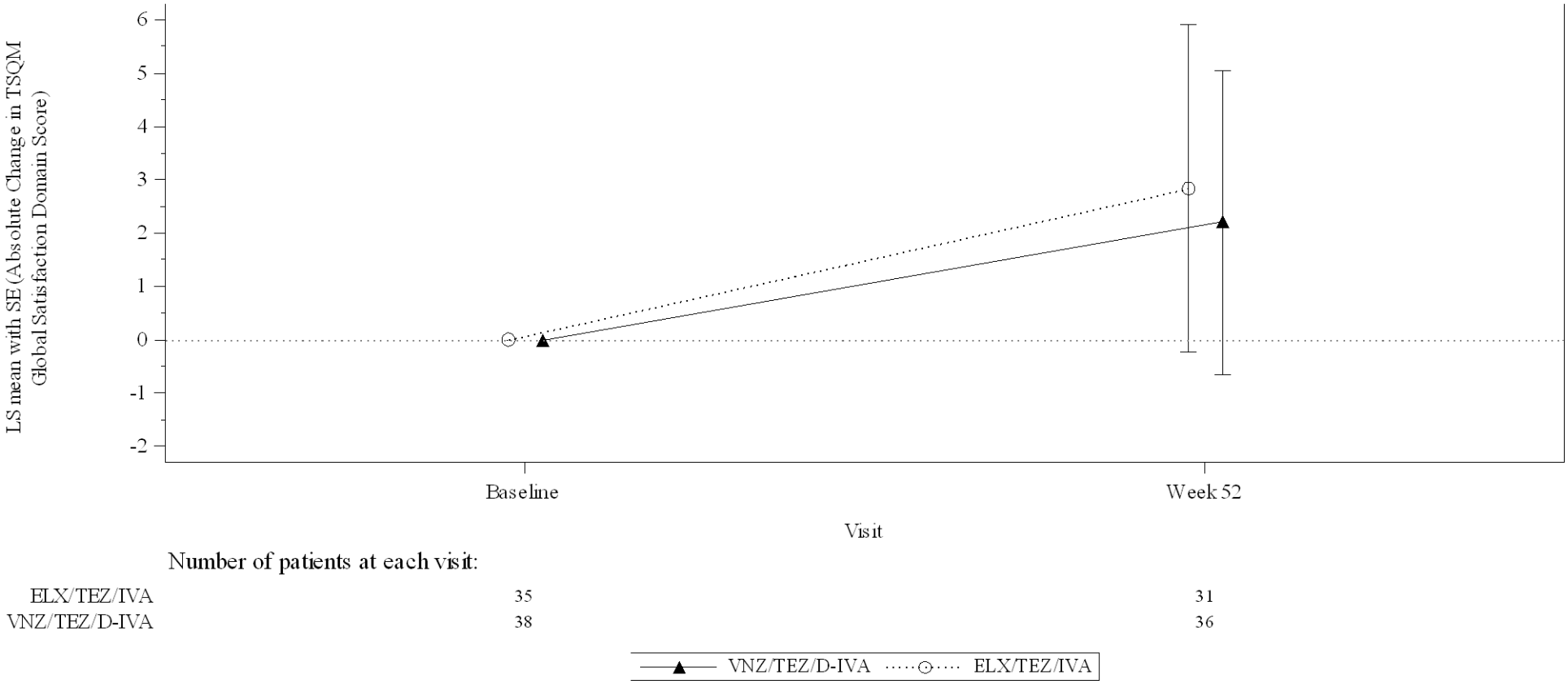
Domain: Convenience



- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 2.2.1.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction



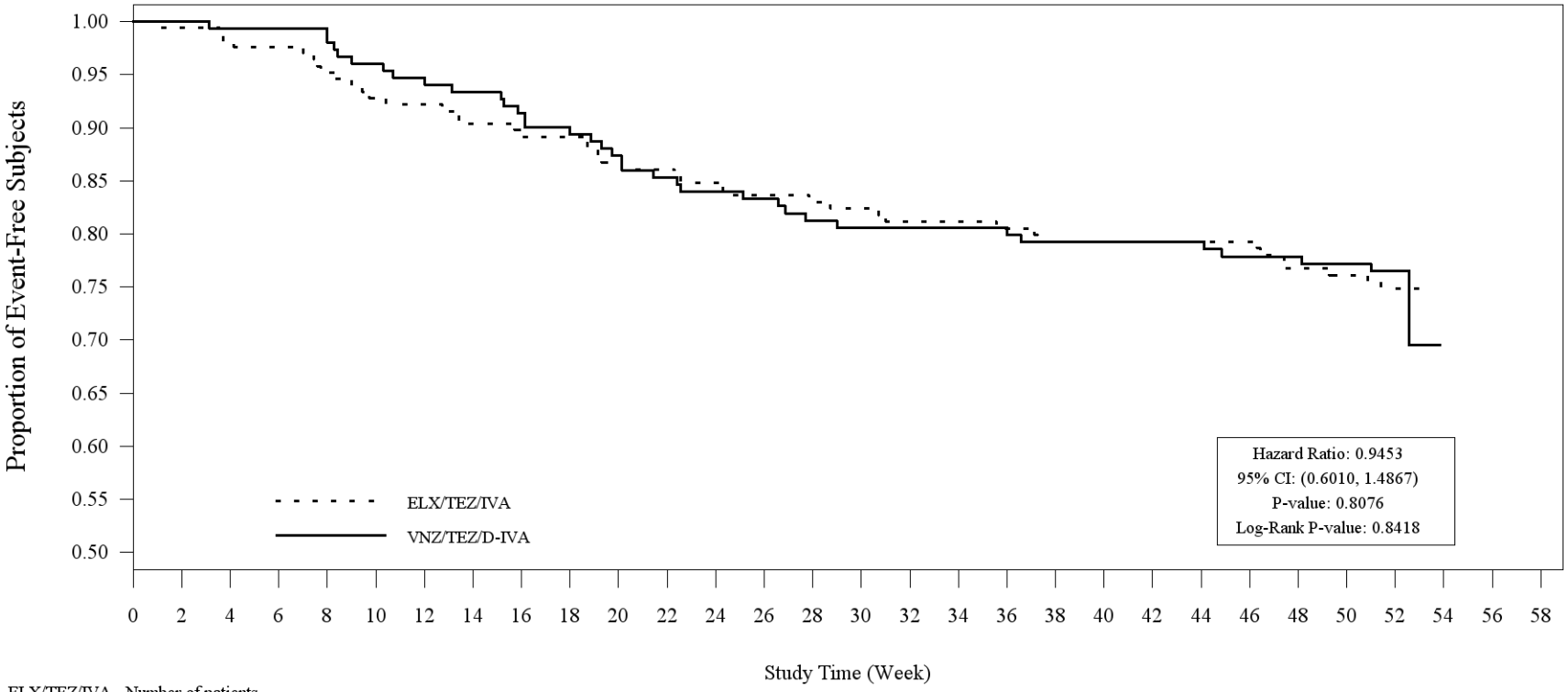
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52 only. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F) and with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: $ppFEV_1$ at Baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	167	153	137	129	122
with event(s)	0	13	25	32	38
censored	0	1	5	6	7
VNZ/TEZ/D-IVA - Number of patients					
at risk	154	143	124	119	114
with event(s)	0	9	24	30	33
censored	0	2	6	5	7

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

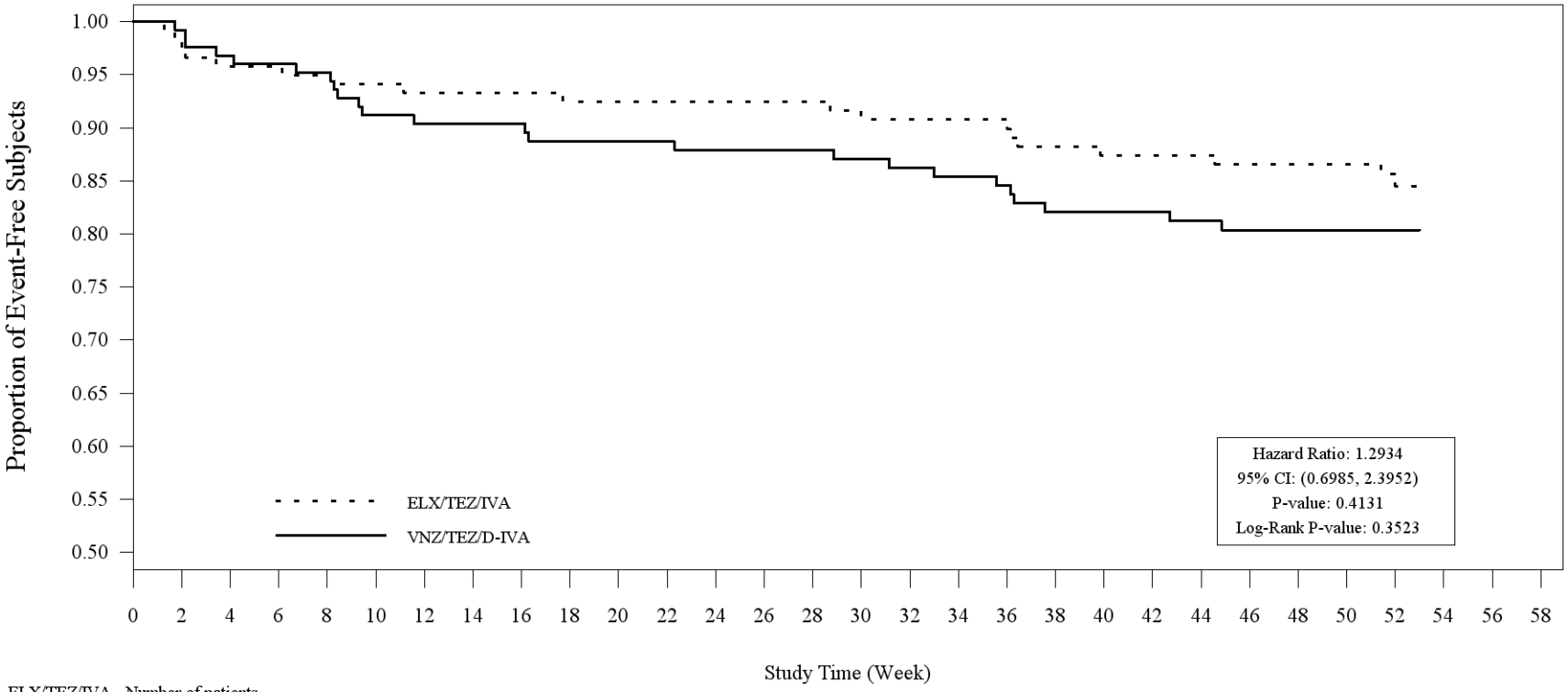
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Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: $ppFEV_1$ at Baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	119	111	110	108	103
with event(s)	0	8	9	12	16
censored	0	0	0	-1	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	125	112	107	101	94
with event(s)	0	12	15	19	24
censored	0	1	3	5	7

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

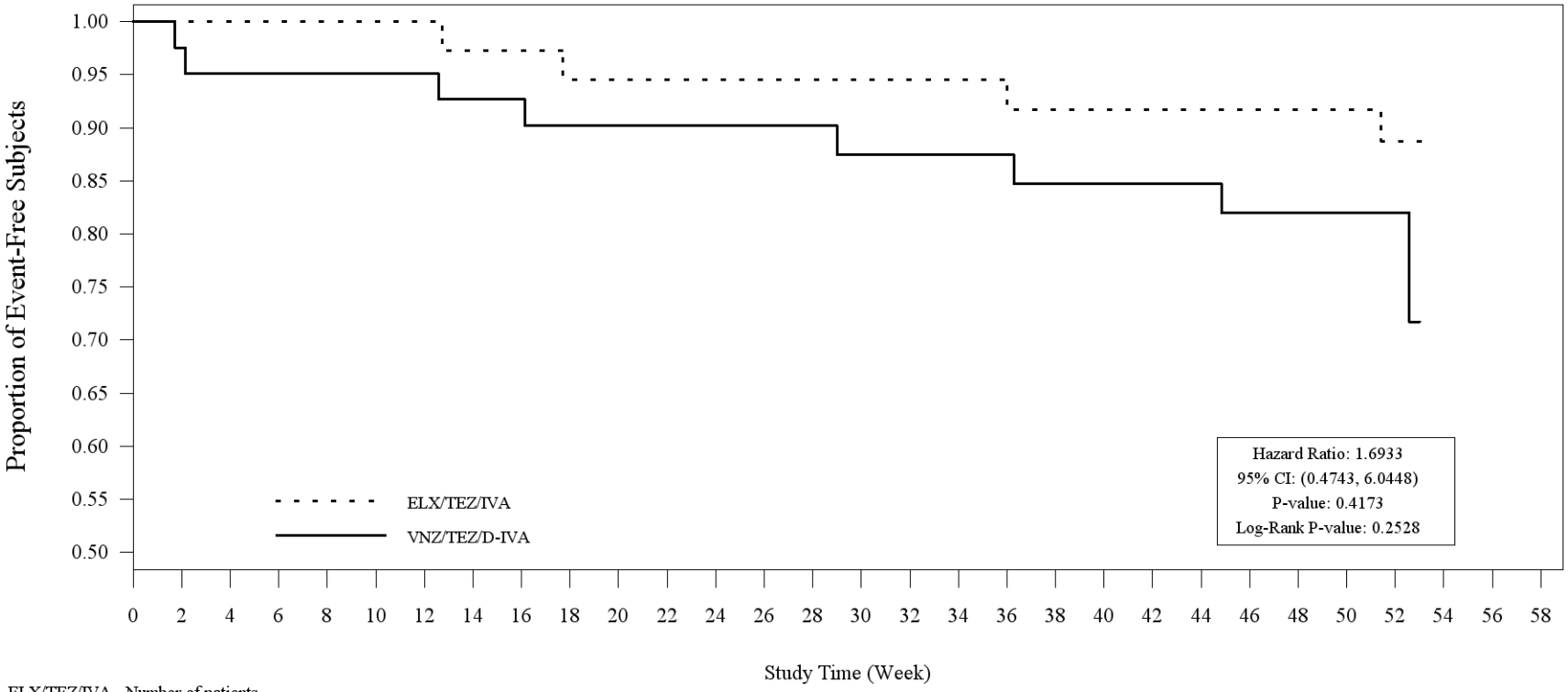
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Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening < 18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	38	37	34	34	33
with event(s)	0	0	2	3	3
censored	0	1	2	1	2
VNZ/TEZ/D-IVA - Number of patients					
at risk	41	39	35	32	30
with event(s)	0	2	4	5	7
censored	0	0	2	4	4

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

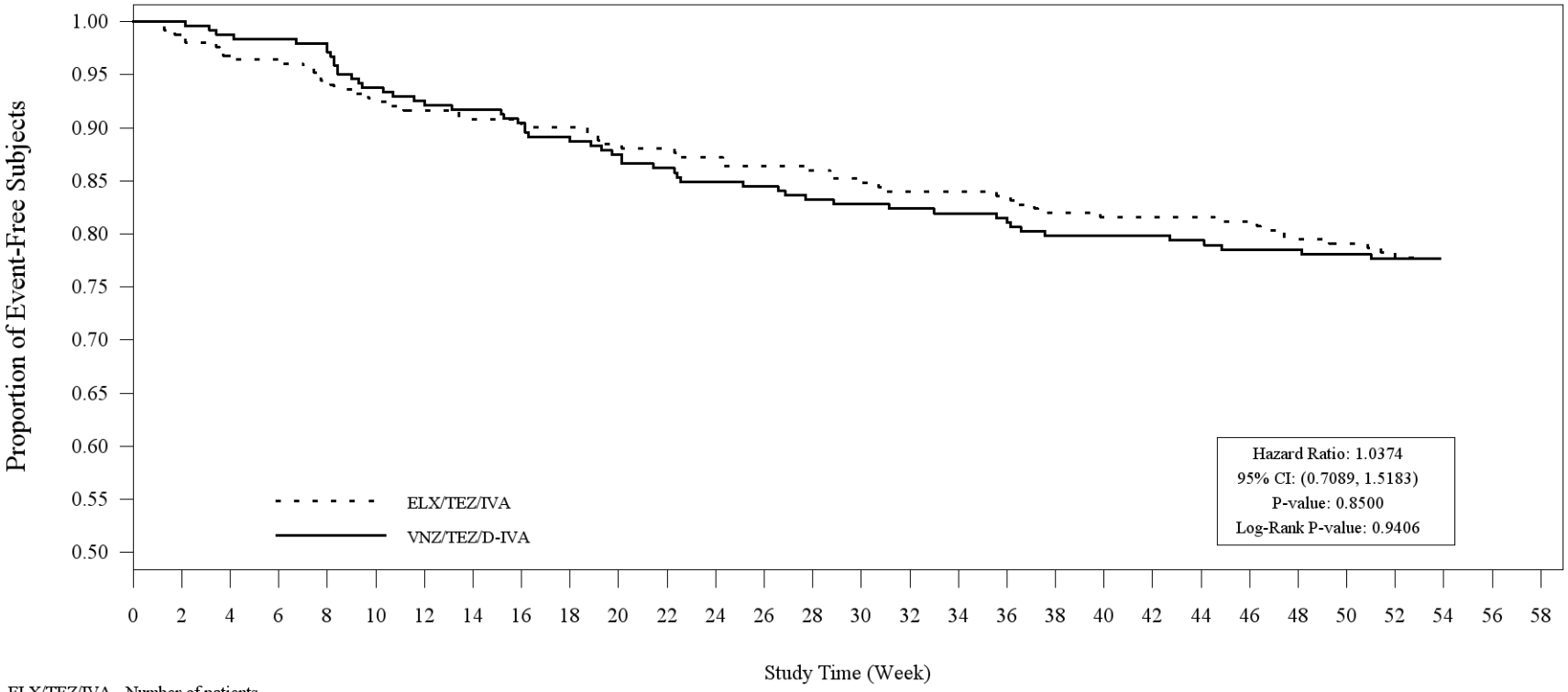
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Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening ≥ 18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	251	230	216	206	195
with event(s)	0	21	32	41	51
censored	0	0	3	4	5
VNZ/TEZ/D-IVA - Number of patients					
at risk	243	221	200	192	182
with event(s)	0	19	36	45	51
censored	0	3	7	6	10

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

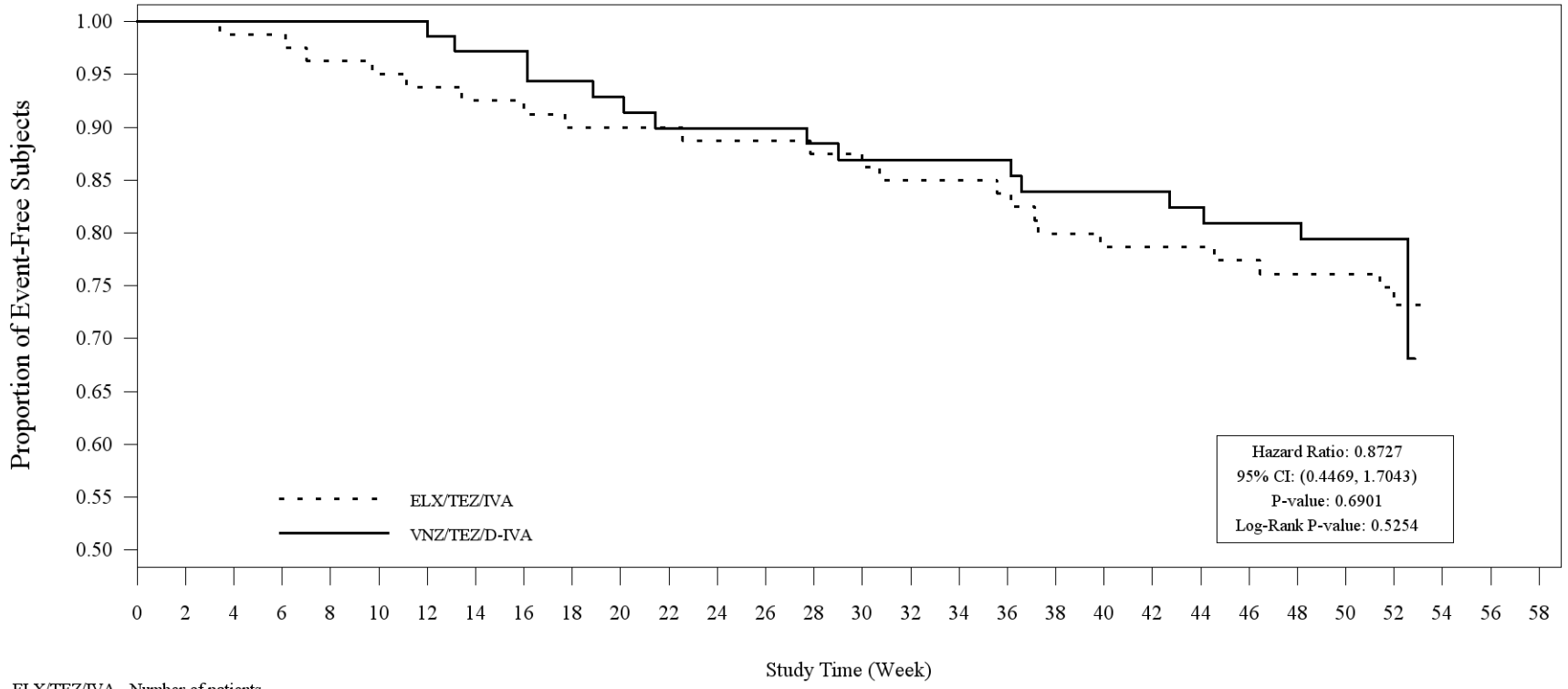
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Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	80	75	71	66	60
with event(s)	0	5	9	13	19
censored	0	0	0	1	1
VNZ/TEZ/D-IVA - Number of patients					
at risk	72	71	61	58	54
with event(s)	0	1	7	9	13
censored	0	0	4	5	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

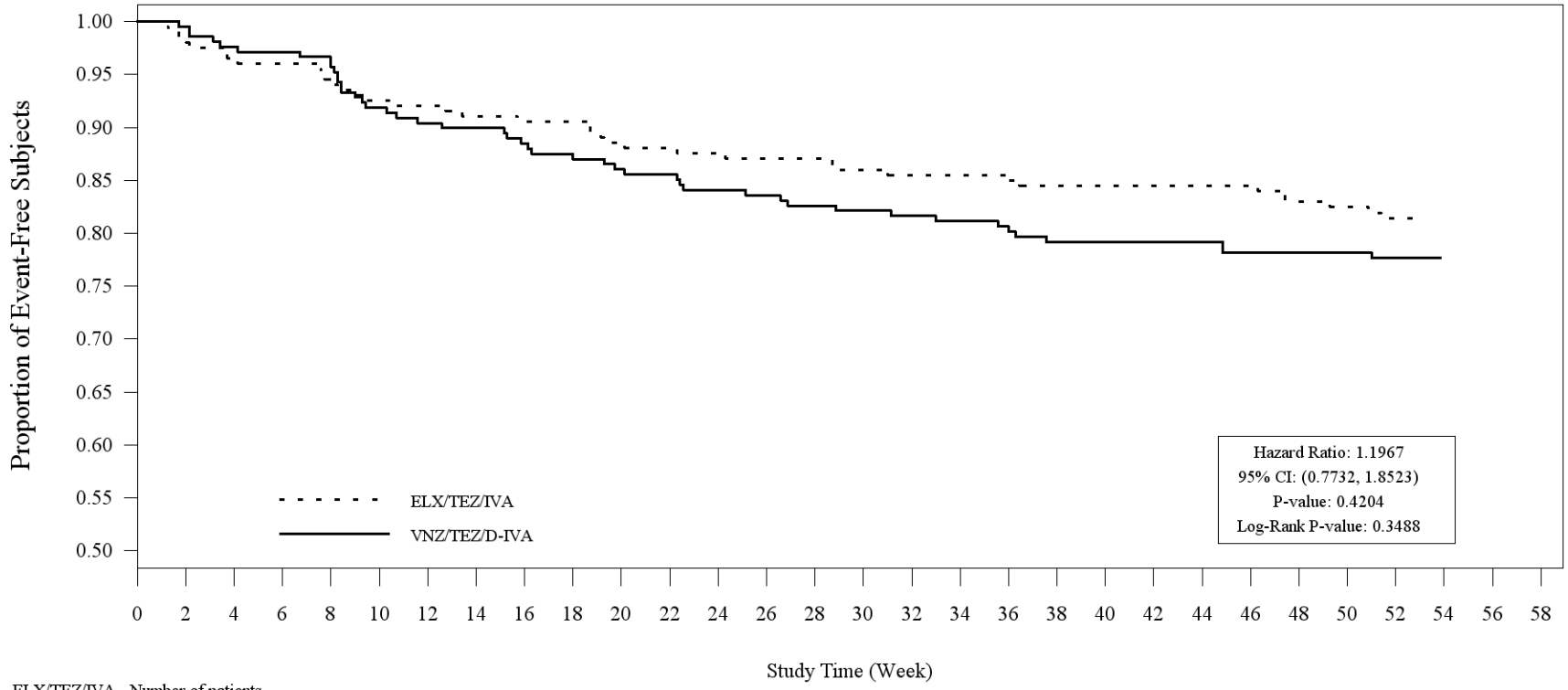
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Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	202	185	173	169	163
with event(s)	0	16	25	30	34
censored	0	1	4	3	5
VNZ/TEZ/D-IVA - Number of patients					
at risk	210	187	172	164	156
with event(s)	0	20	33	41	45
censored	0	3	5	5	9

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

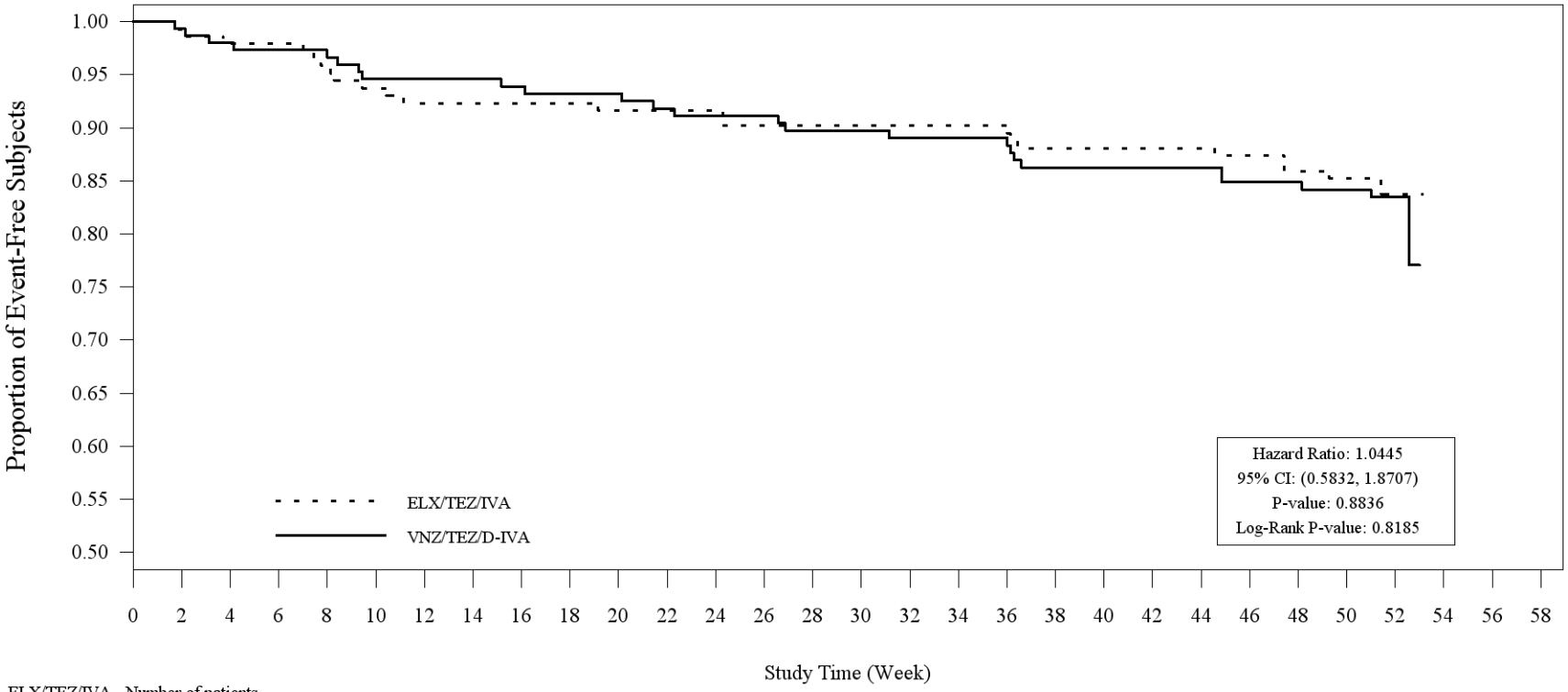
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Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	144	132	129	127	120
with event(s)	0	11	12	15	20
censored	0	1	3	2	4
VNZ/TEZ/D-IVA - Number of patients					
at risk	149	138	131	128	122
with event(s)	0	8	13	17	22
censored	0	3	5	4	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

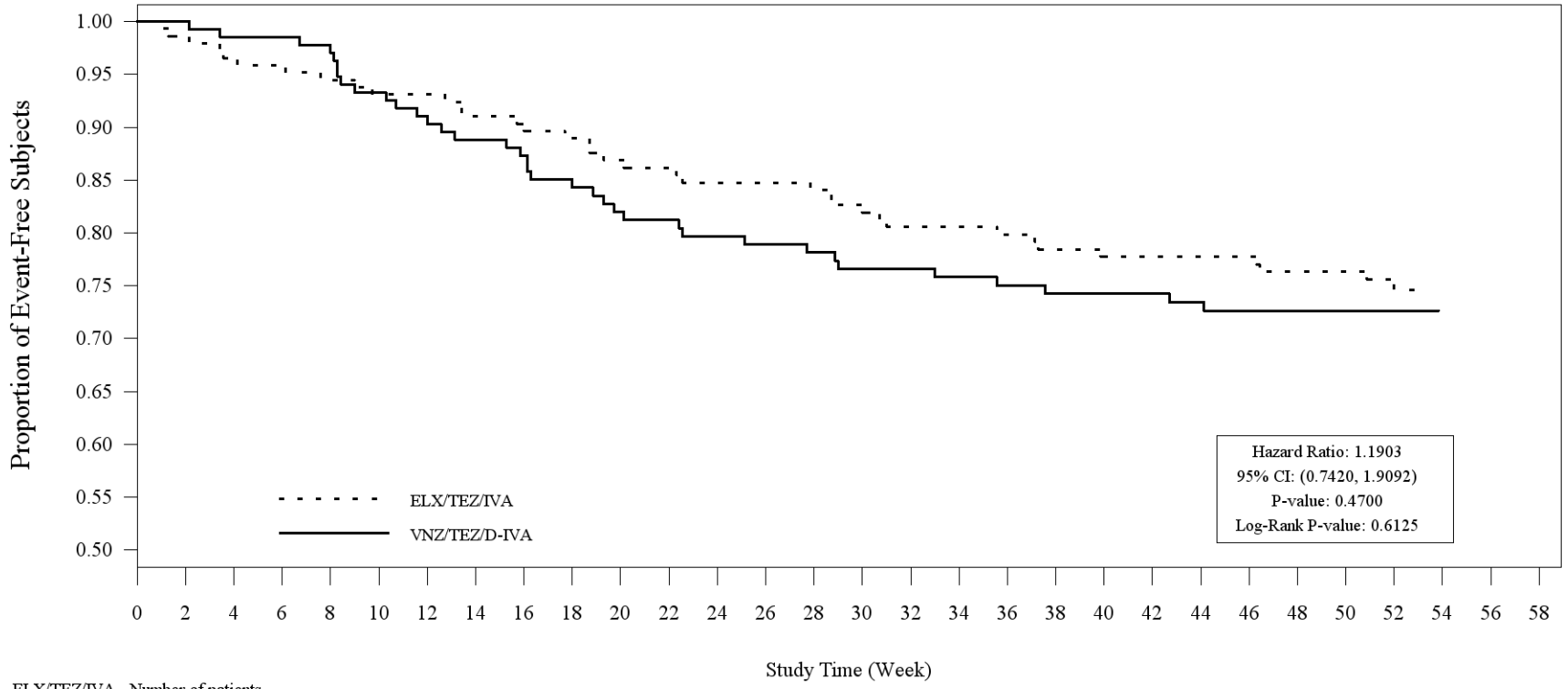
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Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	145	135	121	113	108
with event(s)	0	10	22	29	34
censored	0	0	2	3	3
VNZ/TEZ/D-IVA - Number of patients					
at risk	135	122	104	96	90
with event(s)	0	13	27	33	36
censored	0	0	4	6	9

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

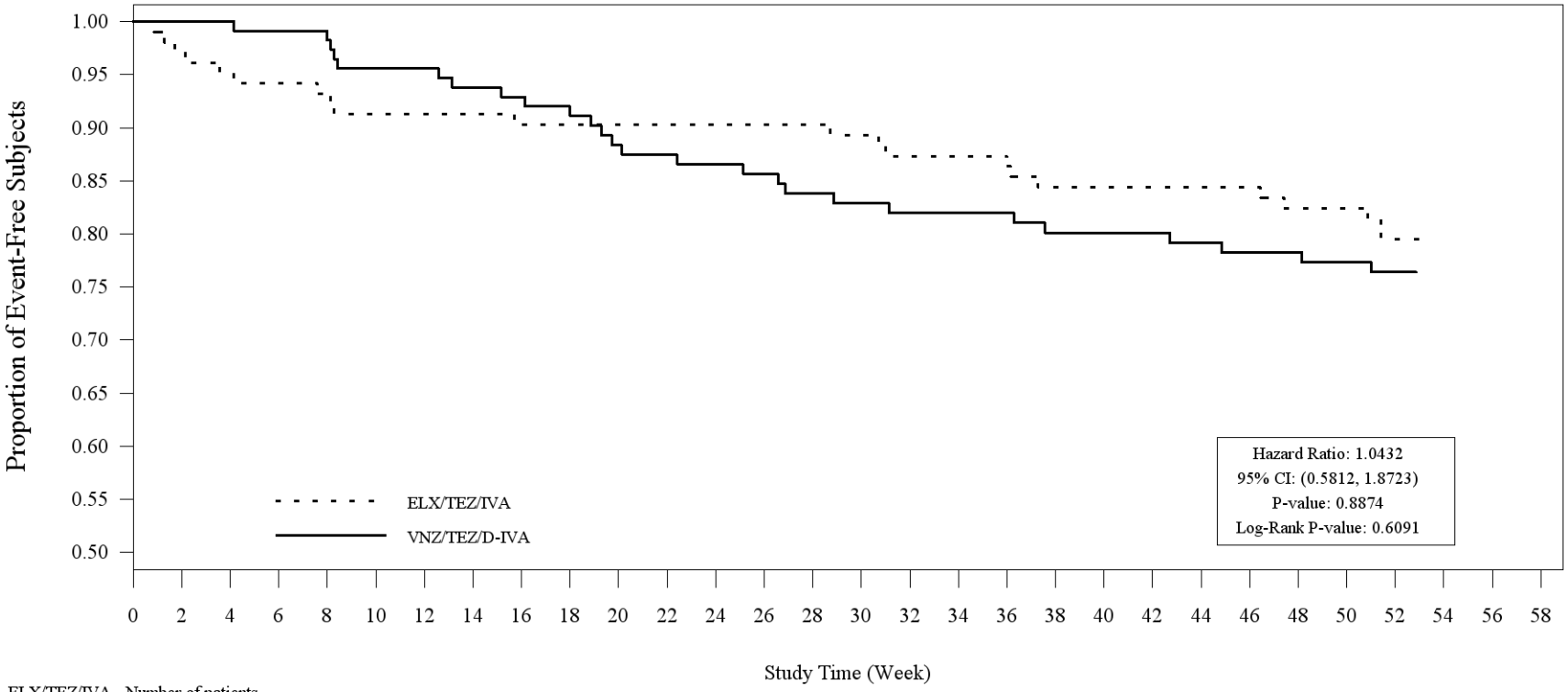
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Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	103	94	92	89	84
with event(s)	0	9	10	14	18
censored	0	0	1	0	1
VNZ/TEZ/D-IVA - Number of patients					
at risk	114	107	95	89	84
with event(s)	0	5	15	20	24
censored	0	2	4	5	6

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

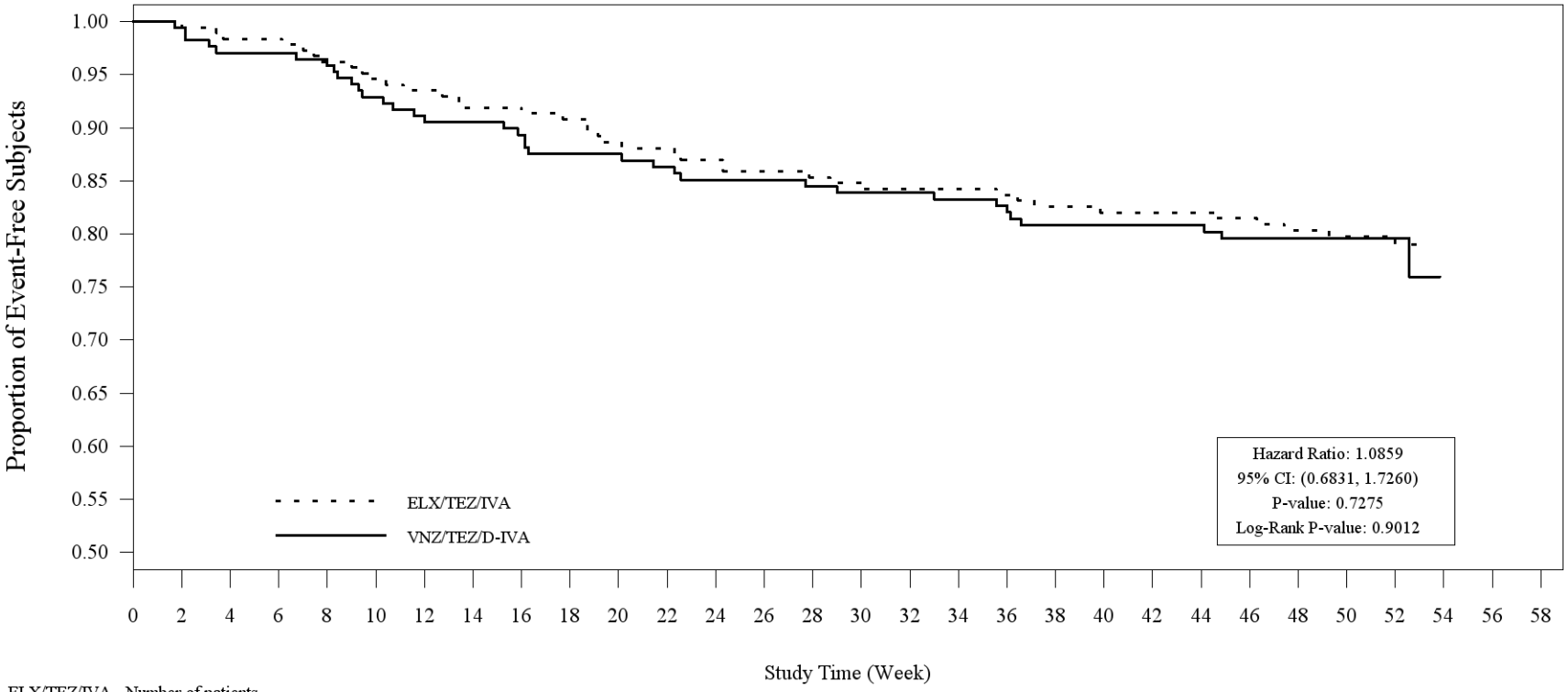
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Figure 2.2.2.6.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = Rest of the World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	186	173	158	151	144
with event(s)	0	12	24	30	36
censored	0	1	4	5	6
VNZ/TEZ/D-IVA - Number of patients					
at risk	170	153	140	135	128
with event(s)	0	16	25	30	34
censored	0	1	5	5	8

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

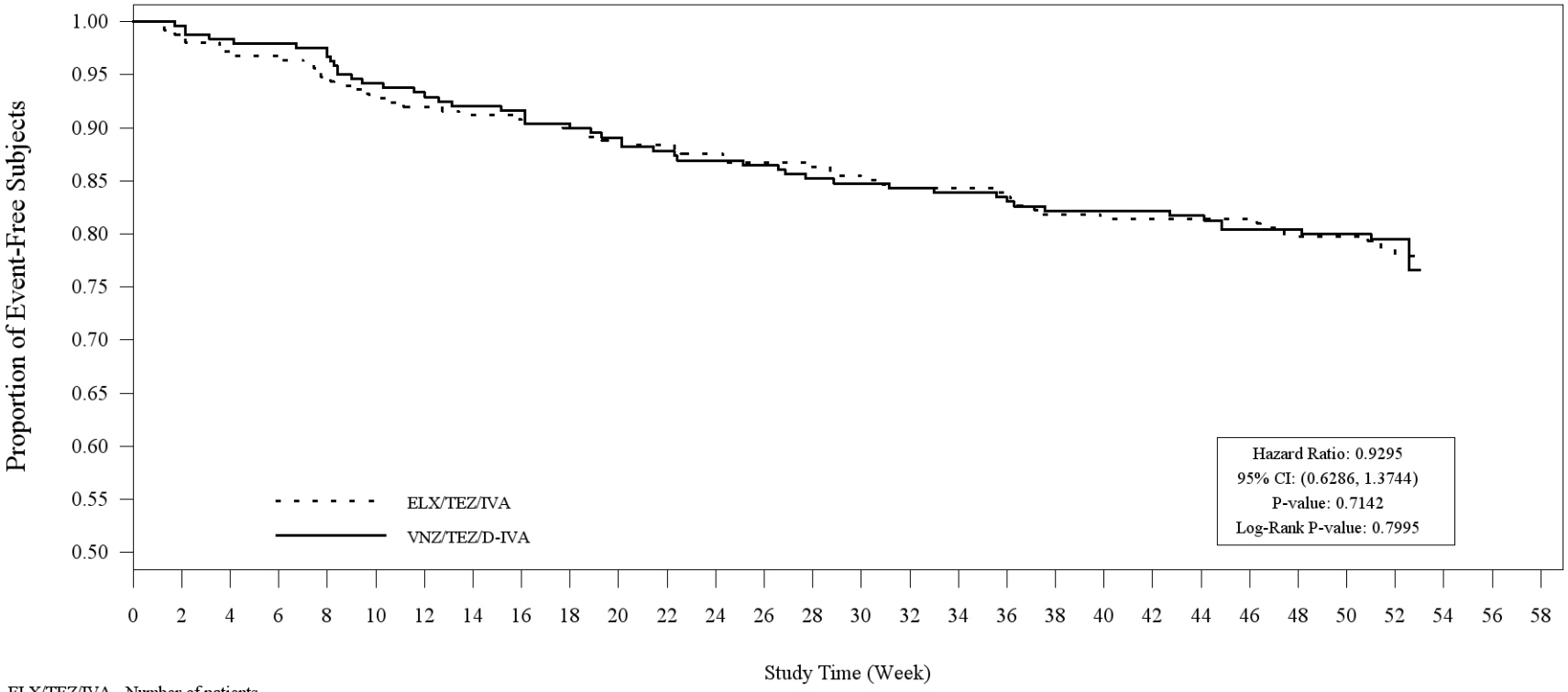
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Figure 2.2.2.6.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	250	229	215	205	195
with event(s)	0	20	31	41	50
censored	0	1	4	4	5
VNZ/TEZ/D-IVA - Number of patients					
at risk	241	222	202	192	183
with event(s)	0	17	31	40	46
censored	0	2	8	9	12

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

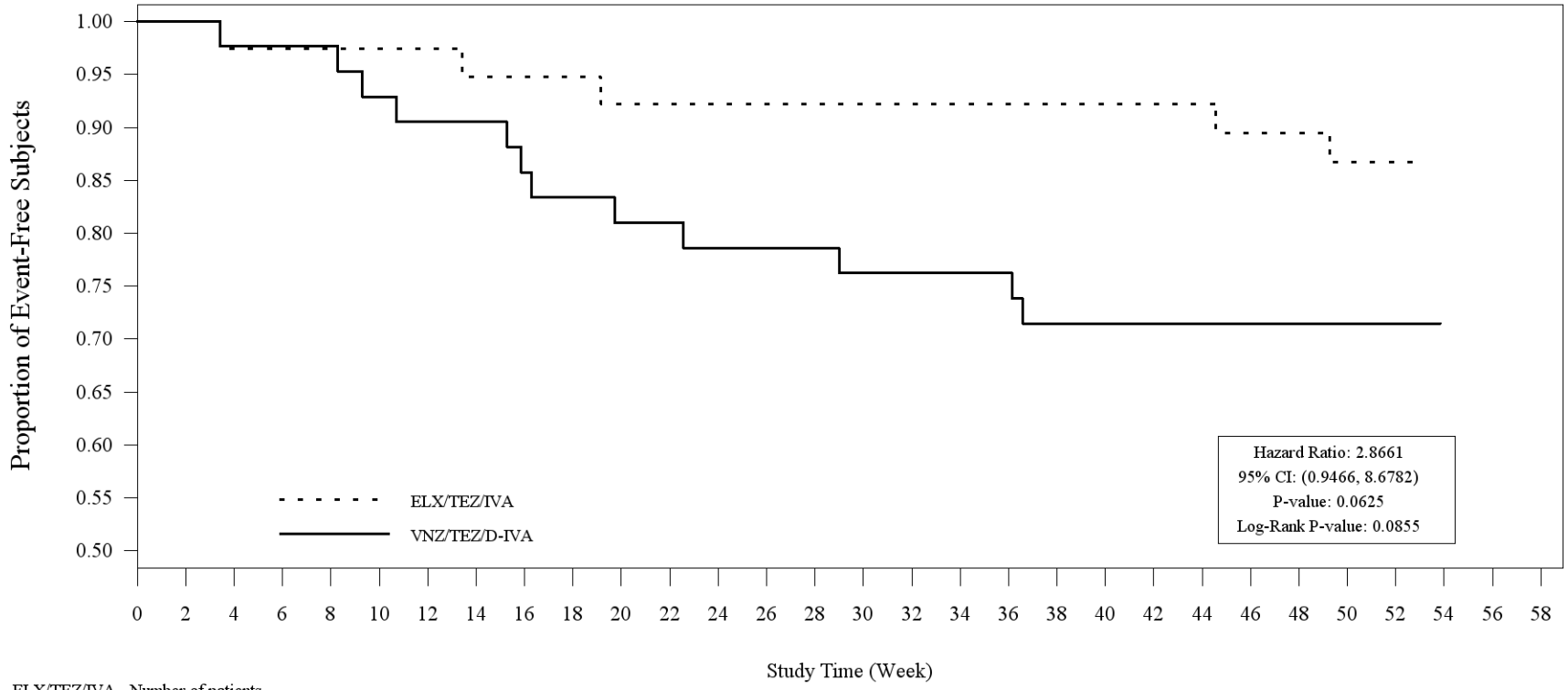
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Figure 2.2.2.6.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	39	38	35	35	33
with event(s)	0	1	3	3	4
censored	0	0	1	1	2
VNZ/TEZ/D-IVA - Number of patients					
at risk	43	38	33	32	29
with event(s)	0	4	9	10	12
censored	0	1	1	1	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

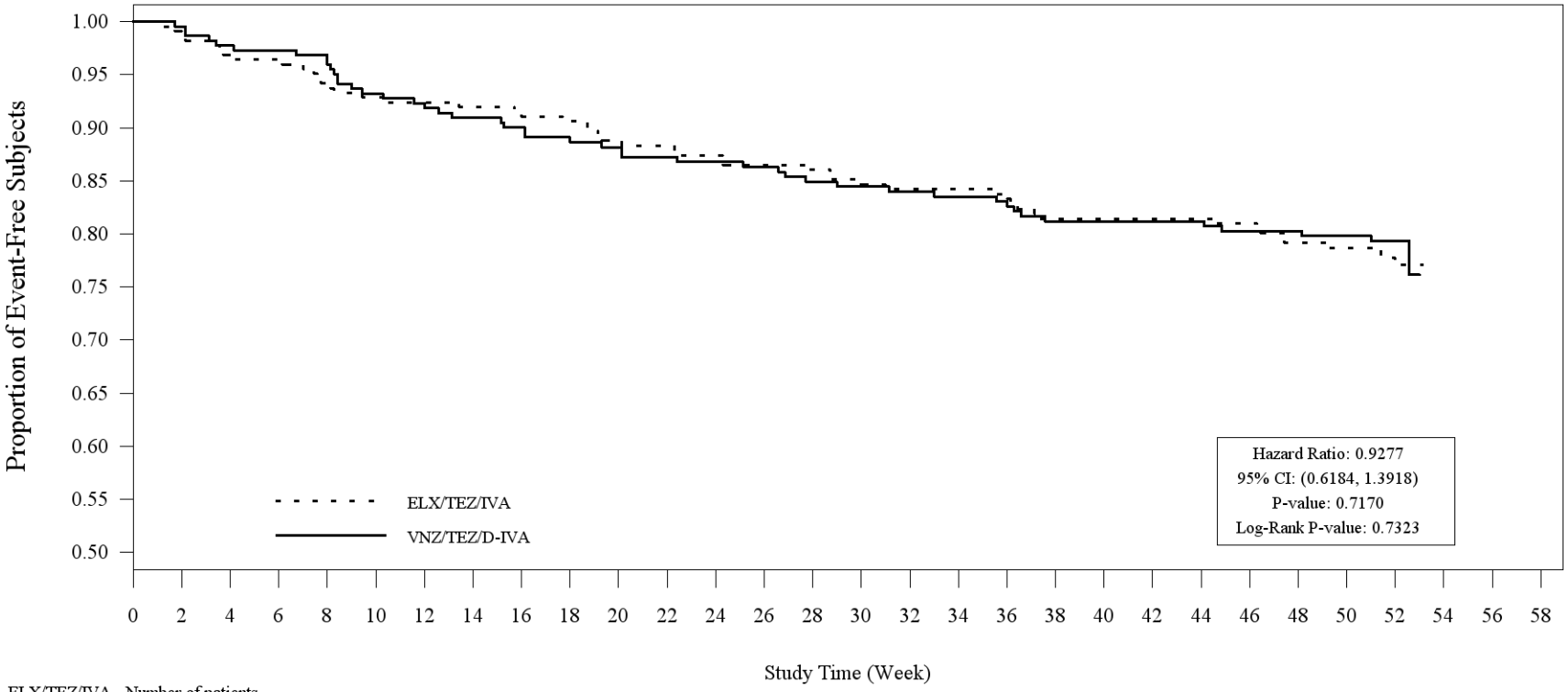
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Figure 2.2.2.6.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Genotype group: F/F

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	224	206	191	182	171
with event(s)	0	17	28	37	46
censored	0	1	5	5	7
VNZ/TEZ/D-IVA - Number of patients					
at risk	222	202	187	179	171
with event(s)	0	18	29	38	43
censored	0	2	6	5	8

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

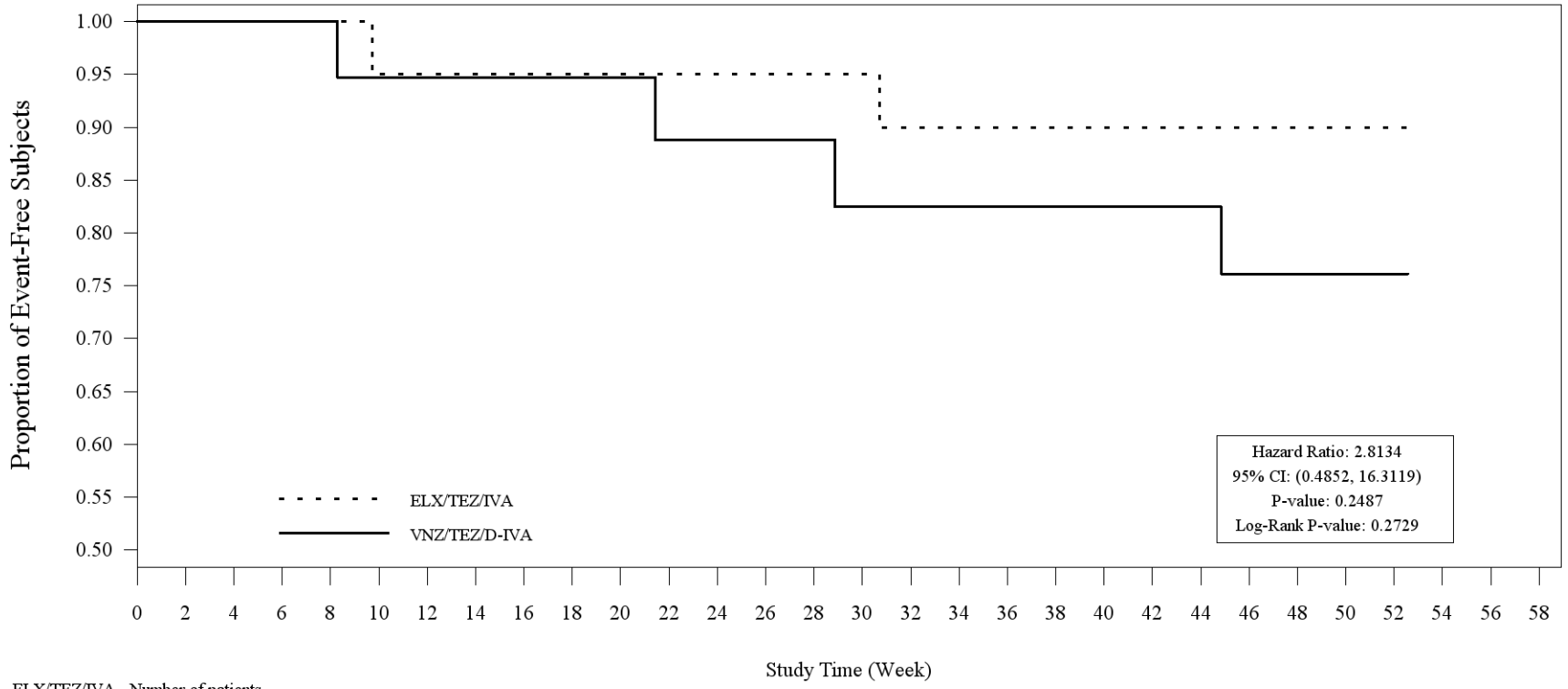
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Figure 2.2.2.6.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Genotype group: F/G

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	20	19	19	18	18
with event(s)	0	1	1	2	2
censored	0	0	0	0	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	19	18	15	13	12
with event(s)	0	1	2	3	4
censored	0	0	2	3	3

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

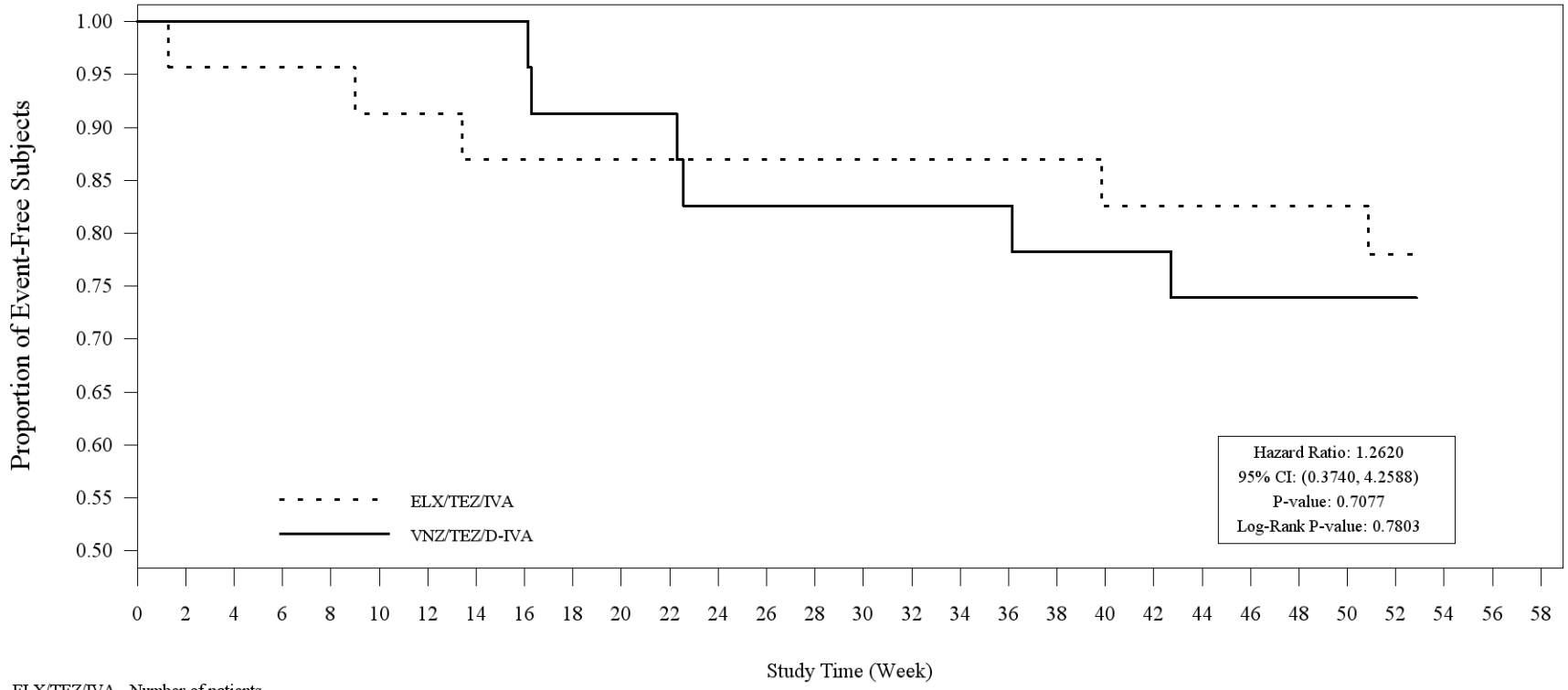
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Figure 2.2.2.6.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Genotype group: F/RF

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	23	21	20	20	19
with event(s)	0	2	3	3	4
censored	0	0	0	0	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	23	23	19	19	17
with event(s)	0	0	4	4	6
censored	0	0	0	0	0

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

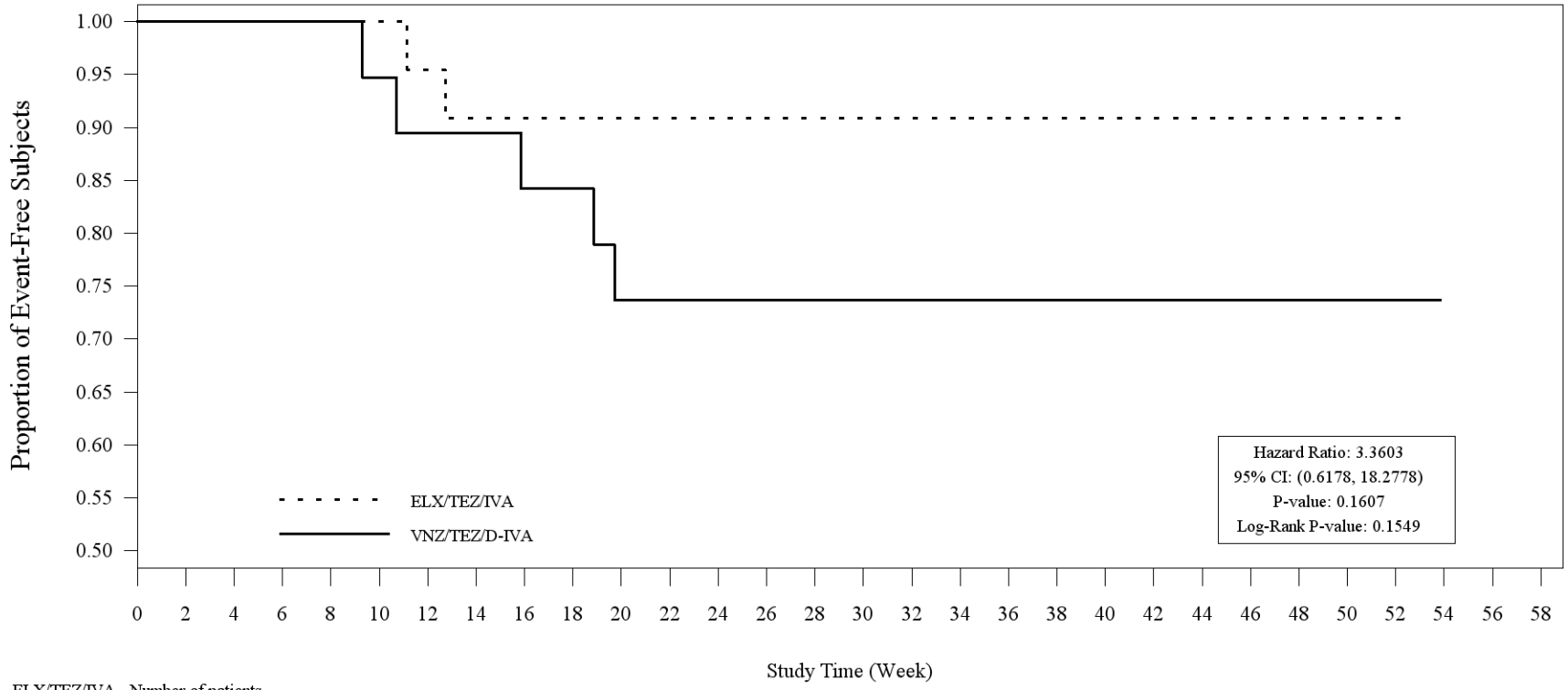
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Figure 2.2.2.6.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Genotype group: TCR/non-F

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	22	21	20	20	20
with event(s)	0	1	2	2	2
censored	0	0	0	0	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	20	17	14	13	12
with event(s)	0	2	5	5	5
censored	0	1	1	2	3

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

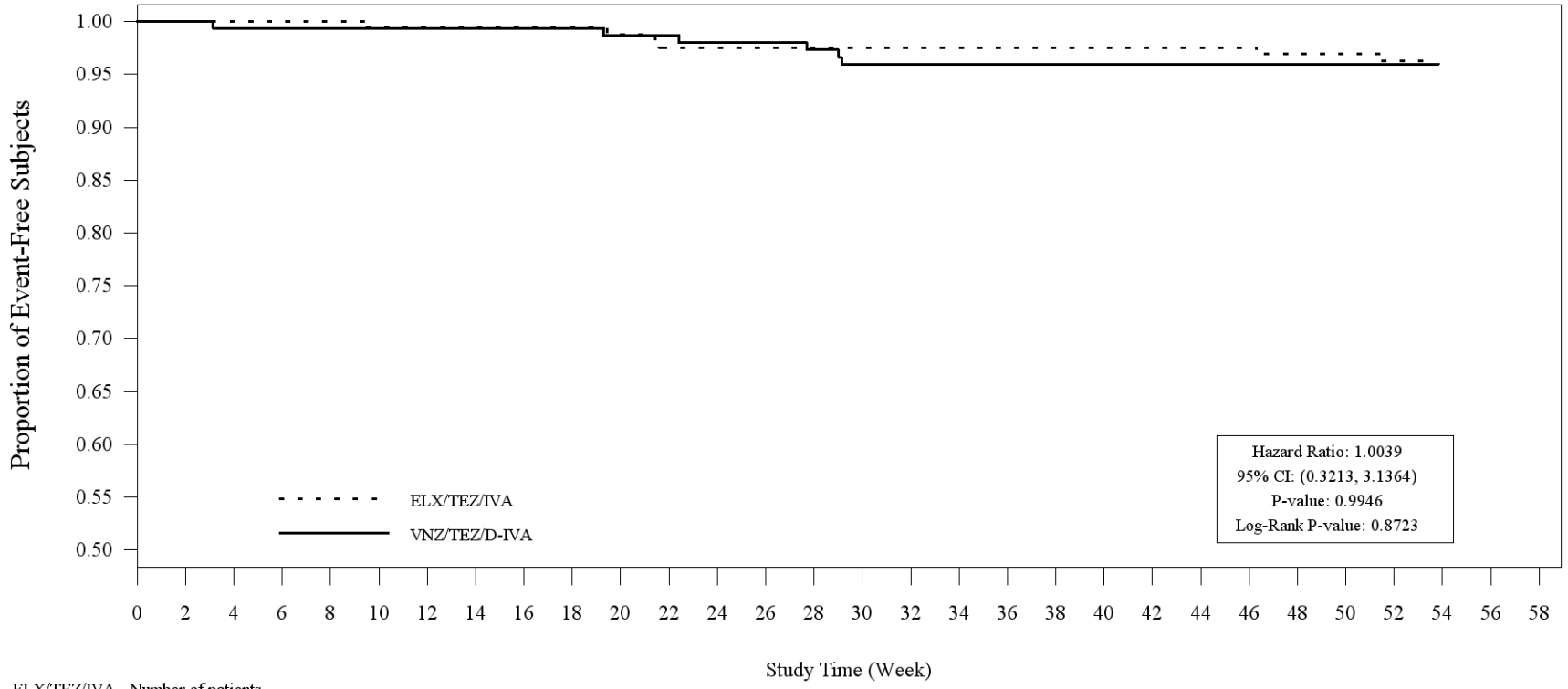
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Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: $ppFEV_1$ at Baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	167	165	158	157	155
with event(s)	0	1	4	4	5
censored	0	1	5	6	7
VNZ/TEZ/D-IVA - Number of patients					
at risk	154	150	145	142	141
with event(s)	0	1	3	6	6
censored	0	3	6	6	7

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

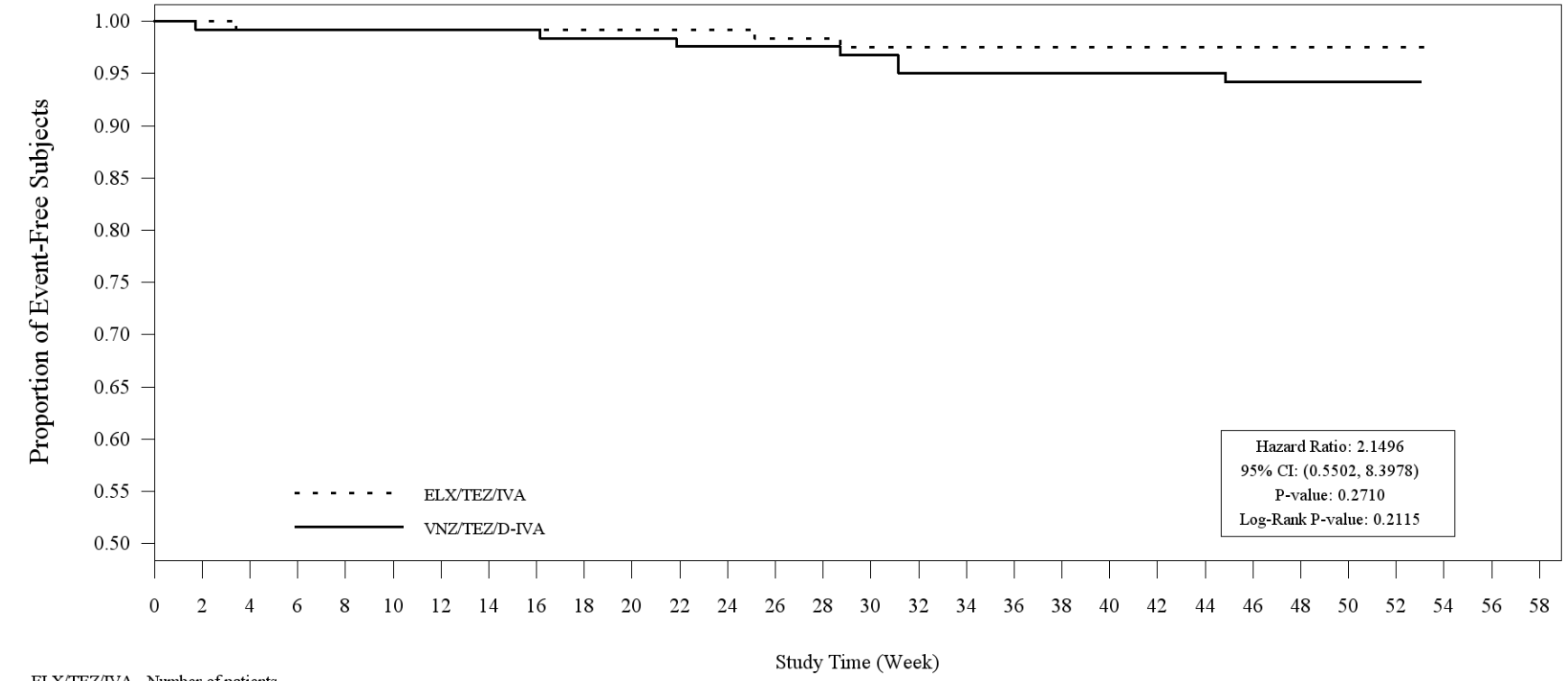
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Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: $ppFEV_1$ at Baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	119	118	118	116	116
with event(s)	0	1	1	3	3
censored	0	0	0	0	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	125	123	119	114	110
with event(s)	0	1	3	6	7
censored	0	1	3	5	8

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

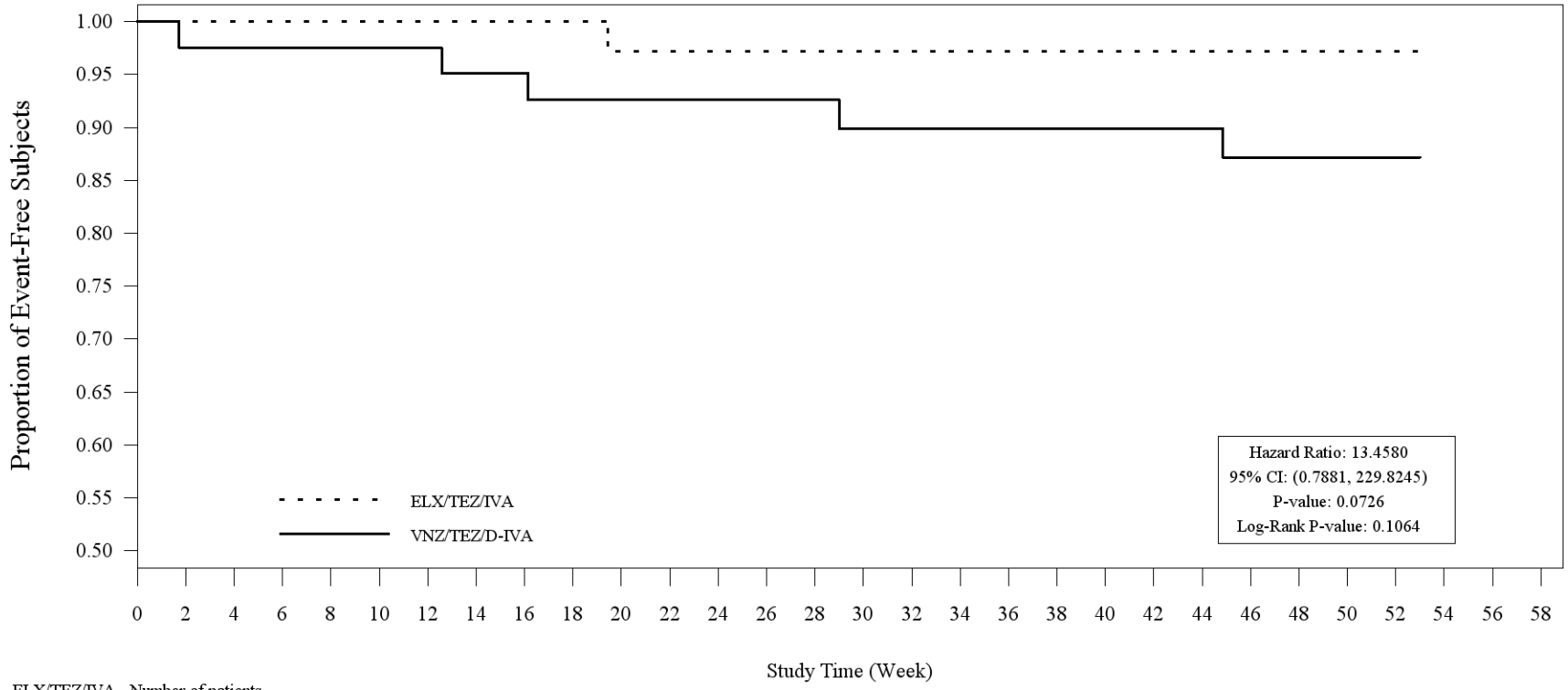
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Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening < 18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	38	37	35	35	35
with event(s)	0	0	1	1	1
censored	0	1	2	2	2
VNZ/TEZ/D-IVA - Number of patients					
at risk	41	40	36	33	32
with event(s)	0	1	3	4	5
censored	0	0	2	4	4

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

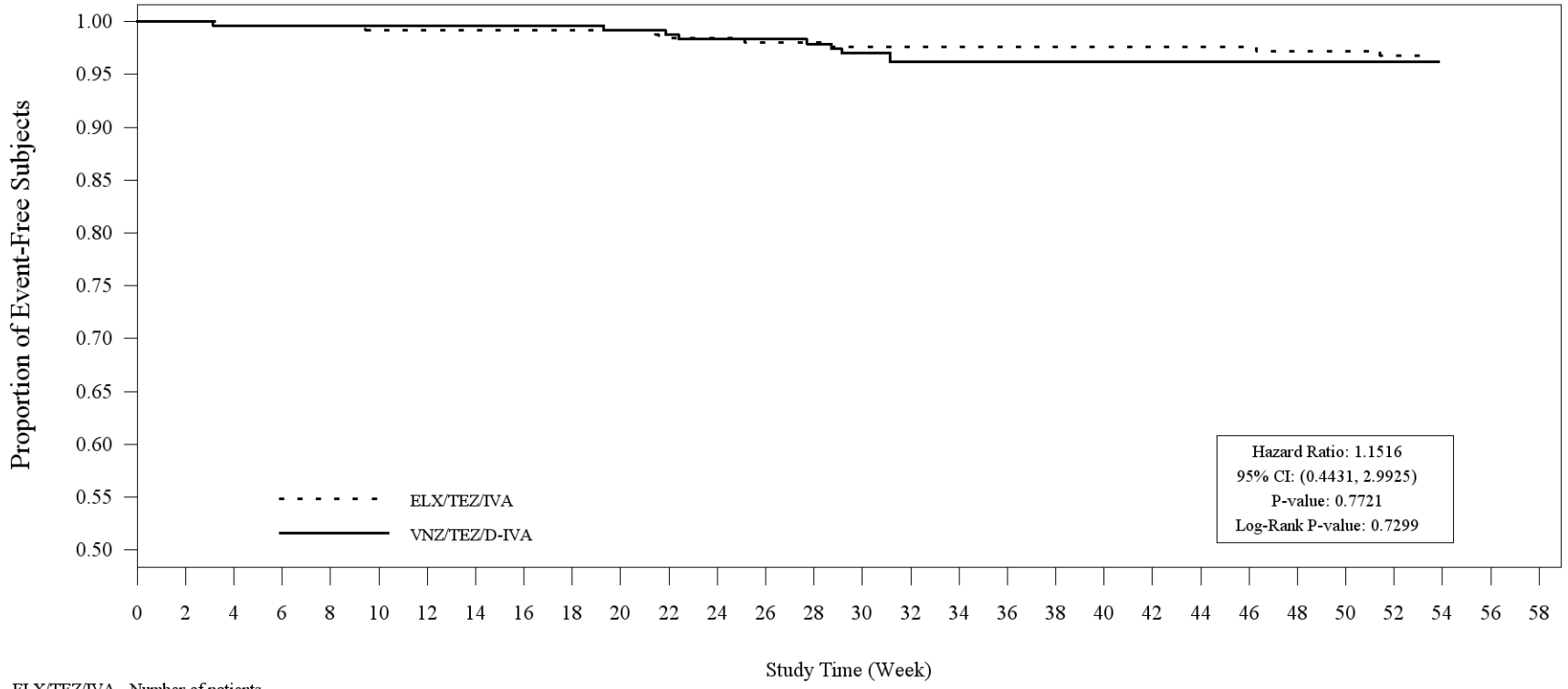
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Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening ≥ 18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	251	249	244	241	239
with event(s)	0	2	4	6	7
censored	0	0	3	4	5
VNZ/TEZ/D-IVA - Number of patients					
at risk	243	238	232	227	223
with event(s)	0	1	4	9	9
censored	0	4	7	7	11

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

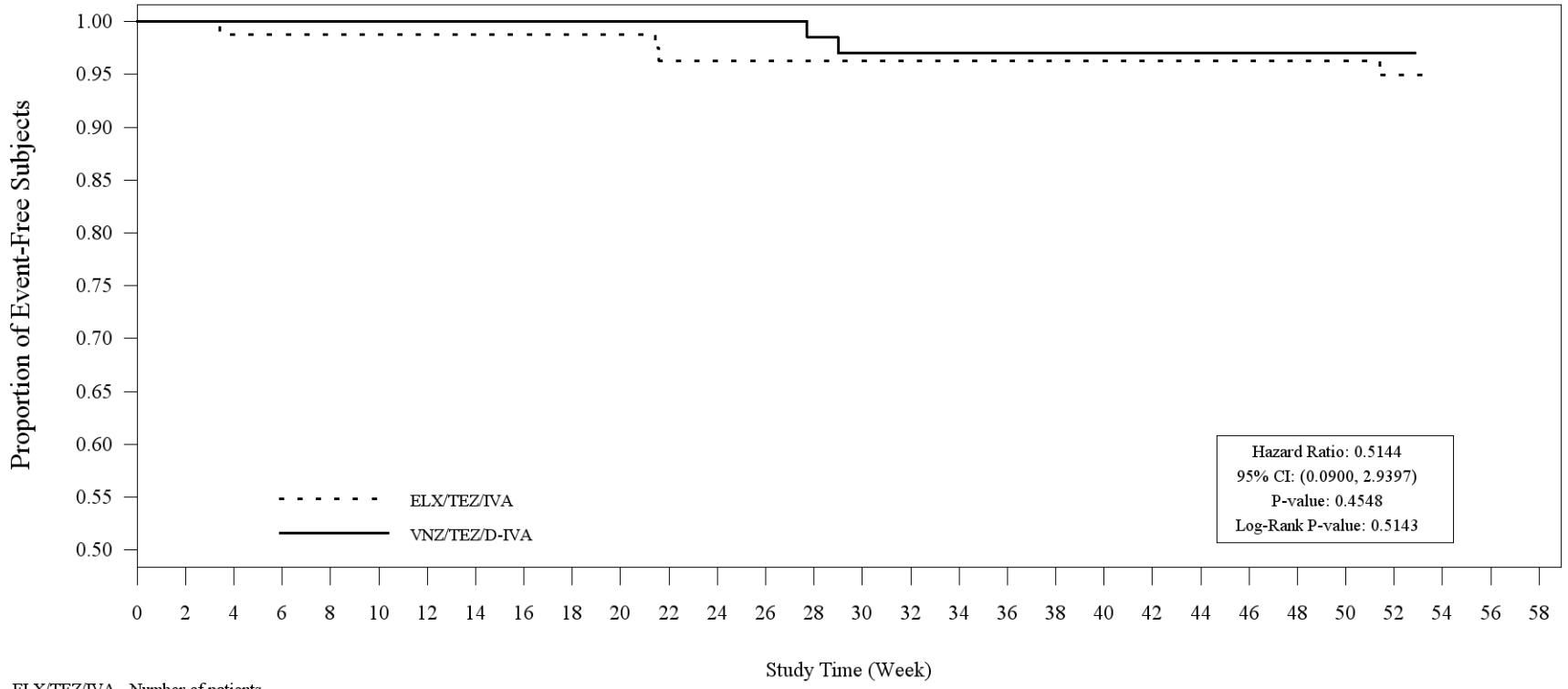
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Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	80	79	77	76	76
with event(s)	0	1	3	3	3
censored	0	0	0	1	1
VNZ/TEZ/D-IVA - Number of patients					
at risk	72	71	68	65	65
with event(s)	0	0	0	2	2
censored	0	1	4	5	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

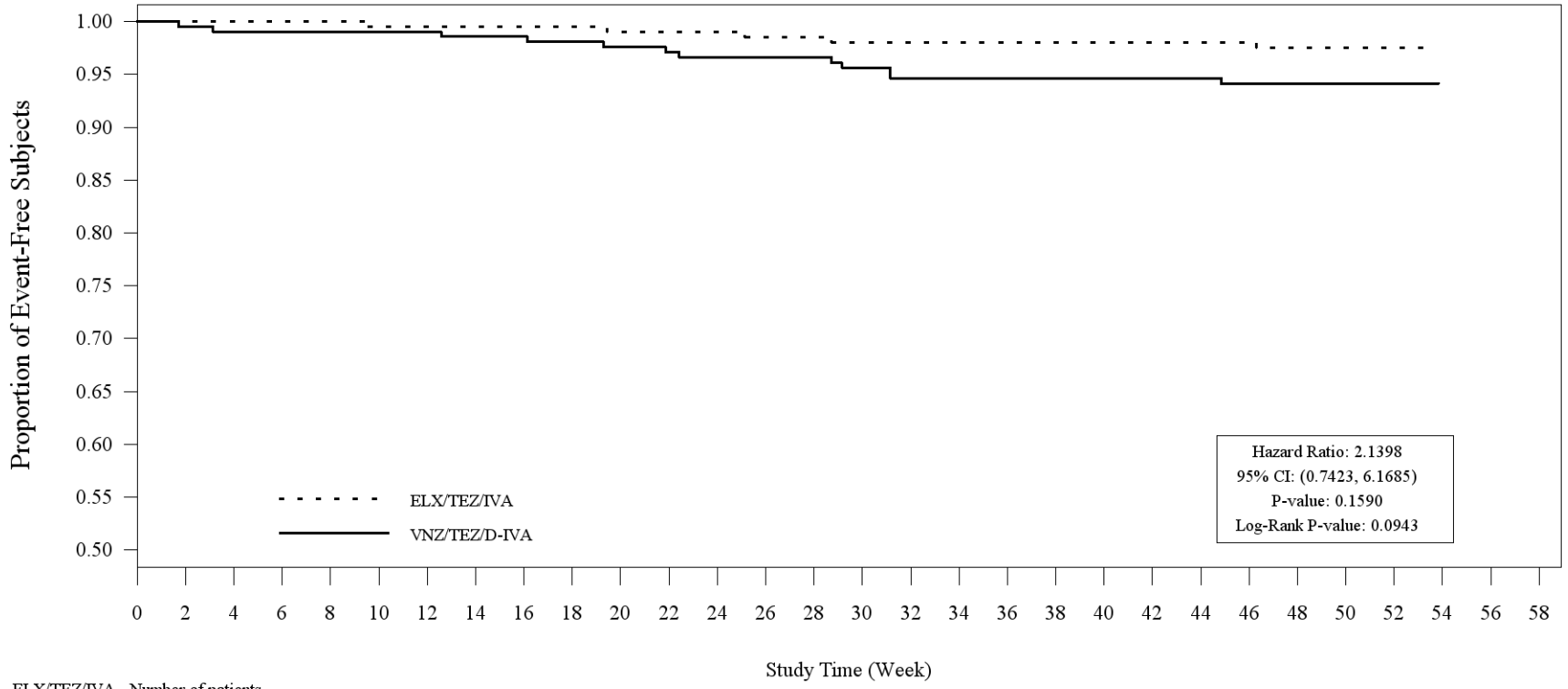
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Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	202	200	196	194	192
with event(s)	0	1	2	4	5
censored	0	1	4	4	5
VNZ/TEZ/D-IVA - Number of patients					
at risk	210	205	198	193	188
with event(s)	0	2	7	11	12
censored	0	3	5	6	10

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

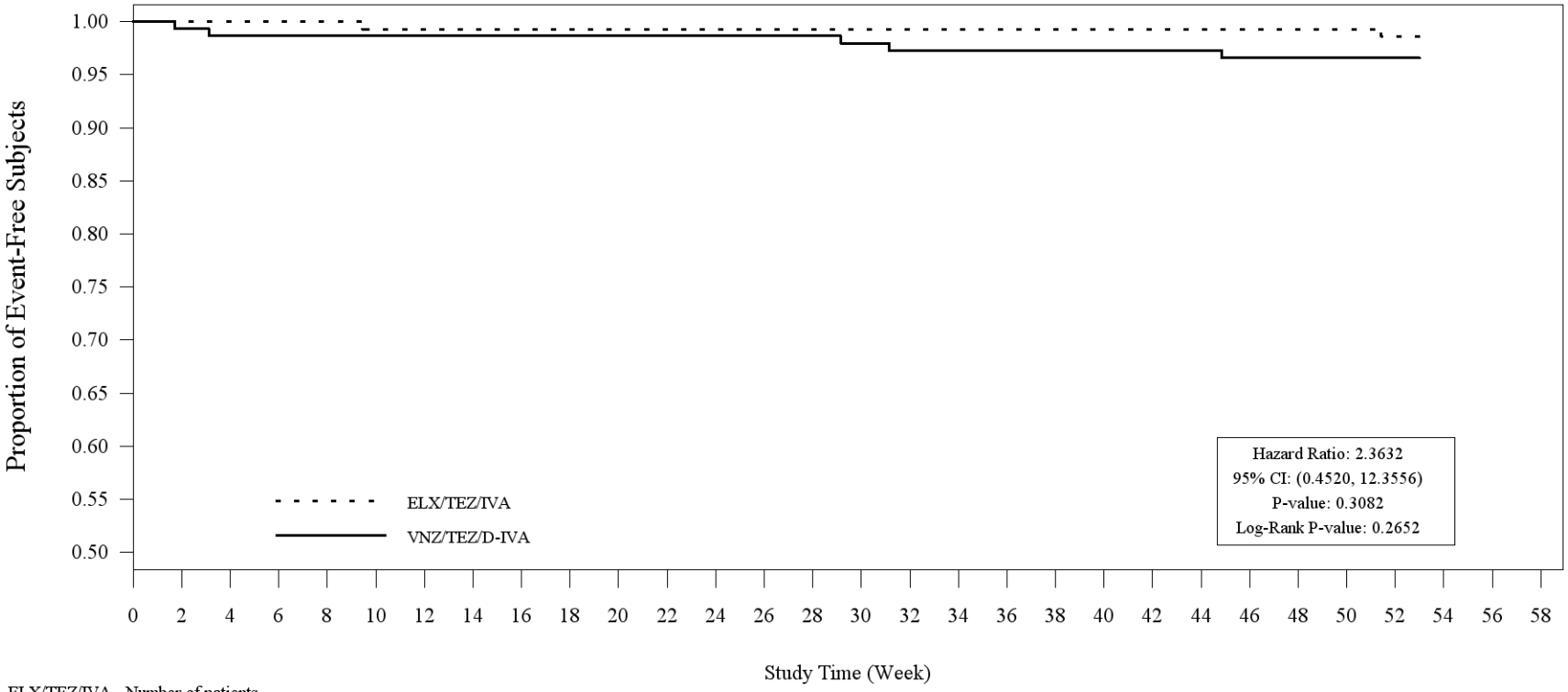
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Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	144	142	140	140	139
with event(s)	0	1	1	1	1
censored	0	1	3	3	4
VNZ/TEZ/D-IVA - Number of patients					
at risk	149	144	142	140	139
with event(s)	0	2	2	4	5
censored	0	3	5	5	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

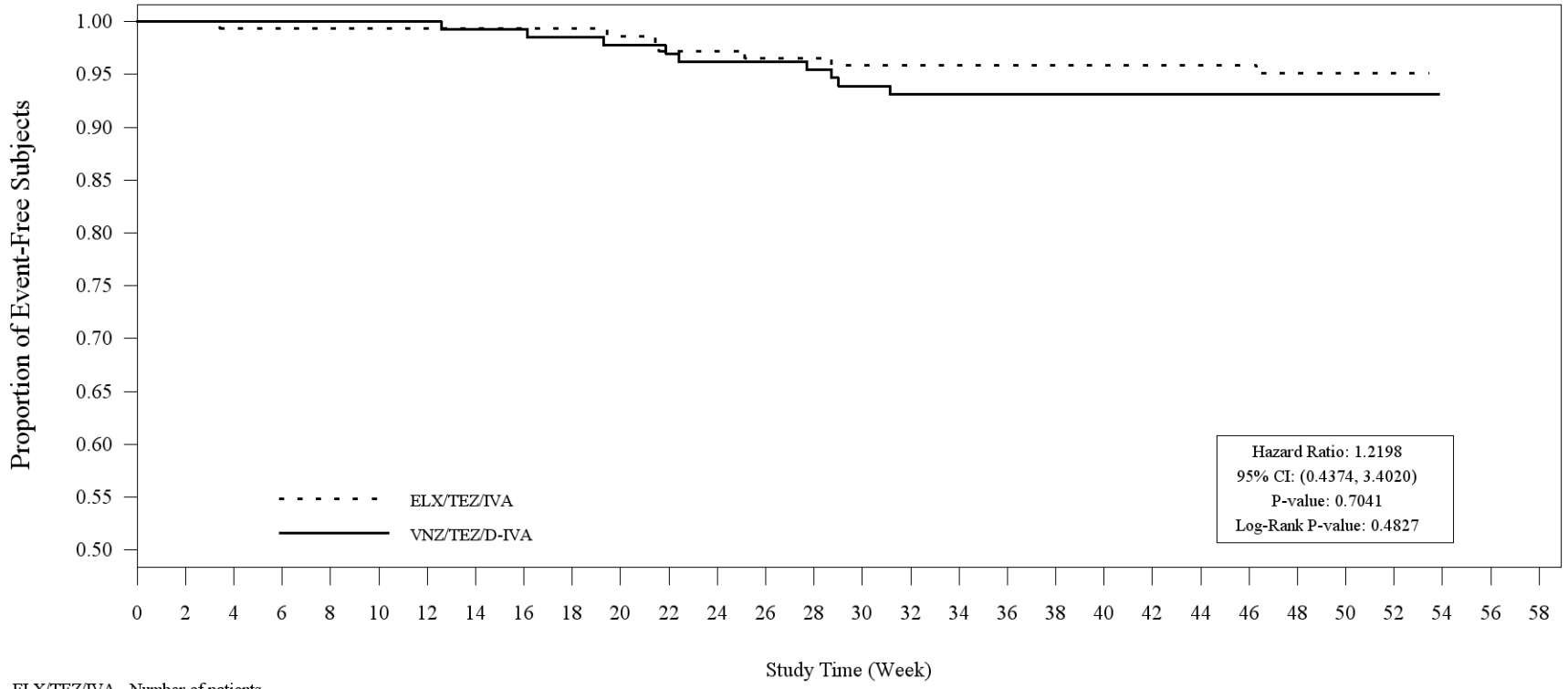
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Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	145	144	139	136	135
with event(s)	0	1	4	6	7
censored	0	0	2	3	3
VNZ/TEZ/D-IVA - Number of patients					
at risk	135	134	126	120	116
with event(s)	0	0	5	9	9
censored	0	1	4	6	10

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

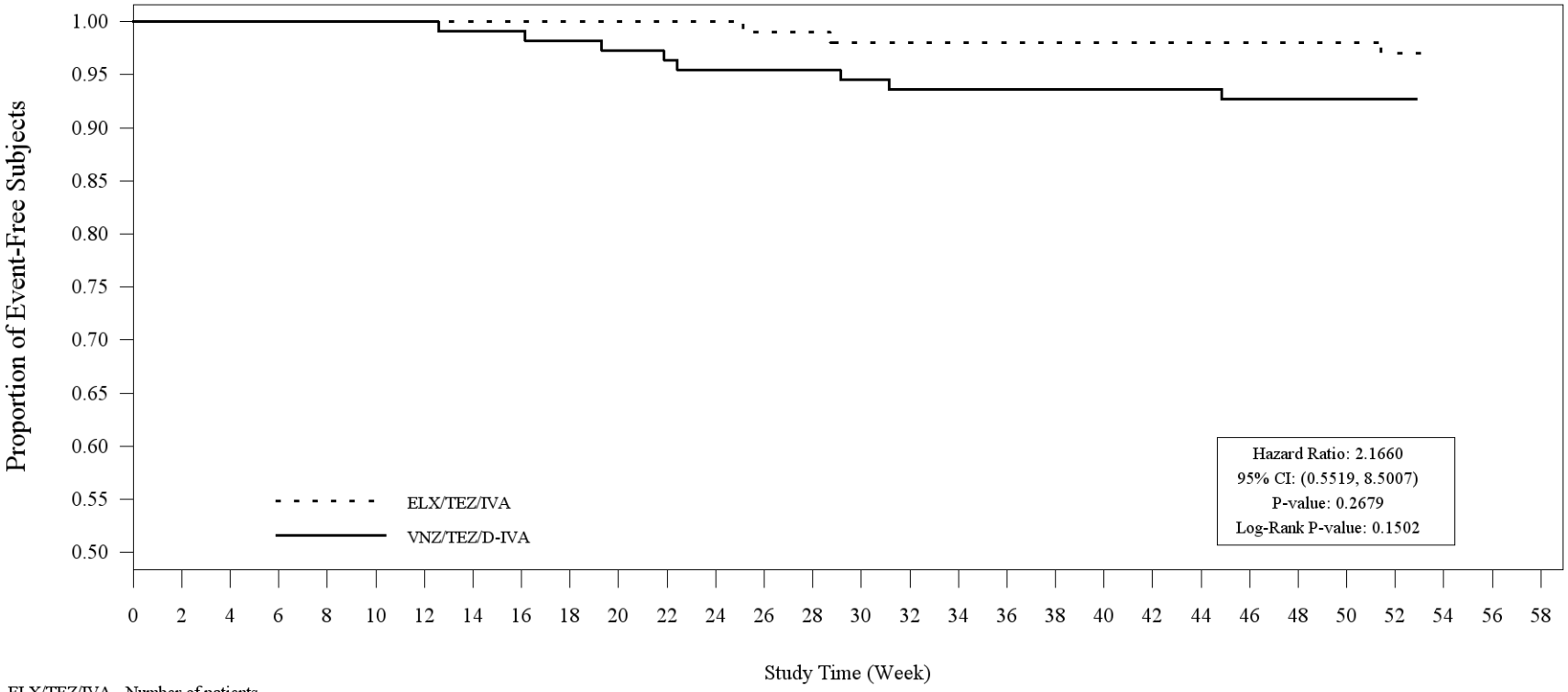
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Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	103	103	102	100	100
with event(s)	0	0	0	2	2
censored	0	0	1	1	1
VNZ/TEZ/D-IVA - Number of patients					
at risk	114	112	105	102	100
with event(s)	0	0	5	7	8
censored	0	2	4	5	6

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

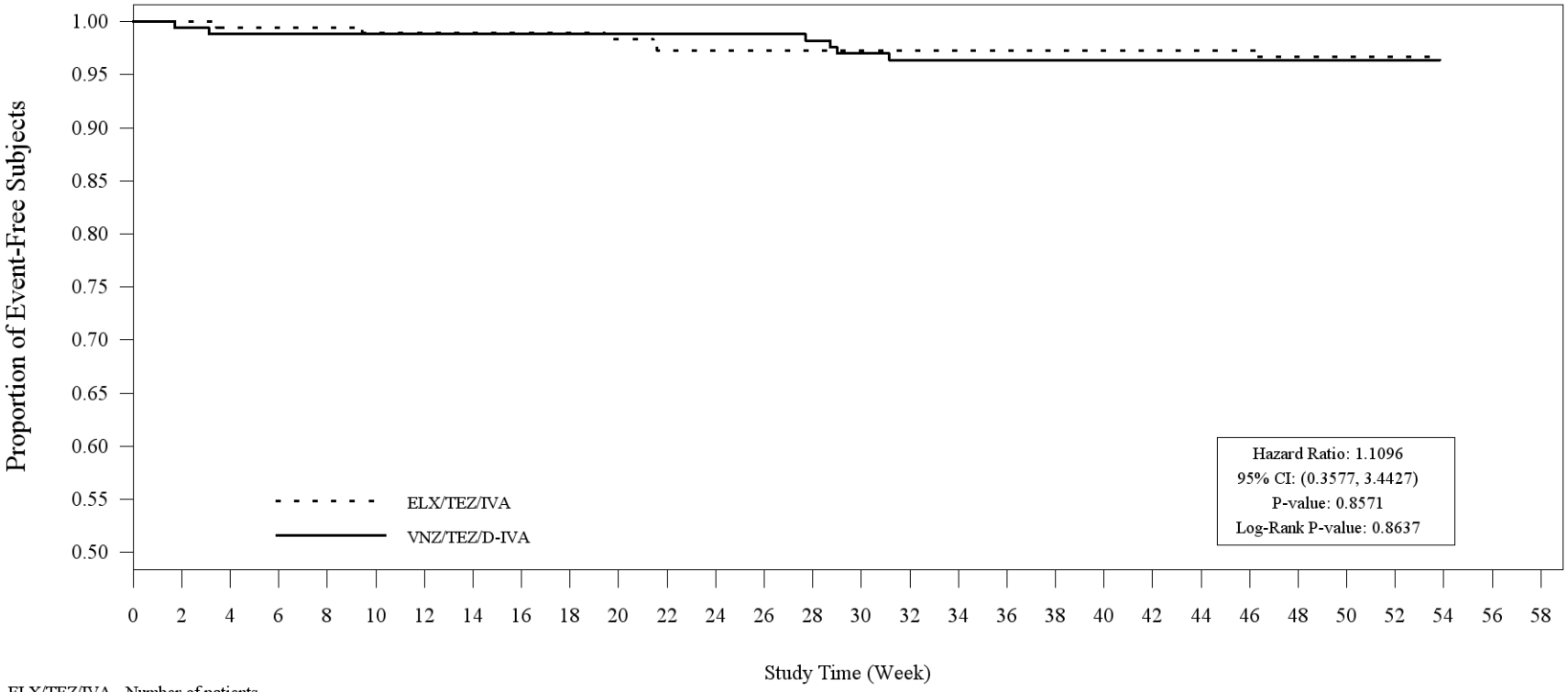
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Figure 2.2.2.7.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = Rest of the World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	186	183	177	176	174
with event(s)	0	2	5	5	6
censored	0	1	4	5	6
VNZ/TEZ/D-IVA - Number of patients					
at risk	170	166	163	158	155
with event(s)	0	2	2	6	6
censored	0	2	5	6	9

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

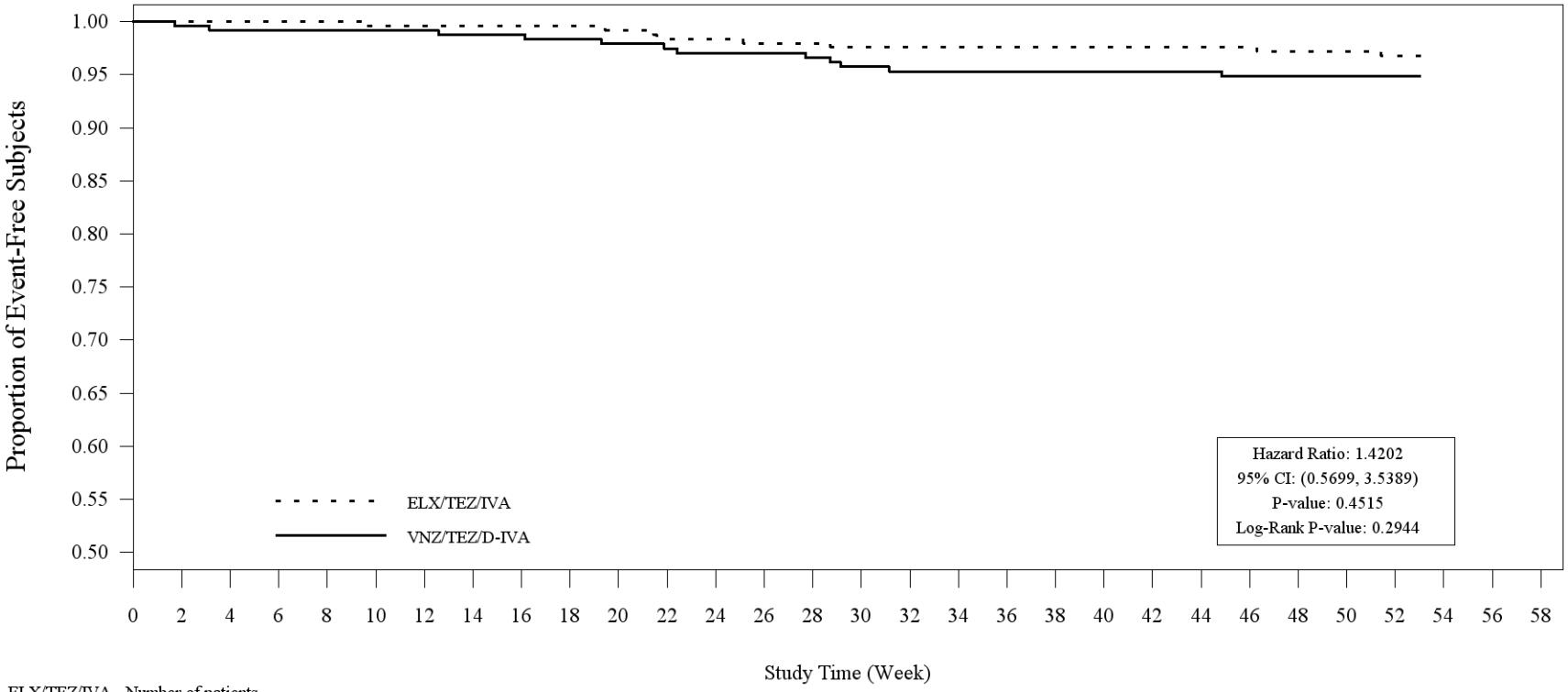
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Figure 2.2.2.7.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, , and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	250	248	242	239	238
with event(s)	0	1	4	6	7
censored	0	1	4	5	5
VNZ/TEZ/D-IVA - Number of patients					
at risk	241	236	226	220	216
with event(s)	0	2	7	11	12
censored	0	3	8	10	13

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, , and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

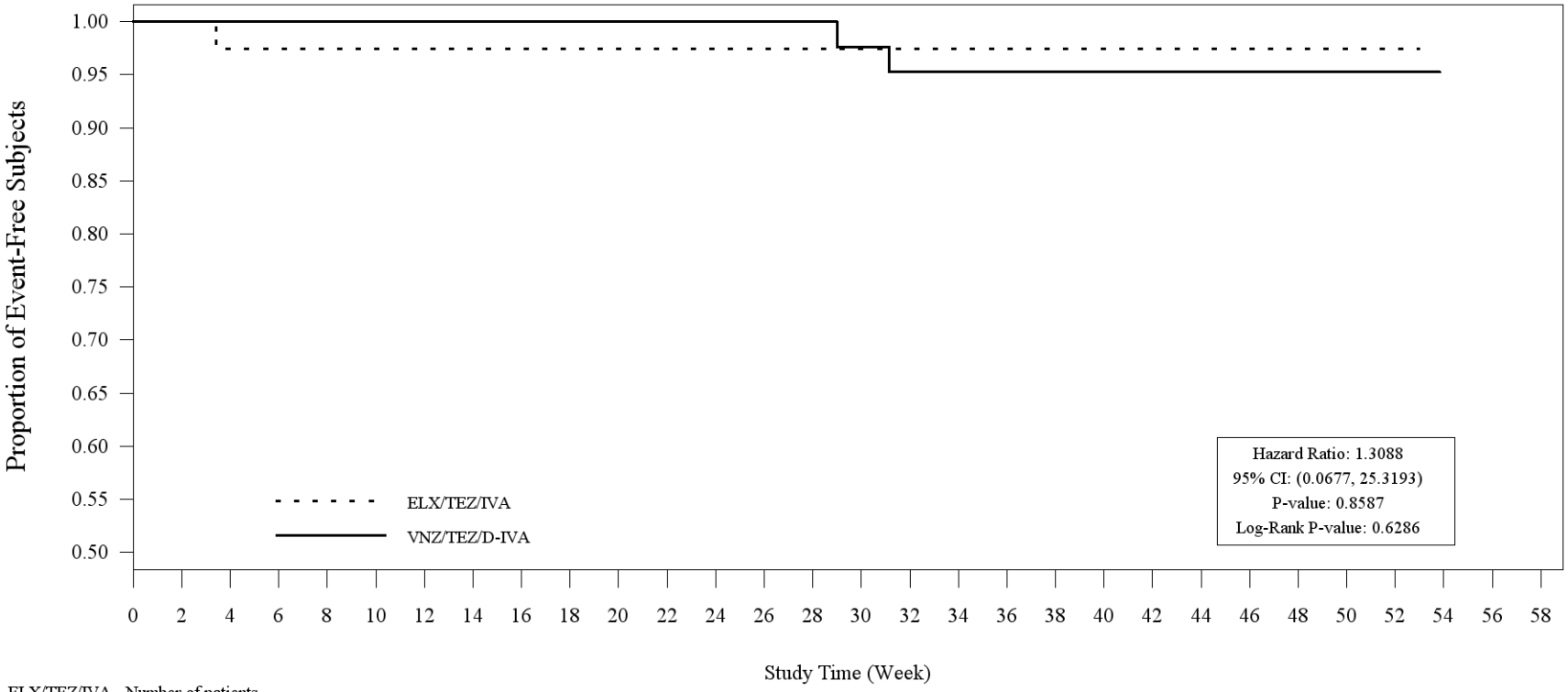
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Figure 2.2.2.7.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, , and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	39	38	37	37	36
with event(s)	0	1	1	1	1
censored	0	0	1	1	2
VNZ/TEZ/D-IVA - Number of patients					
at risk	43	42	42	40	39
with event(s)	0	0	0	2	2
censored	0	1	1	1	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, , and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

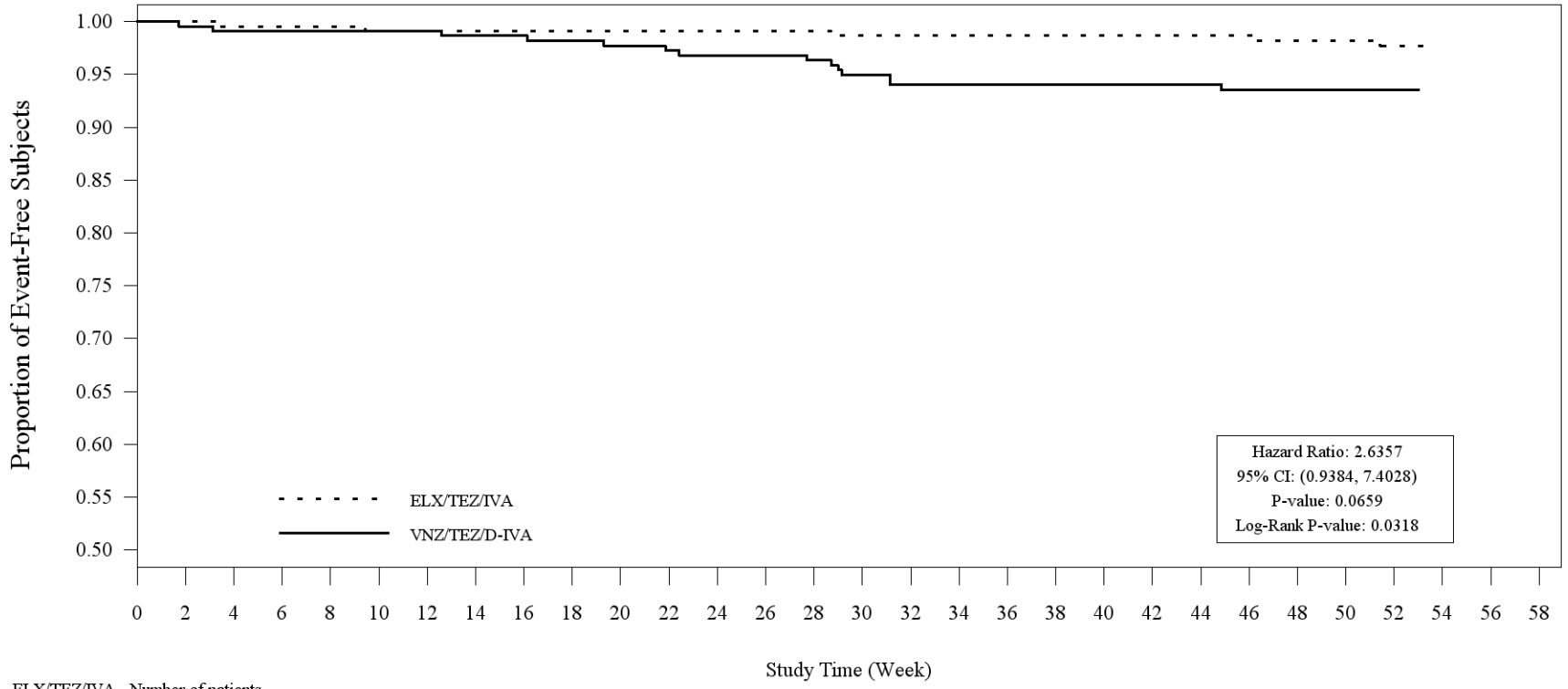
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Figure 2.2.2.7.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Genotype group: F/F

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, , and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	224	221	217	215	213
with event(s)	0	2	2	3	4
censored	0	1	5	6	7
VNZ/TEZ/D-IVA - Number of patients					
at risk	222	217	209	203	199
with event(s)	0	2	7	13	14
censored	0	3	6	6	9

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, , and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

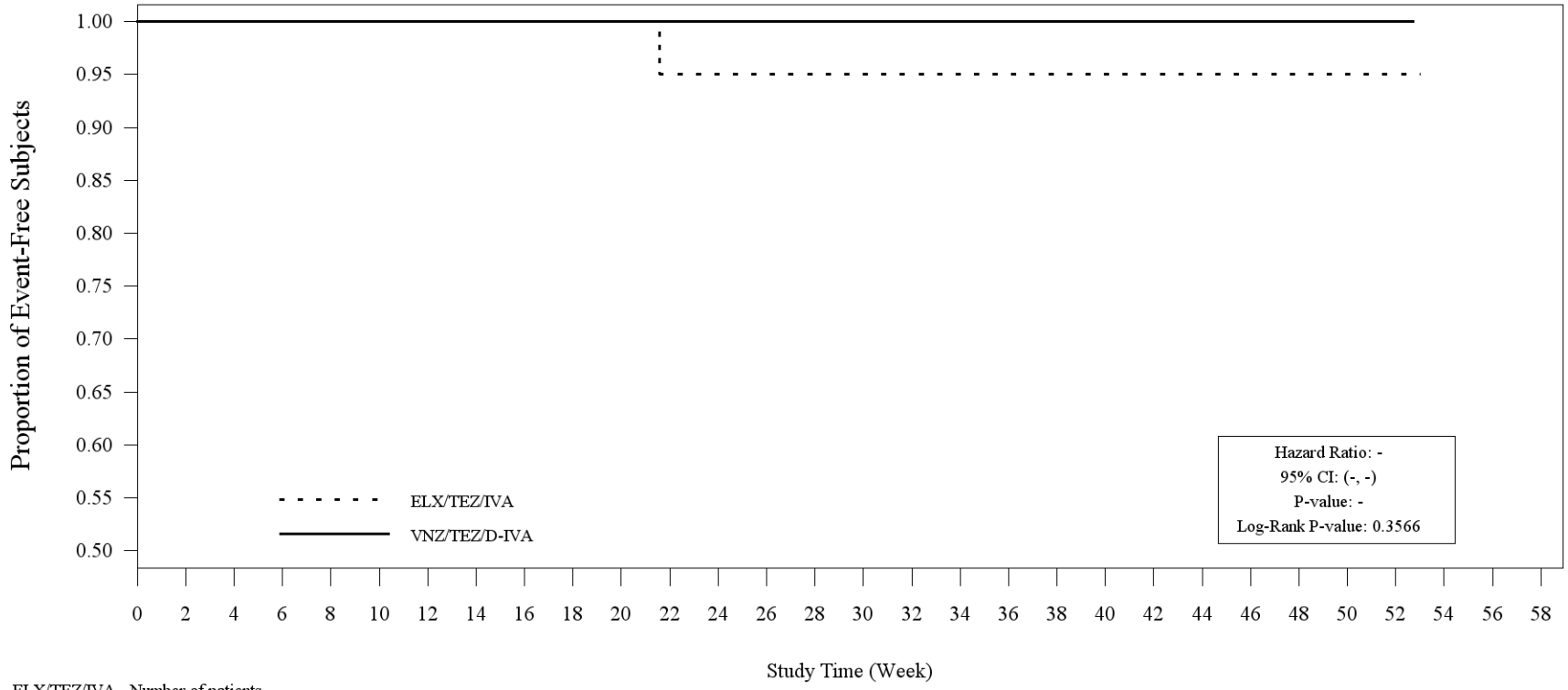
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Figure 2.2.2.7.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Genotype group: F/G

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, , and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	20	20	19	19	19
with event(s)	0	0	1	1	1
censored	0	0	0	0	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	19	19	17	16	16
with event(s)	0	0	0	0	0
censored	0	0	2	3	3

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, , and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

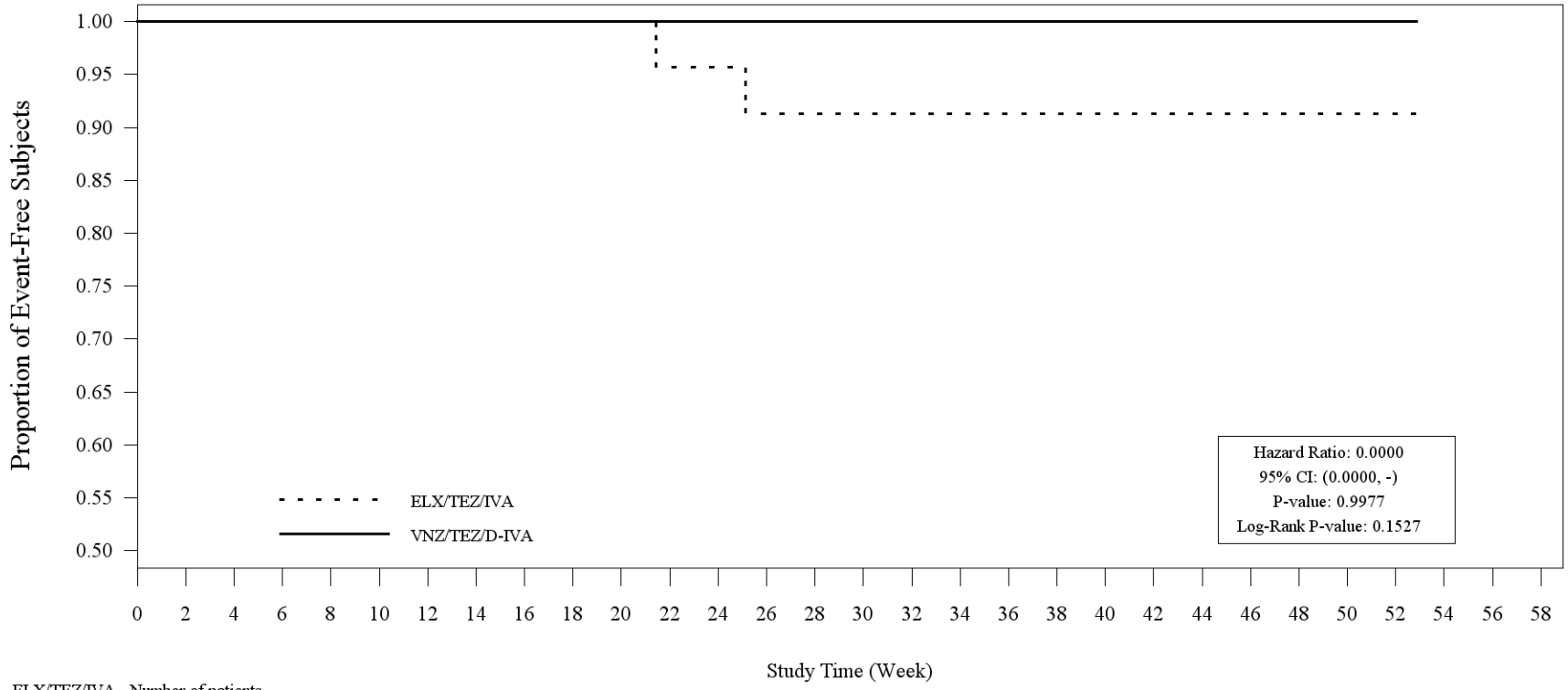
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Figure 2.2.2.7.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Genotype group: F/RF

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, , and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	23	23	22	21	21
with event(s)	0	0	1	2	2
censored	0	0	0	0	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	23	23	23	23	23
with event(s)	0	0	0	0	0
censored	0	0	0	0	0

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, , and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

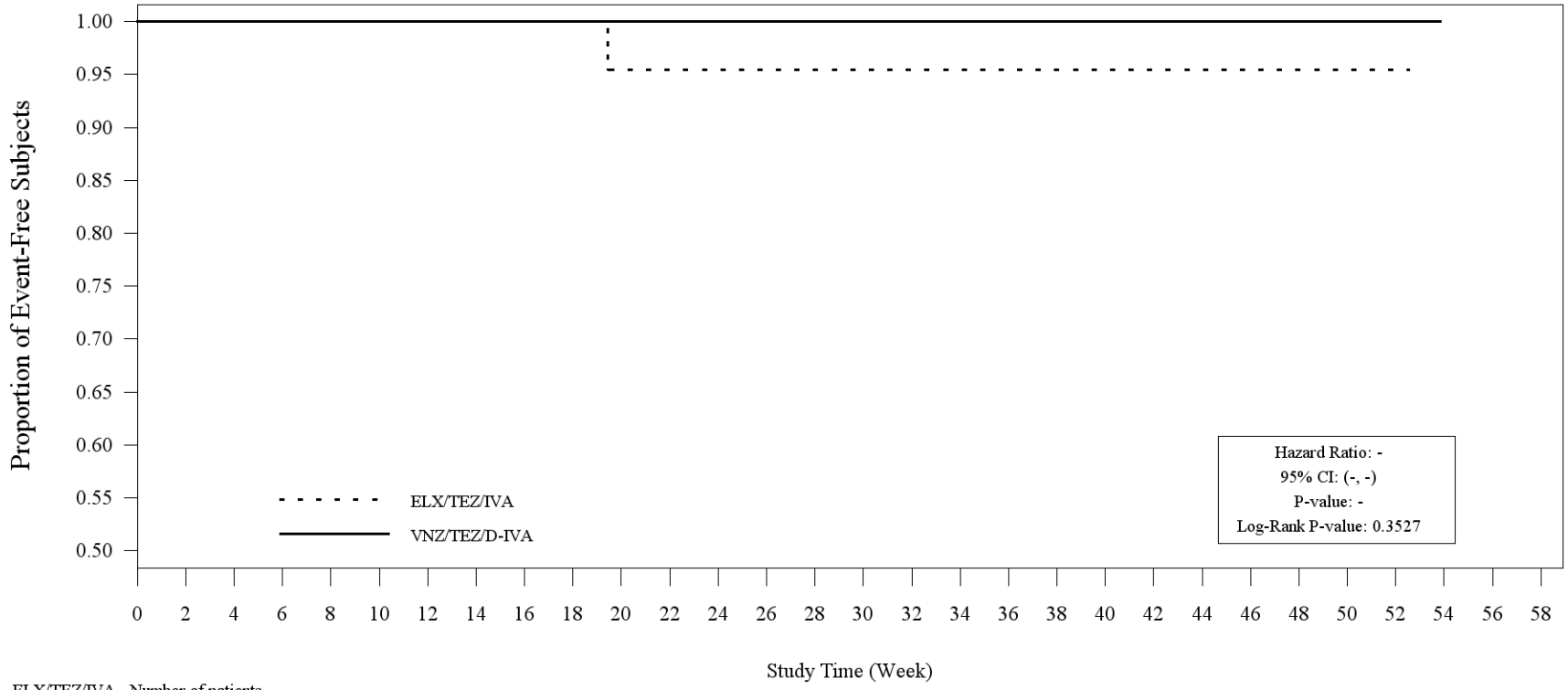
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Figure 2.2.2.7.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Genotype group: TCR/non-F

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, , and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	22	22	21	21	21
with event(s)	0	0	1	1	1
censored	0	0	0	0	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	20	19	19	18	17
with event(s)	0	0	0	0	0
censored	0	1	1	2	3

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, , and age at screening (<18 vs ≥18 years). Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

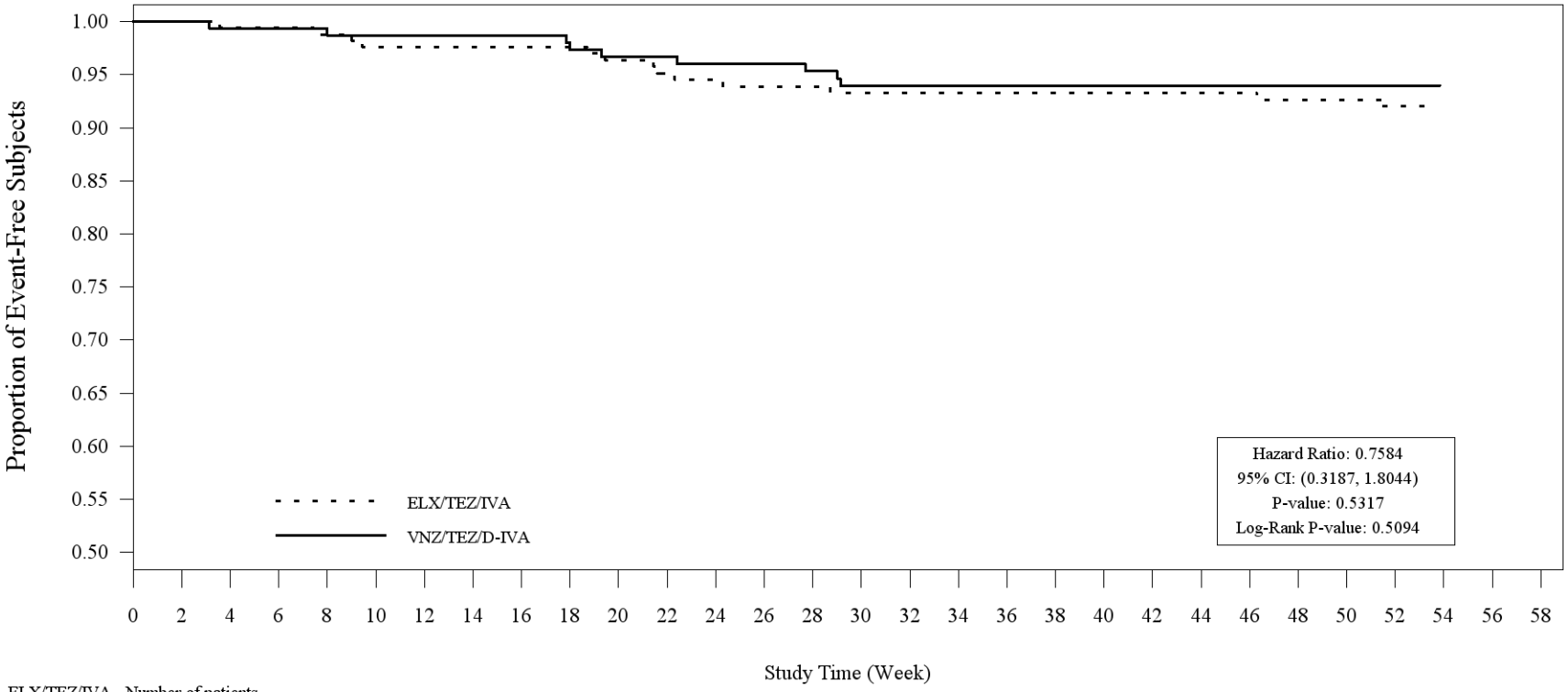
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Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: $ppFEV_1$ at Baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	167	162	153	150	148
with event(s)	0	4	9	11	12
censored	0	1	5	6	7
VNZ/TEZ/D-IVA - Number of patients					
at risk	154	149	142	139	138
with event(s)	0	2	6	9	9
censored	0	3	6	6	7

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

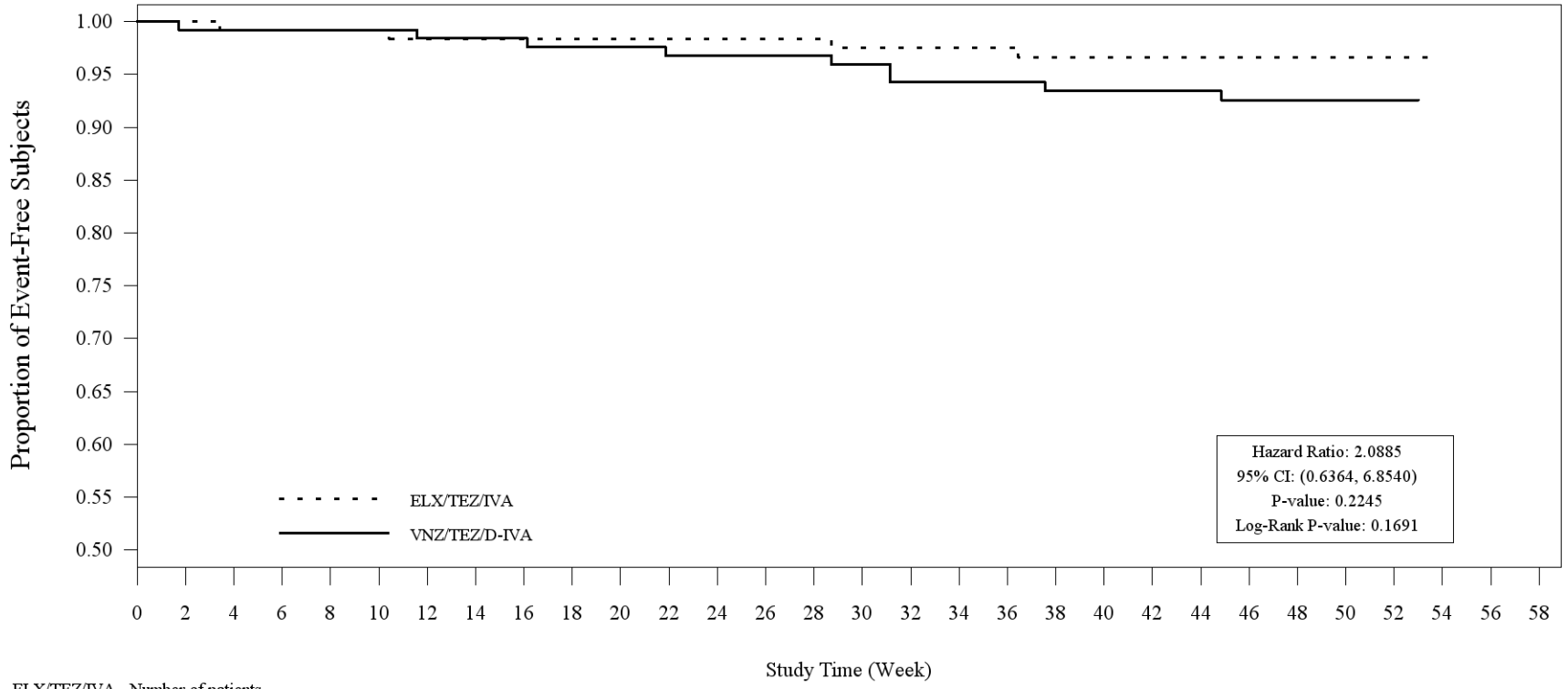
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Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: $ppFEV_1$ at Baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline $ppFEV_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	119	117	117	116	115
with event(s)	0	2	2	3	4
censored	0	0	0	0	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	125	122	118	113	108
with event(s)	0	2	4	7	9
censored	0	1	3	5	8

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

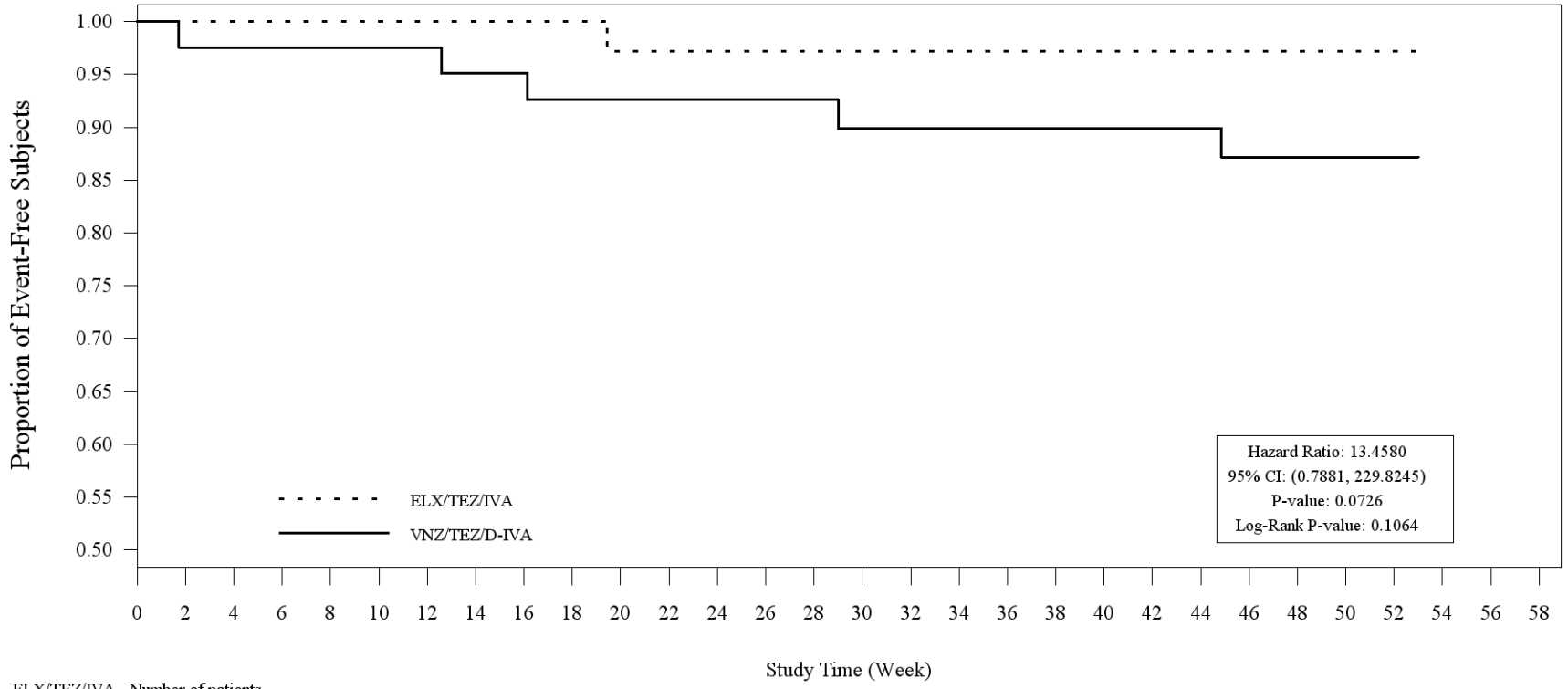
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Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening < 18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	38	37	35	35	35
with event(s)	0	0	1	1	1
censored	0	1	2	2	2
VNZ/TEZ/D-IVA - Number of patients					
at risk	41	40	36	33	32
with event(s)	0	1	3	4	5
censored	0	0	2	4	4

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

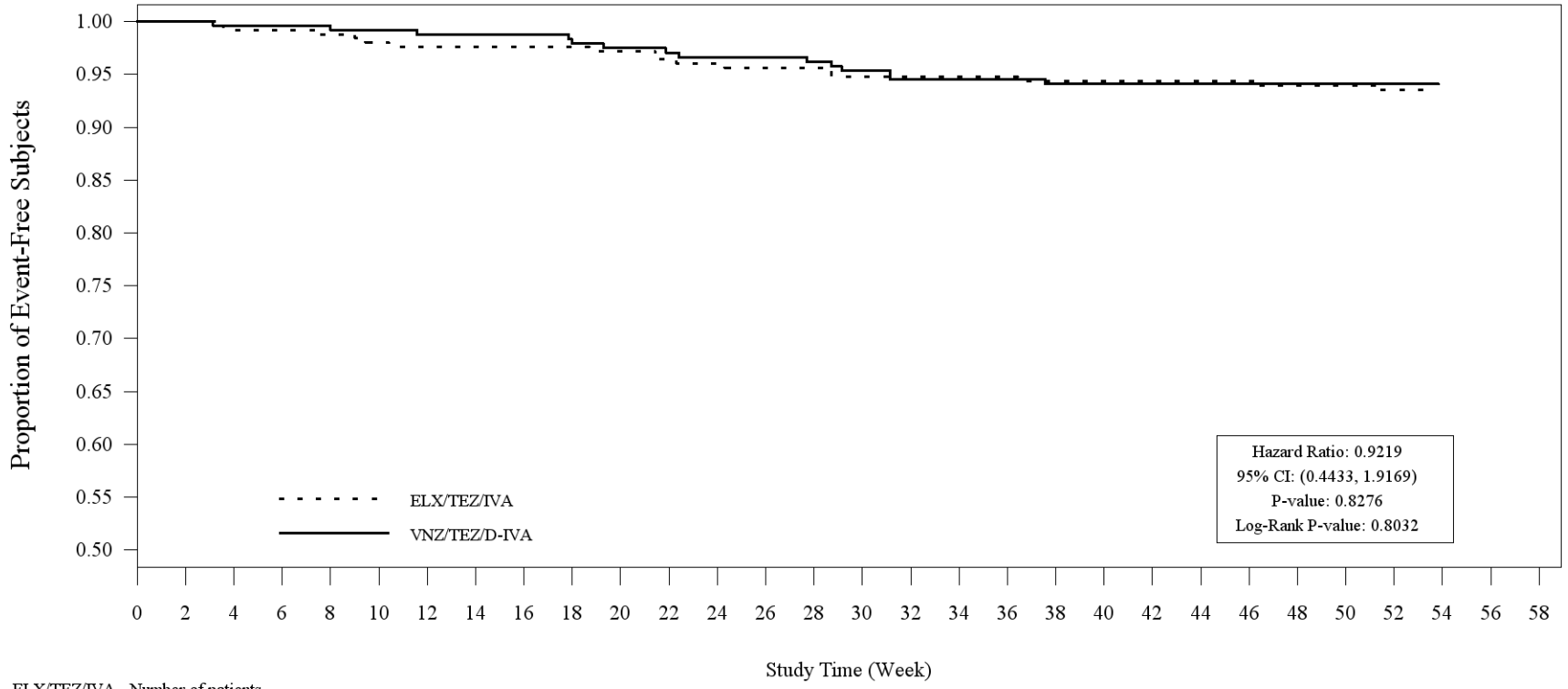
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Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Age at Screening ≥ 18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	251	245	238	234	231
with event(s)	0	6	10	13	15
censored	0	0	3	4	5
VNZ/TEZ/D-IVA - Number of patients					
at risk	243	236	228	223	218
with event(s)	0	3	8	13	14
censored	0	4	7	7	11

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

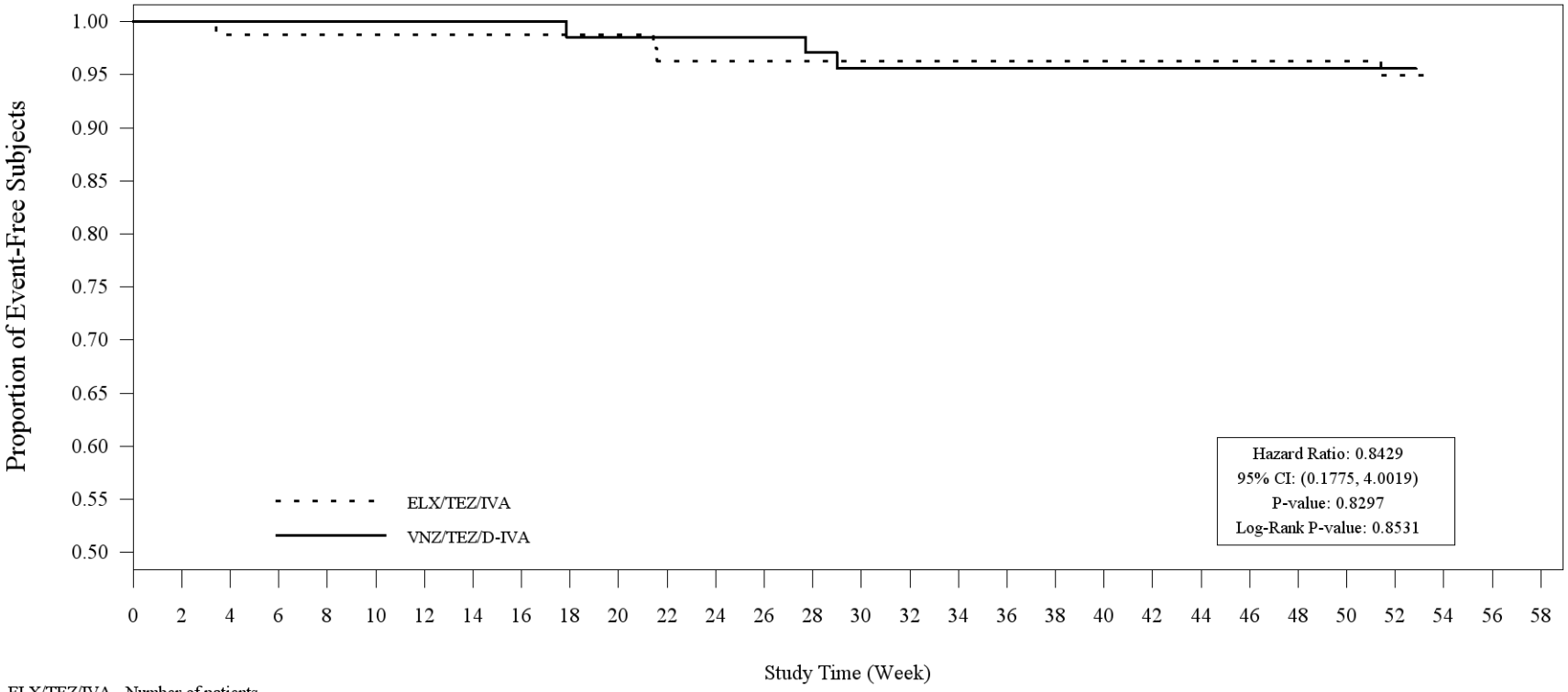
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Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	80	79	77	76	76
with event(s)	0	1	3	3	3
censored	0	0	0	1	1
VNZ/TEZ/D-IVA - Number of patients					
at risk	72	71	67	64	64
with event(s)	0	0	1	3	3
censored	0	1	4	5	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

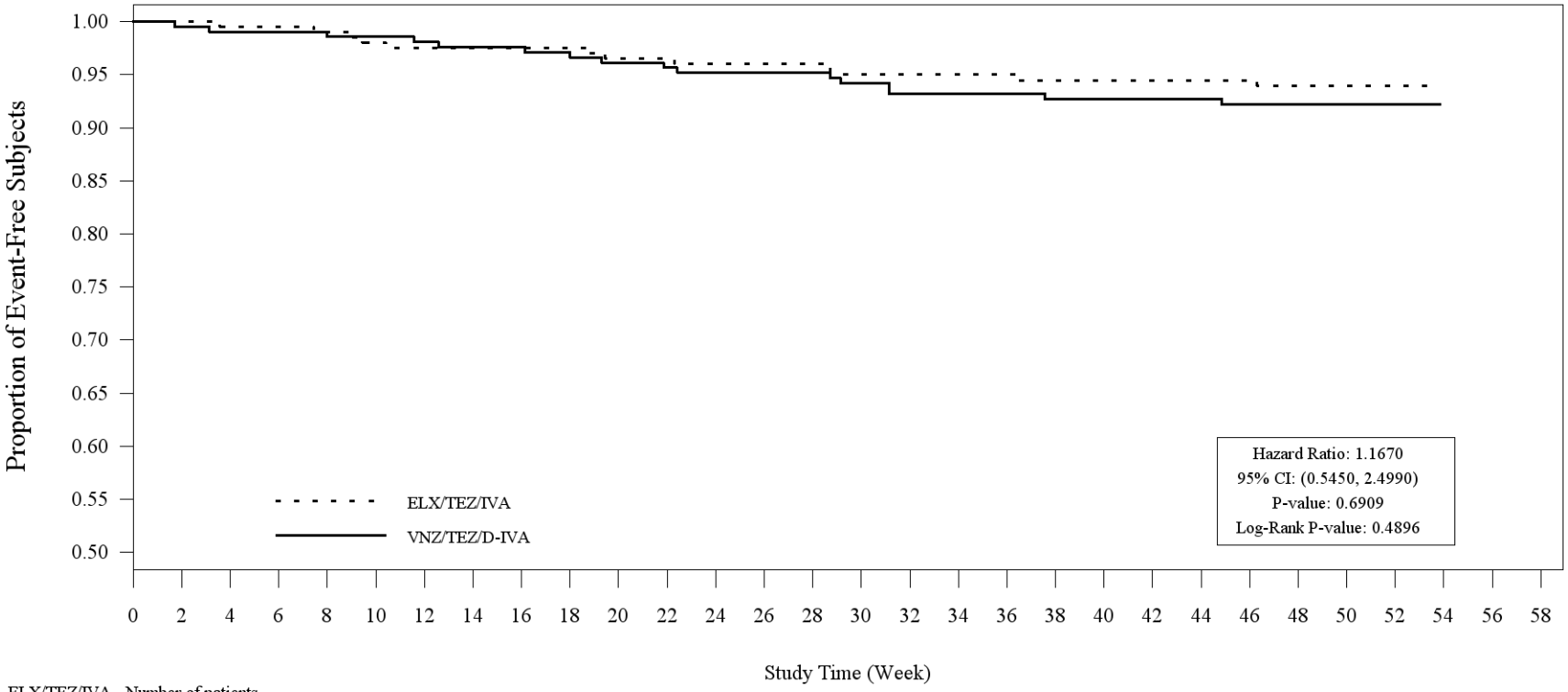
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Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	202	196	190	188	185
with event(s)	0	5	8	10	12
censored	0	1	4	4	5
VNZ/TEZ/D-IVA - Number of patients					
at risk	210	203	195	190	184
with event(s)	0	4	10	14	16
censored	0	3	5	6	10

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

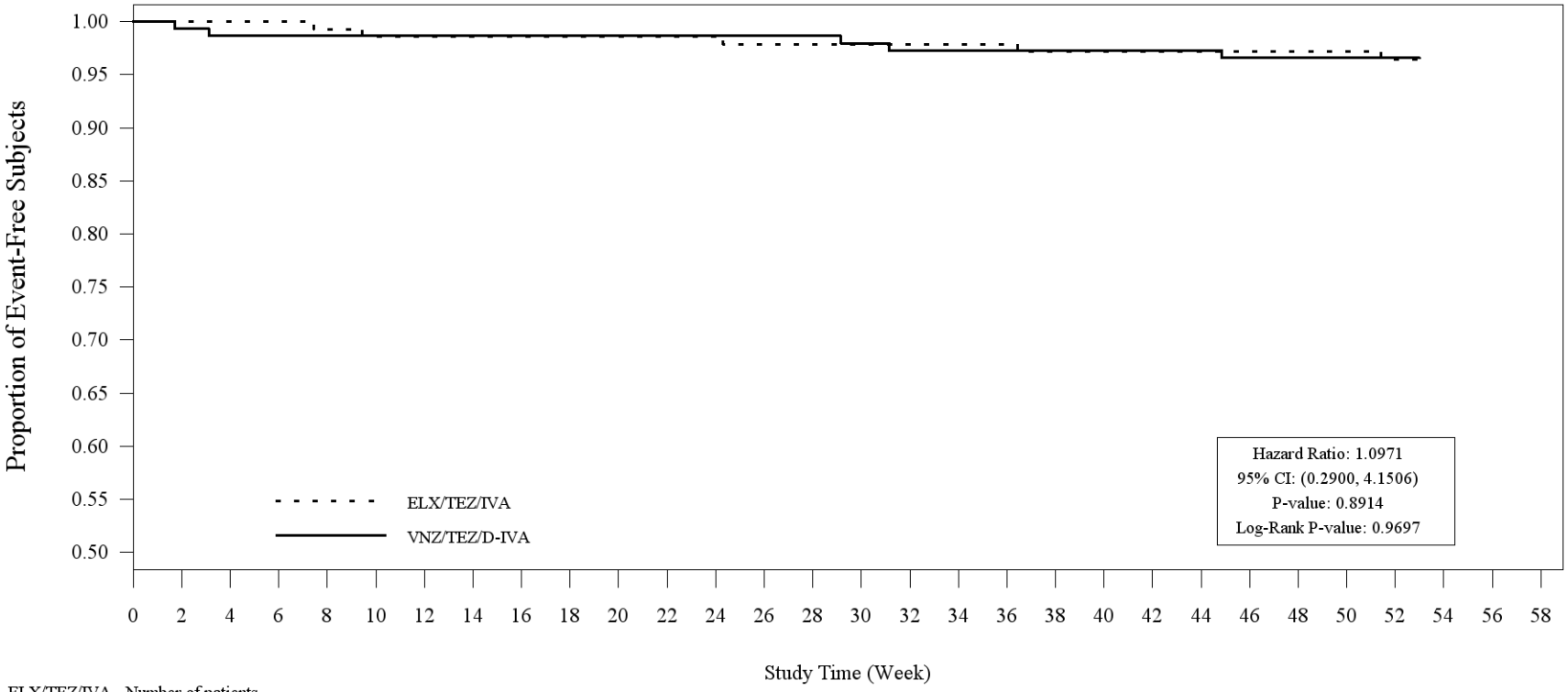
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Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	144	141	139	138	136
with event(s)	0	2	2	3	4
censored	0	1	3	3	4
VNZ/TEZ/D-IVA - Number of patients					
at risk	149	144	142	140	139
with event(s)	0	2	2	4	5
censored	0	3	5	5	5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

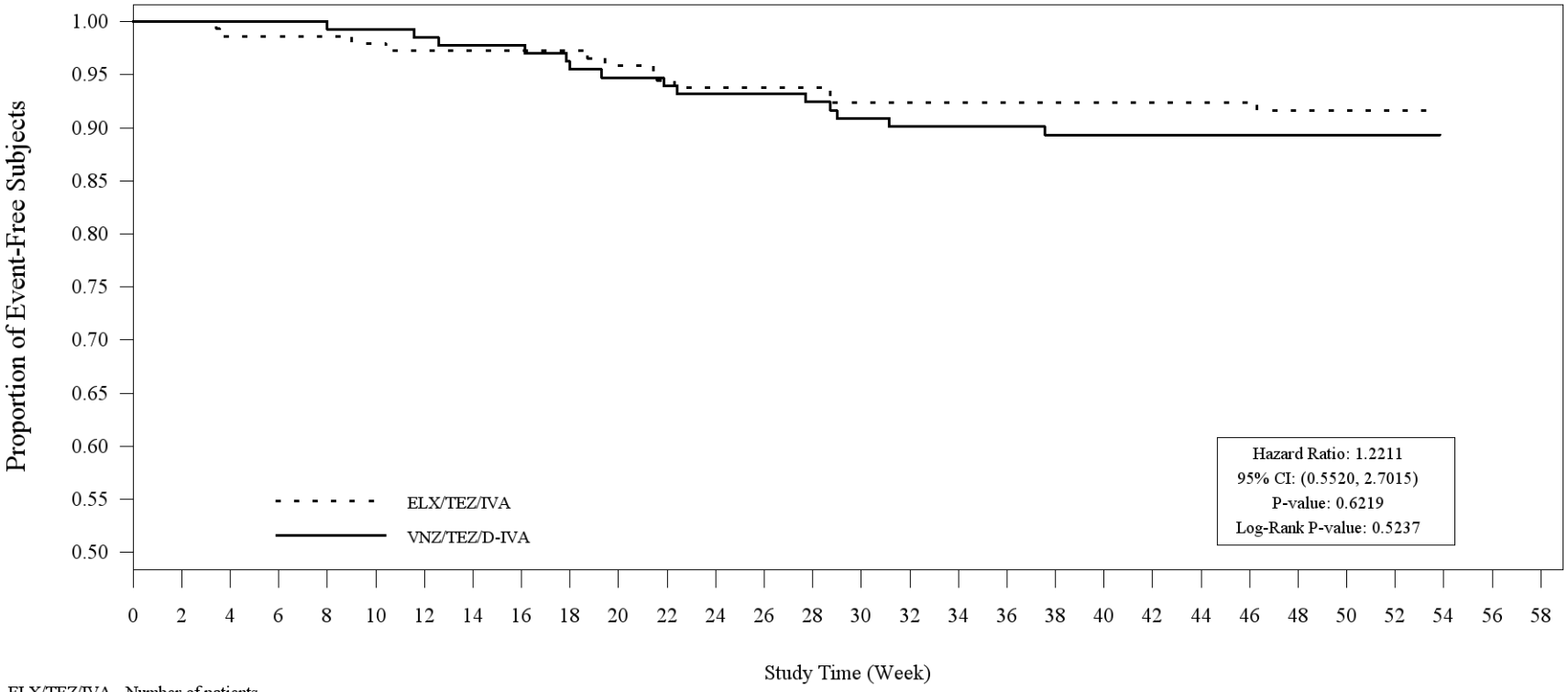
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Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	145	141	134	131	130
with event(s)	0	4	9	11	12
censored	0	0	2	3	3
VNZ/TEZ/D-IVA - Number of patients					
at risk	135	132	122	116	111
with event(s)	0	2	9	13	14
censored	0	1	4	6	10

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

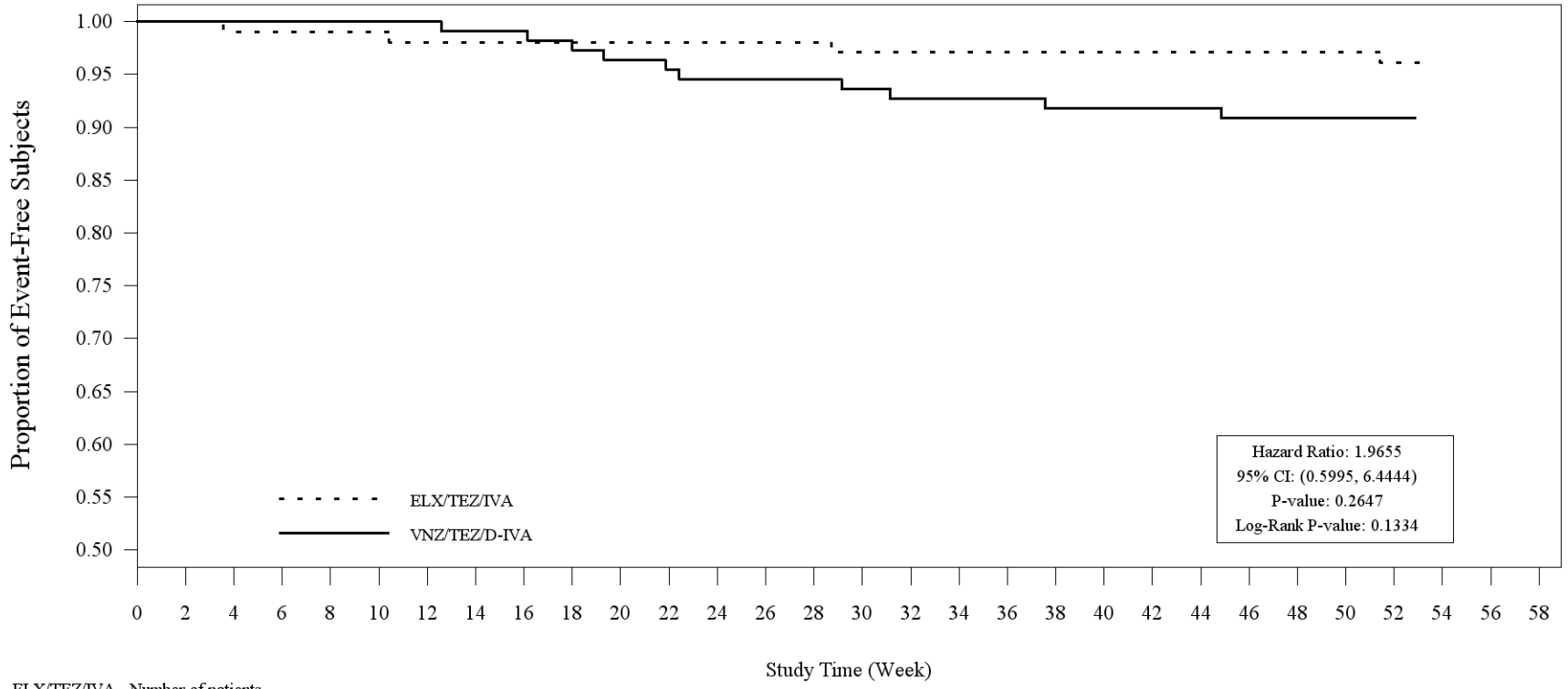
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Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	103	101	100	99	99
with event(s)	0	2	2	3	3
censored	0	0	1	1	1
VNZ/TEZ/D-IVA - Number of patients					
at risk	114	112	104	101	98
with event(s)	0	0	6	8	10
censored	0	2	4	5	6

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

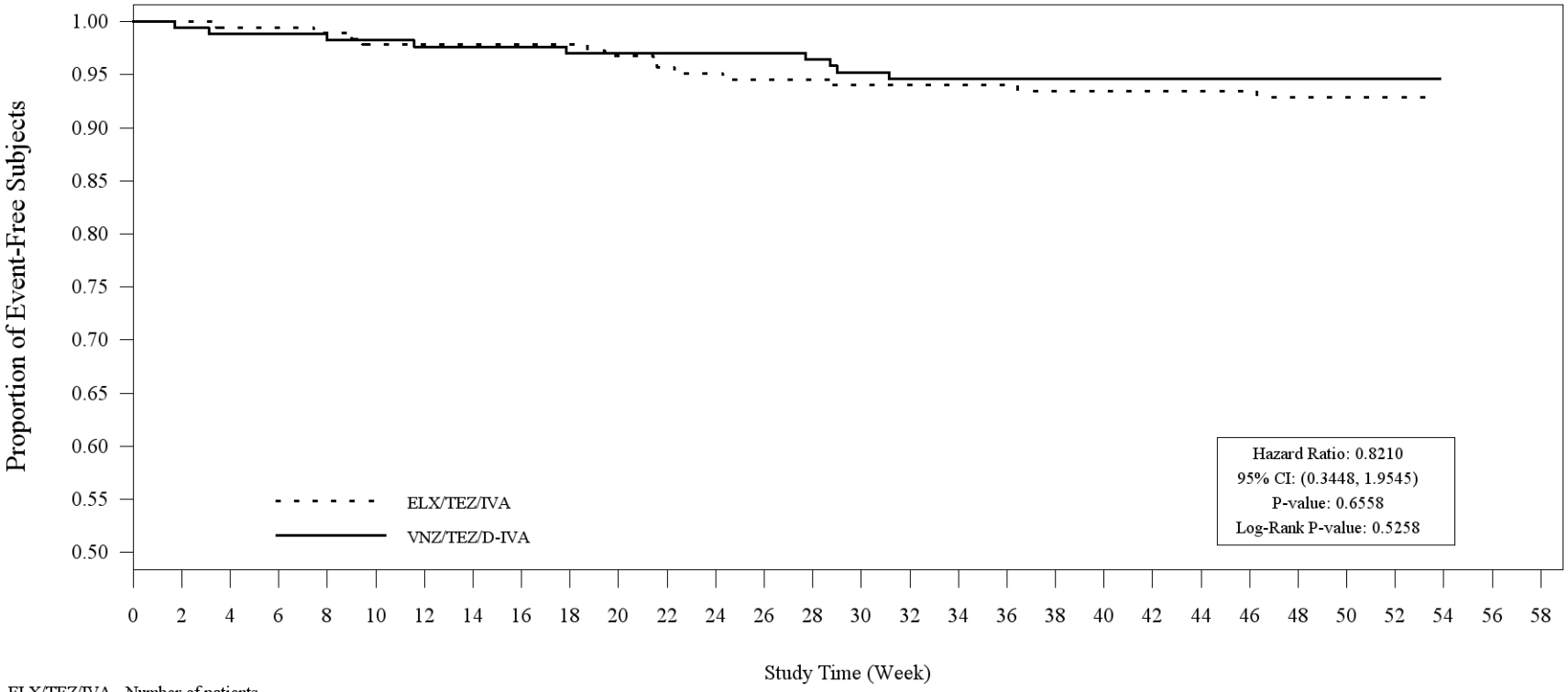
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Figure 2.2.2.8.2
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups
Full Analysis Set

Subgroup: Region = Rest of the World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	186	181	173	170	167
with event(s)	0	4	9	11	13
censored	0	1	4	5	6
VNZ/TEZ/D-IVA - Number of patients					
at risk	170	164	160	155	152
with event(s)	0	4	5	9	9
censored	0	2	5	6	9

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Age at screening" subgroup factor, age covariate is removed from analysis model.

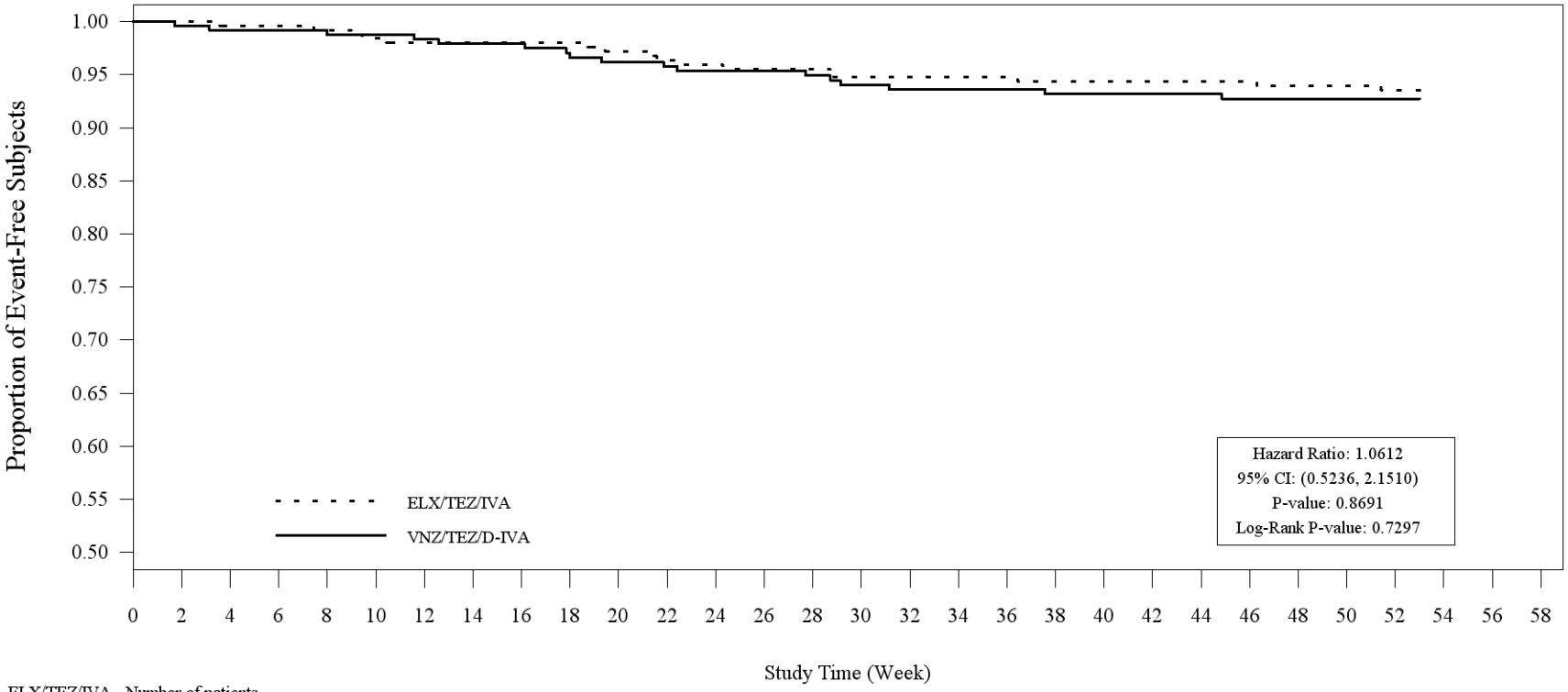
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Figure 2.2.2.8.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Prior CFTR modulator use: Yes

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	250	244	236	232	230
with event(s)	0	5	10	13	15
censored	0	1	4	5	5
VNZ/TEZ/D-IVA - Number of patients					
at risk	241	234	222	216	211
with event(s)	0	4	11	15	17
censored	0	3	8	10	13

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

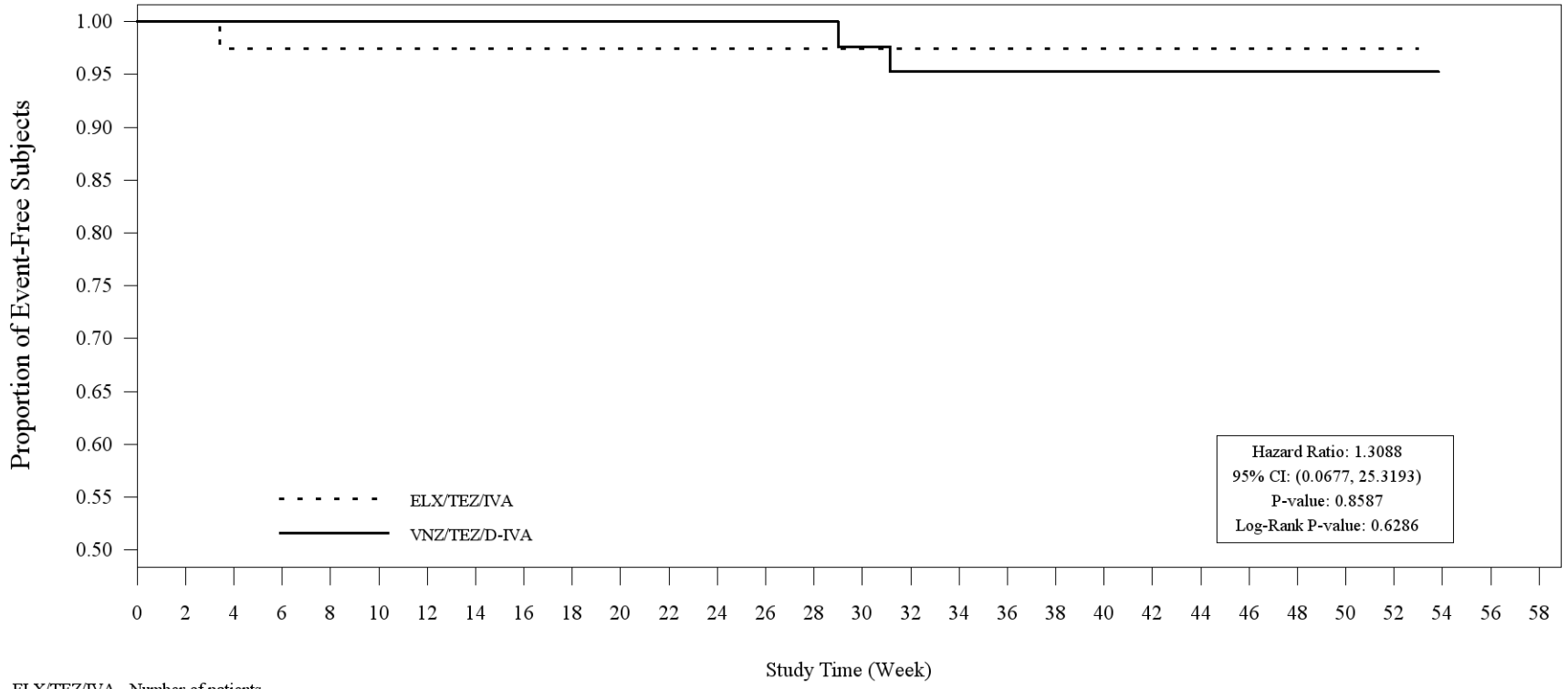
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Figure 2.2.2.8.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Prior CFTR modulator use: No

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	39	38	37	37	36
with event(s)	0	1	1	1	1
censored	0	0	1	1	2
VNZ/TEZ/D-IVA - Number of patients					
at risk	43	42	42	40	39
with event(s)	0	0	0	2	2
censored	0	1	1	1	2

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

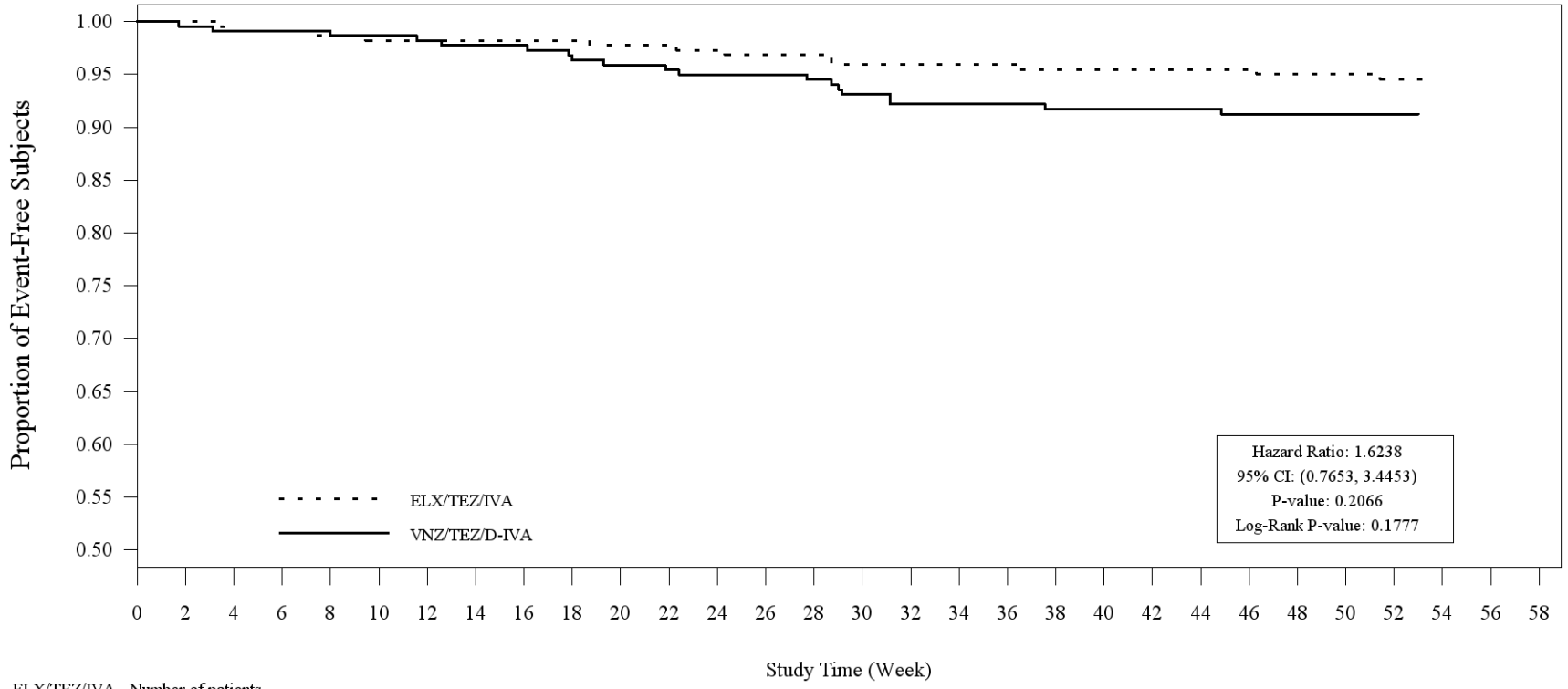
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Figure 2.2.2.8.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Genotype group: F/F

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	224	219	213	209	206
with event(s)	0	4	6	9	11
censored	0	1	5	6	7
VNZ/TEZ/D-IVA - Number of patients					
at risk	222	215	205	199	194
with event(s)	0	4	11	17	19
censored	0	3	6	6	9

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

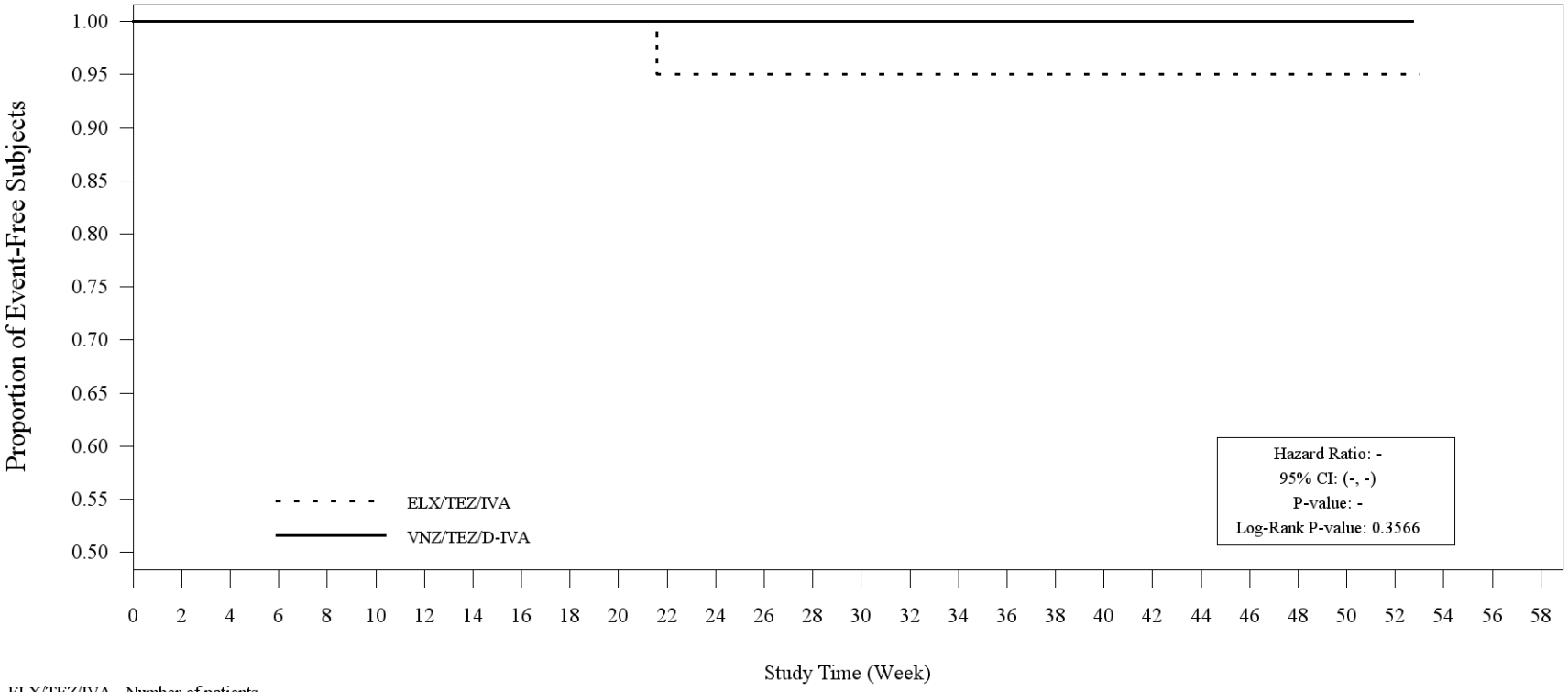
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Figure 2.2.2.8.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Genotype group: F/G

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	20	20	19	19	19
with event(s)	0	0	1	1	1
censored	0	0	0	0	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	19	19	17	16	16
with event(s)	0	0	0	0	0
censored	0	0	2	3	3

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

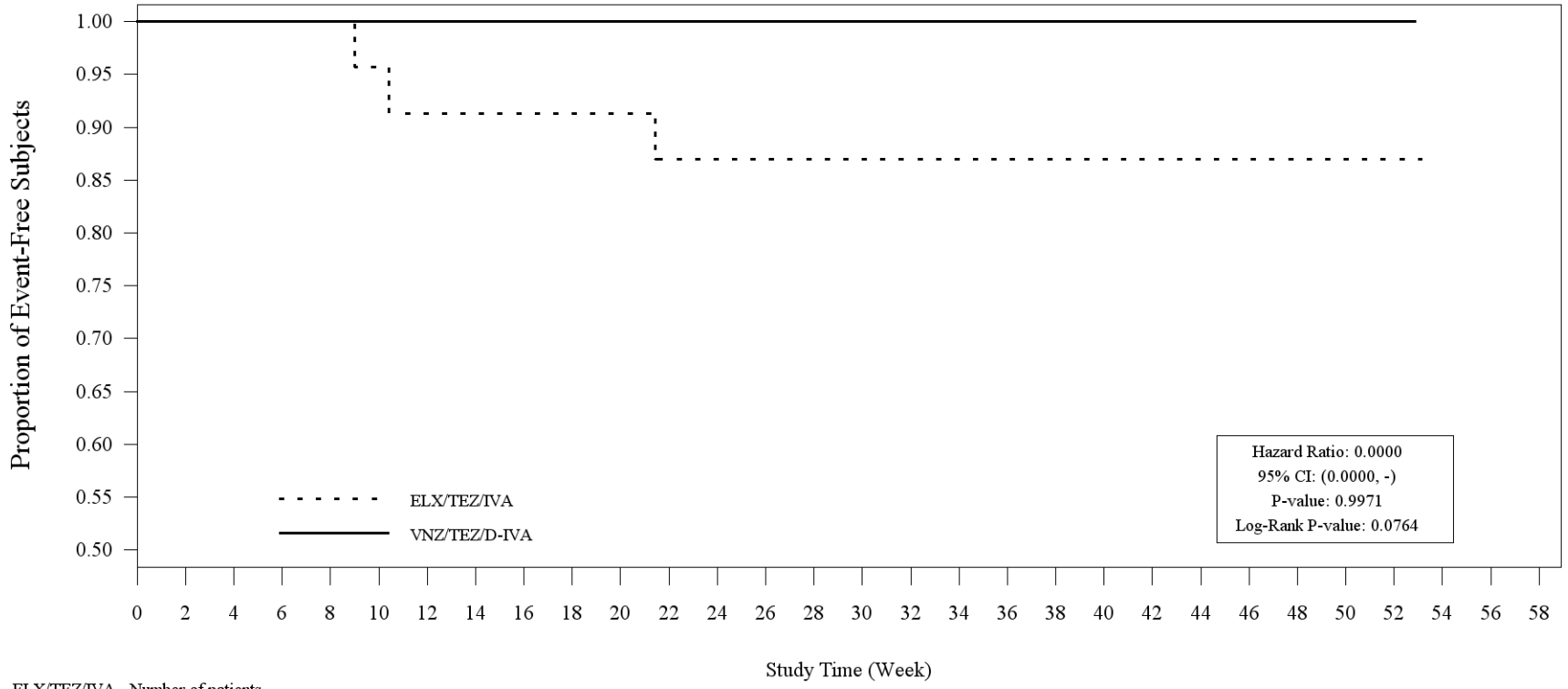
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Figure 2.2.2.8.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Genotype group: F/RF

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	23	21	20	20	20
with event(s)	0	2	3	3	3
censored	0	0	0	0	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	23	23	23	23	23
with event(s)	0	0	0	0	0
censored	0	0	0	0	0

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

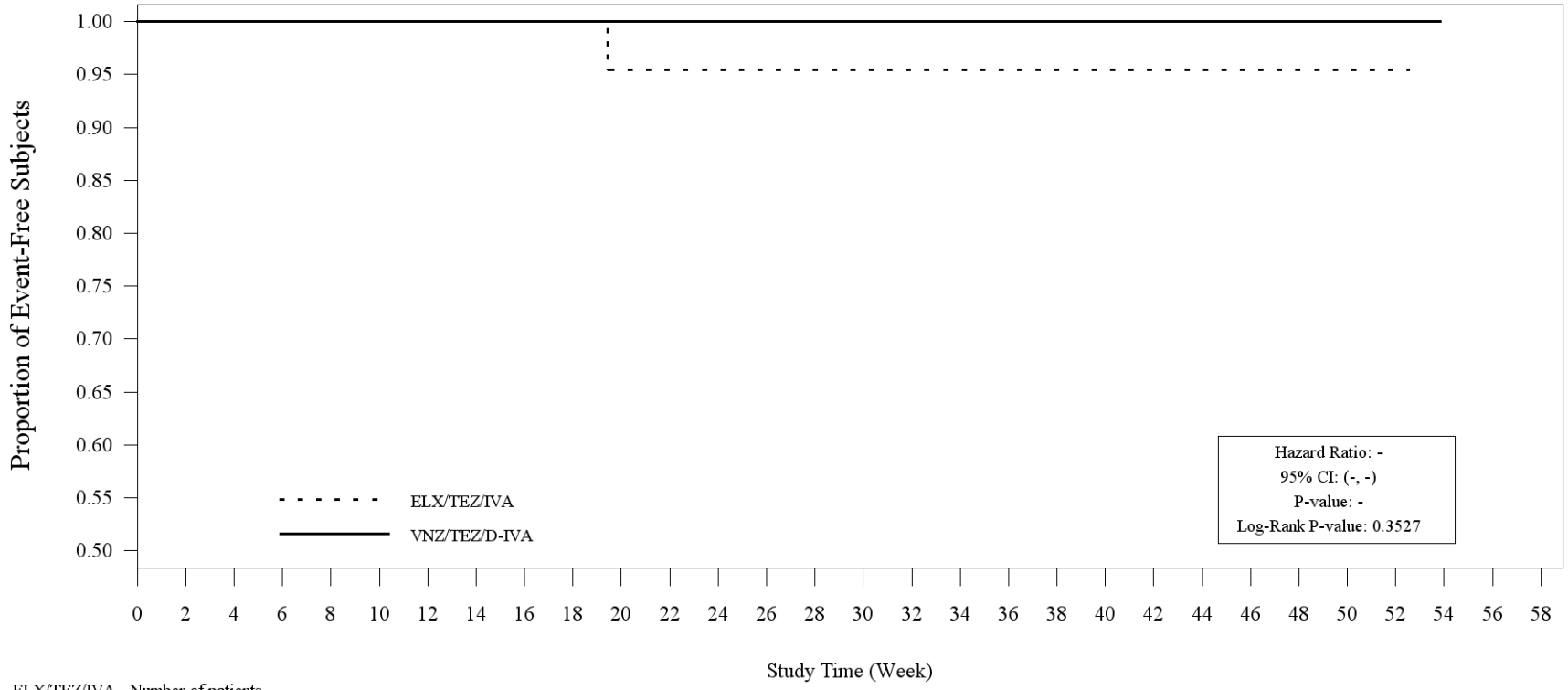
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Figure 2.2.2.8.2.1
Study VX20-121-103: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Intravenous Antibiotics through Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

Subgroup: Genotype group: TCR/non-F

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

Zusatzanalysen zur Studie VX20-121-103



ELX/TEZ/IVA - Number of patients					
at risk	22	22	21	21	21
with event(s)	0	0	1	1	1
censored	0	0	0	0	0
VNZ/TEZ/D-IVA - Number of patients					
at risk	20	19	19	18	17
with event(s)	0	0	0	0	0
censored	0	1	1	2	3

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Cox regression: time is the time-to-first pulmonary exacerbation or censoring, with adjustment for treatment, baseline ppFEV$_1$, baseline sweat chloride, and age at screening (<18 vs ≥18 years), genotype. Hazard ratio, CI and p-values from Cox regression.
- For "Genotype group" subgroup factor, genotype covariate is removed from the model.

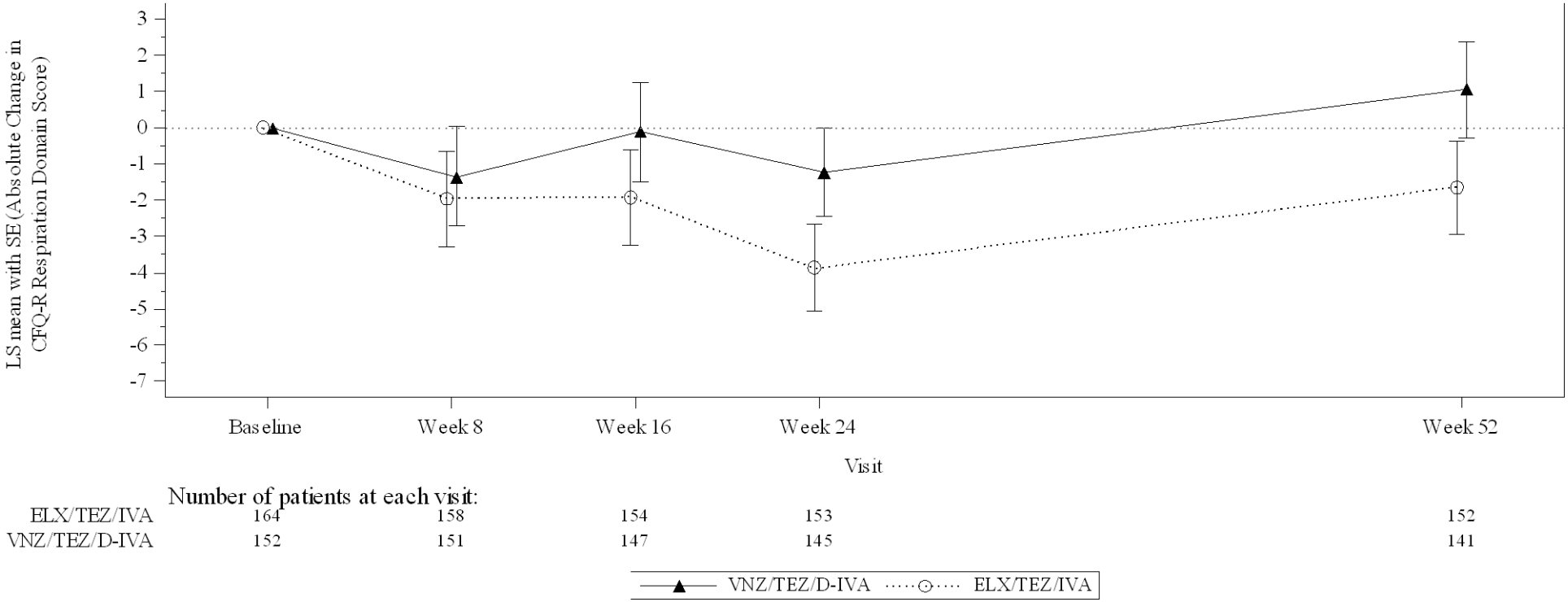
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

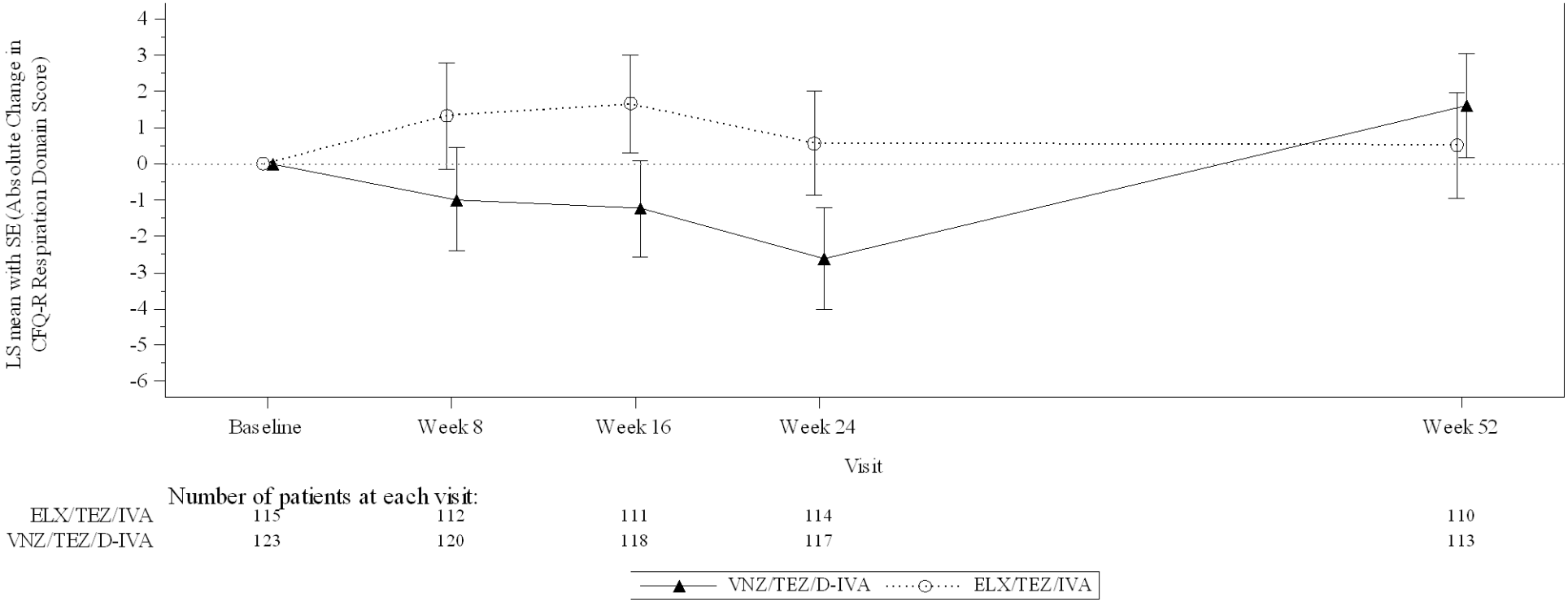
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

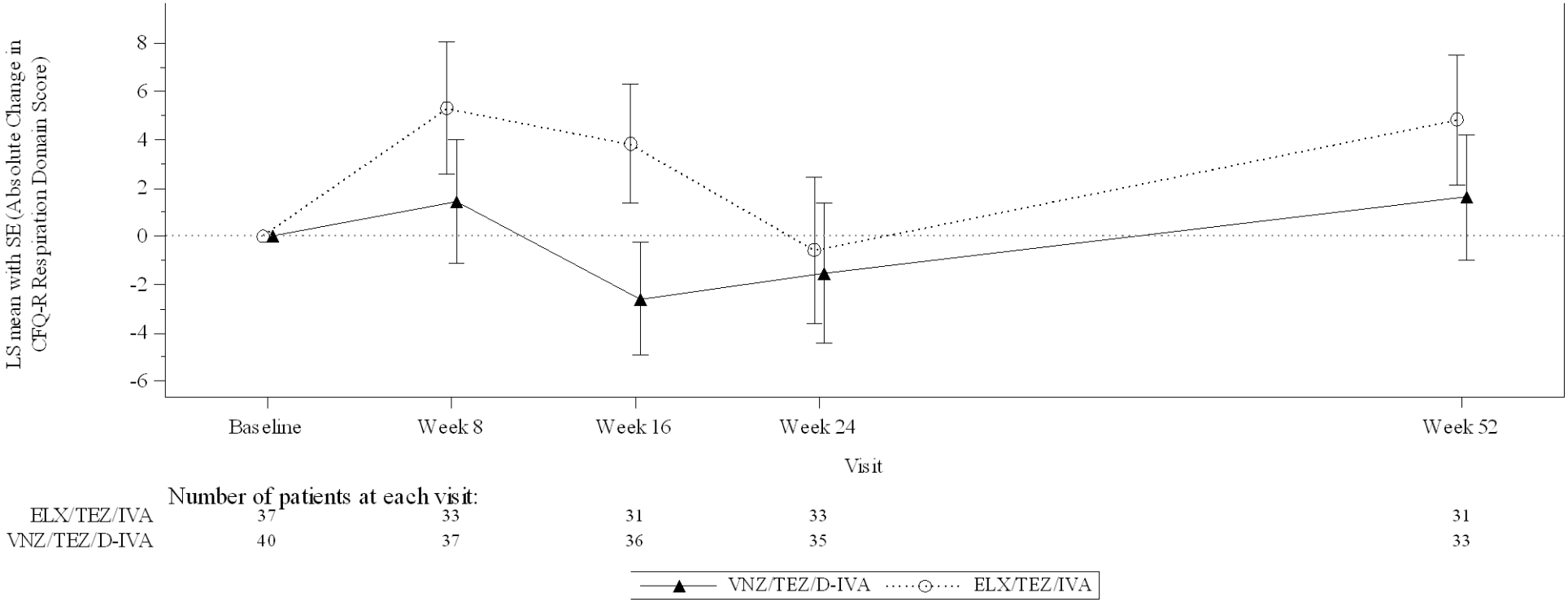
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

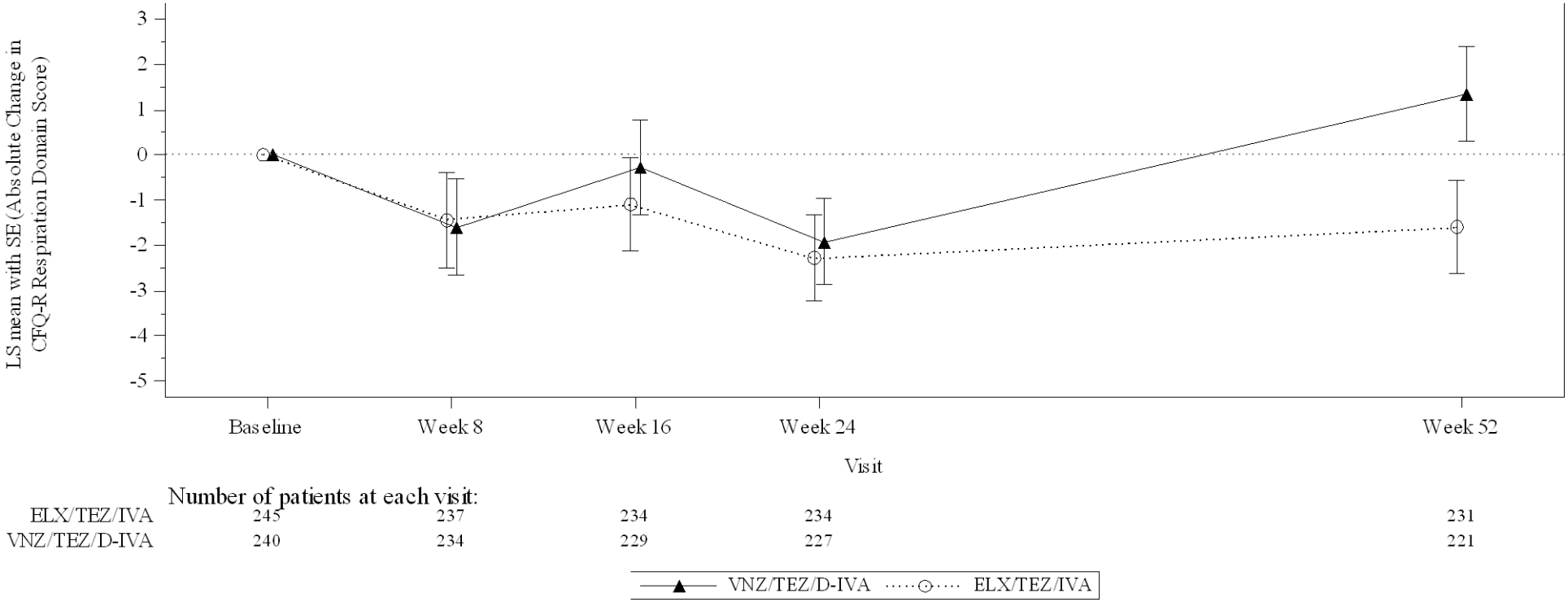
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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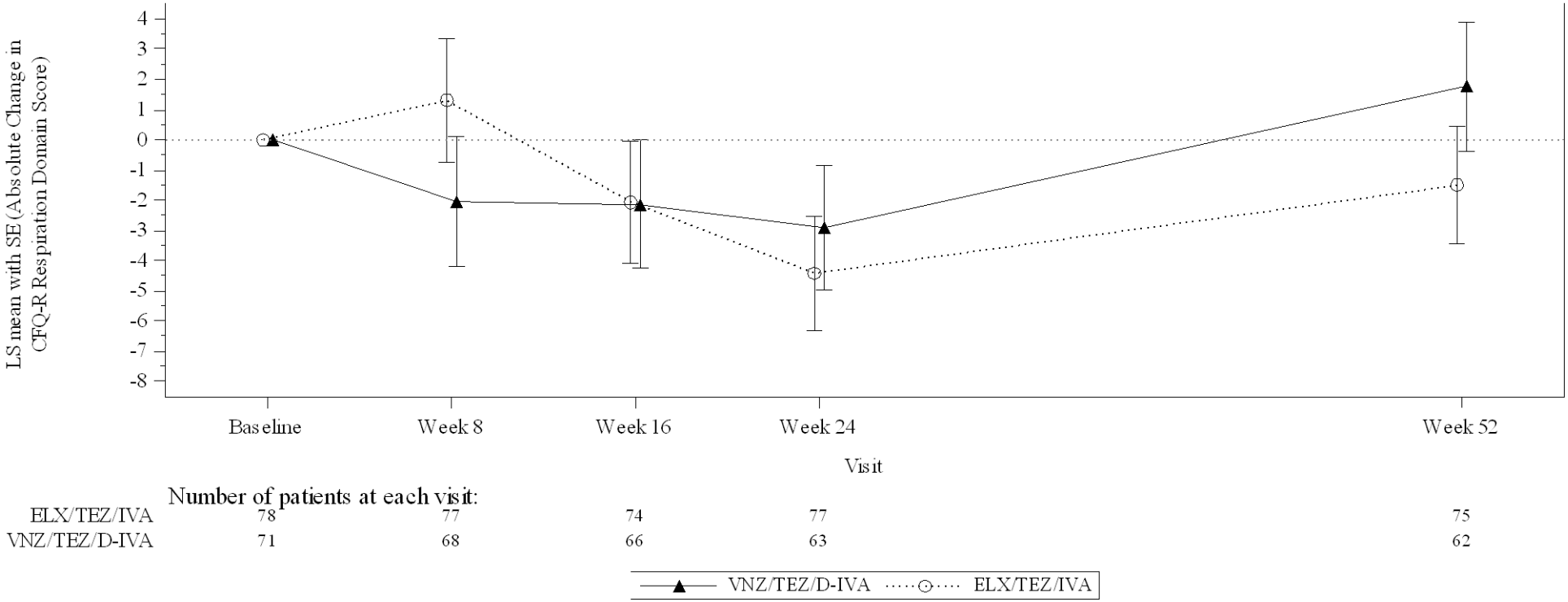
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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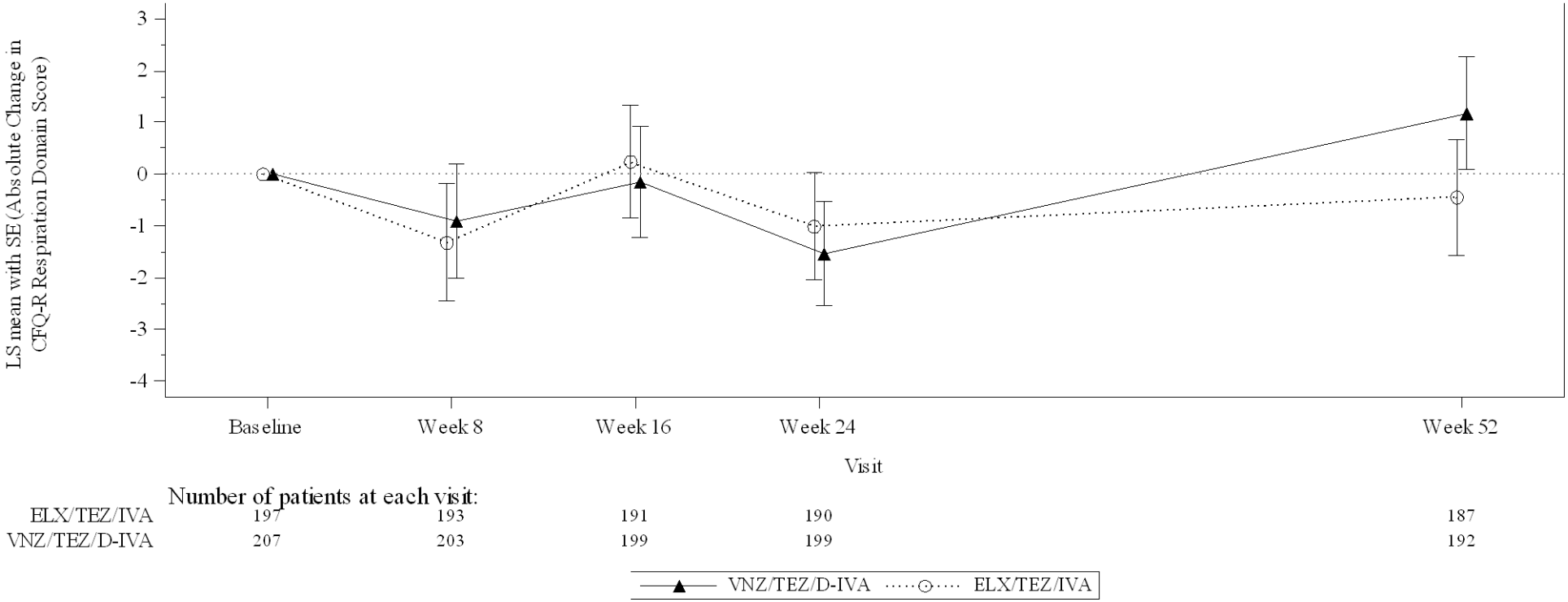
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

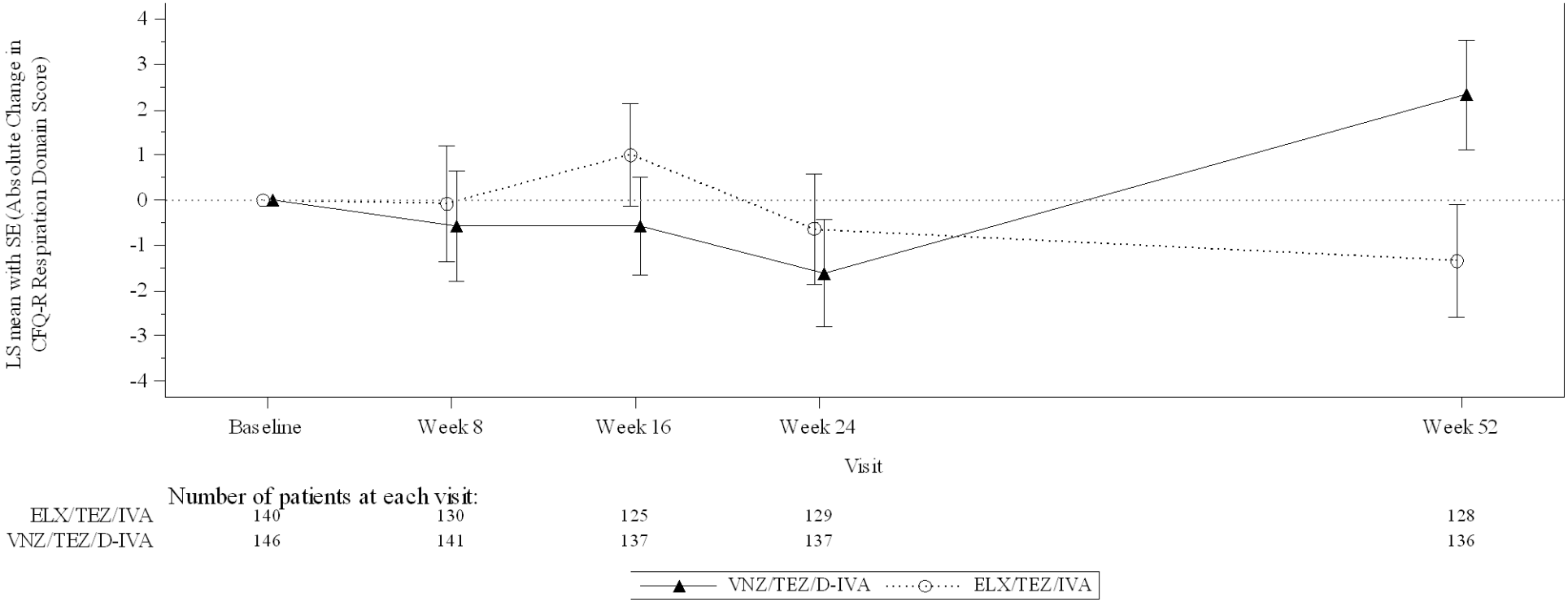
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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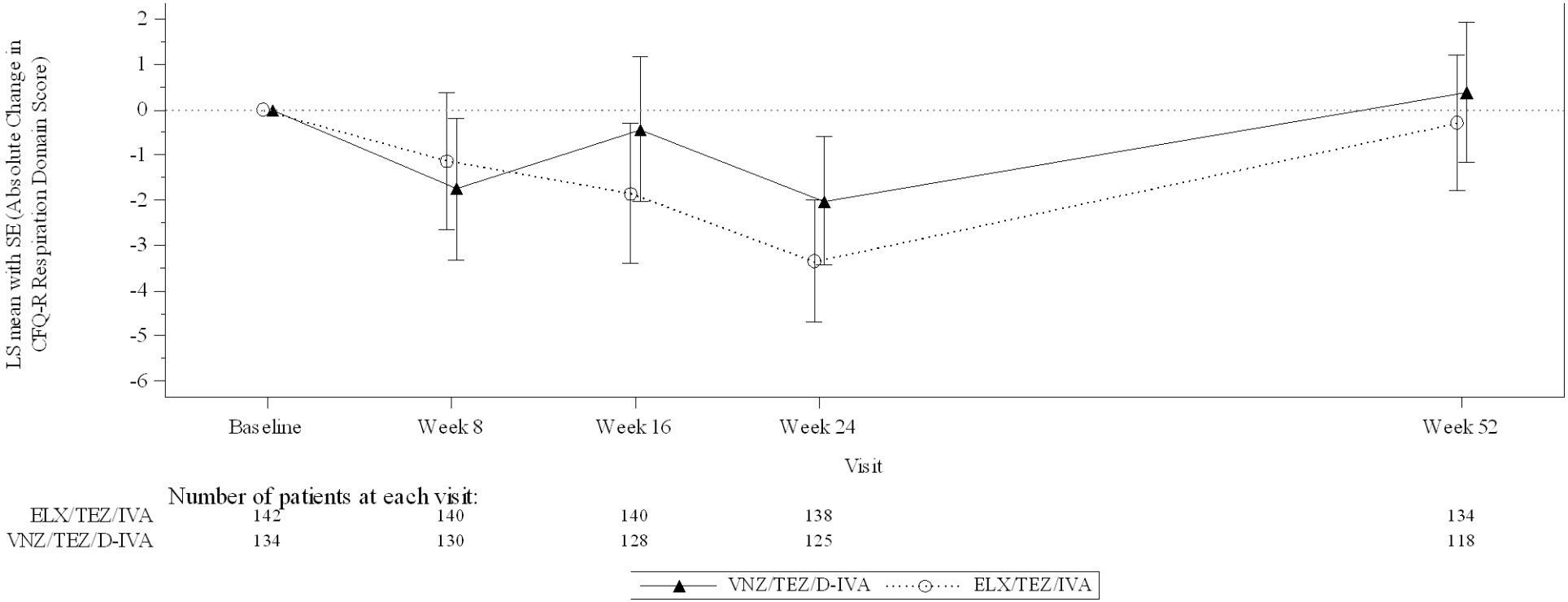
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



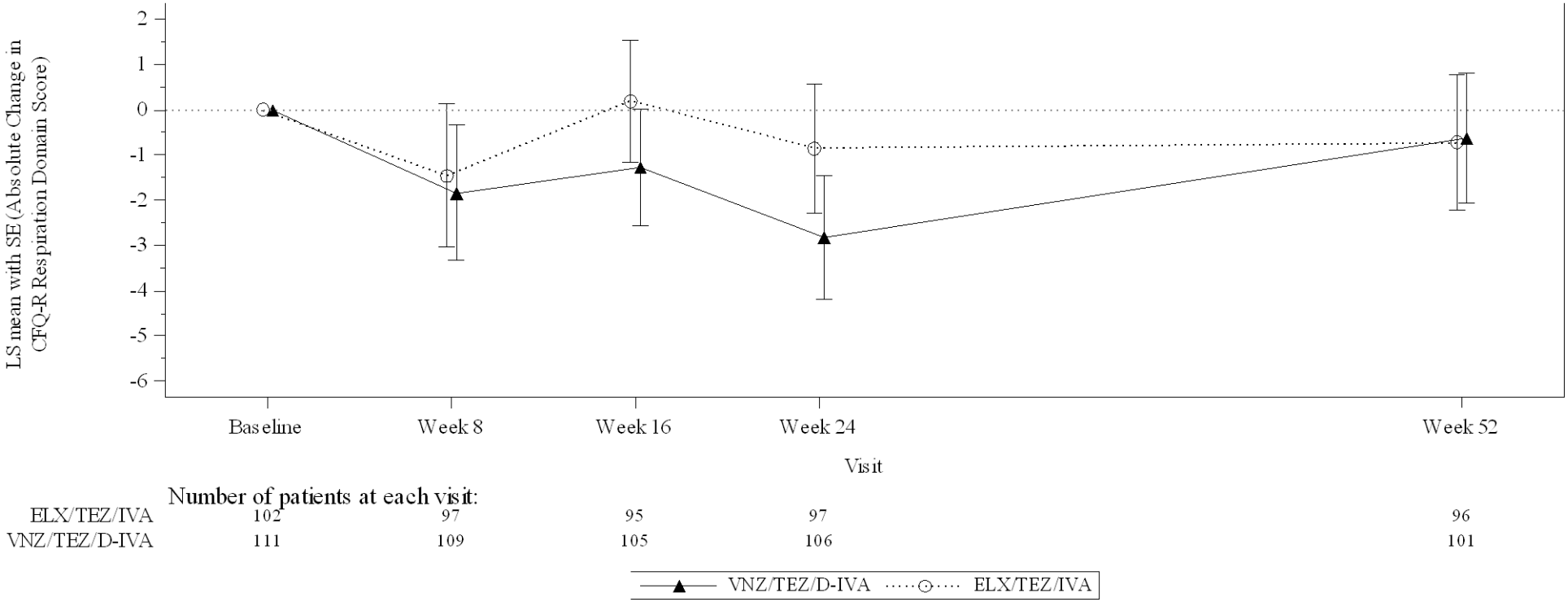
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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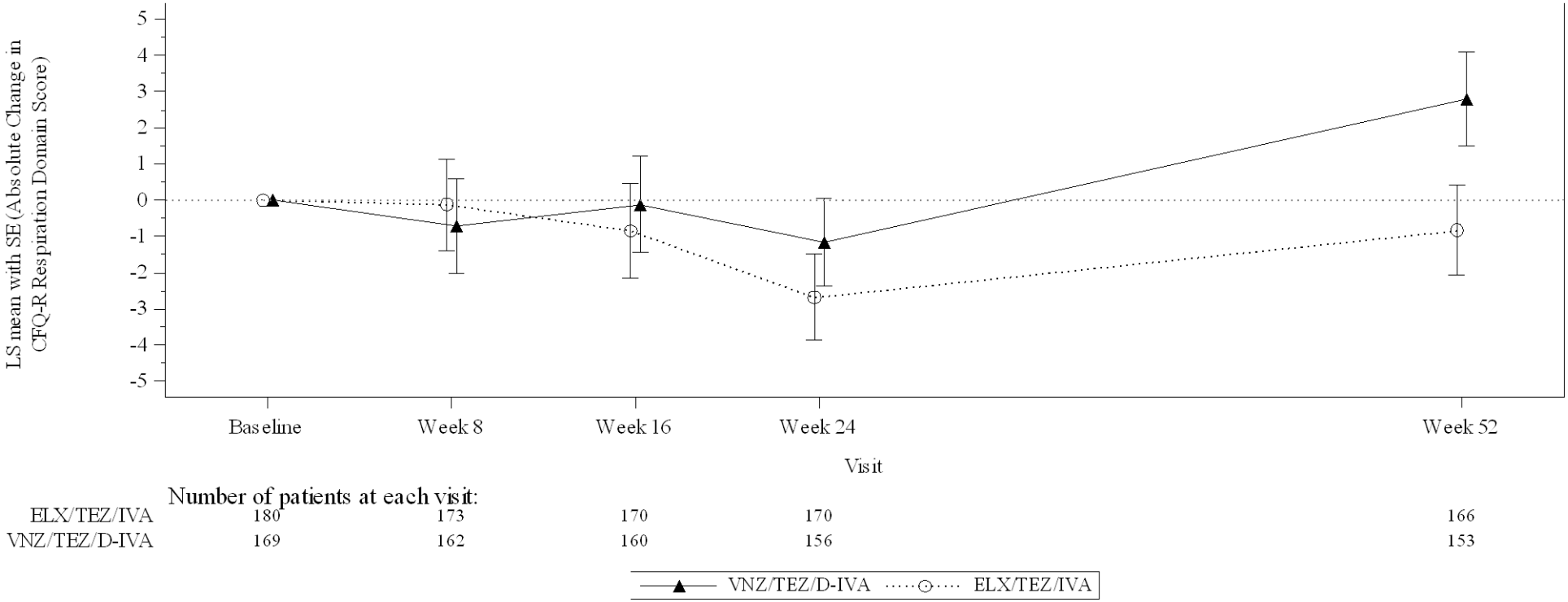
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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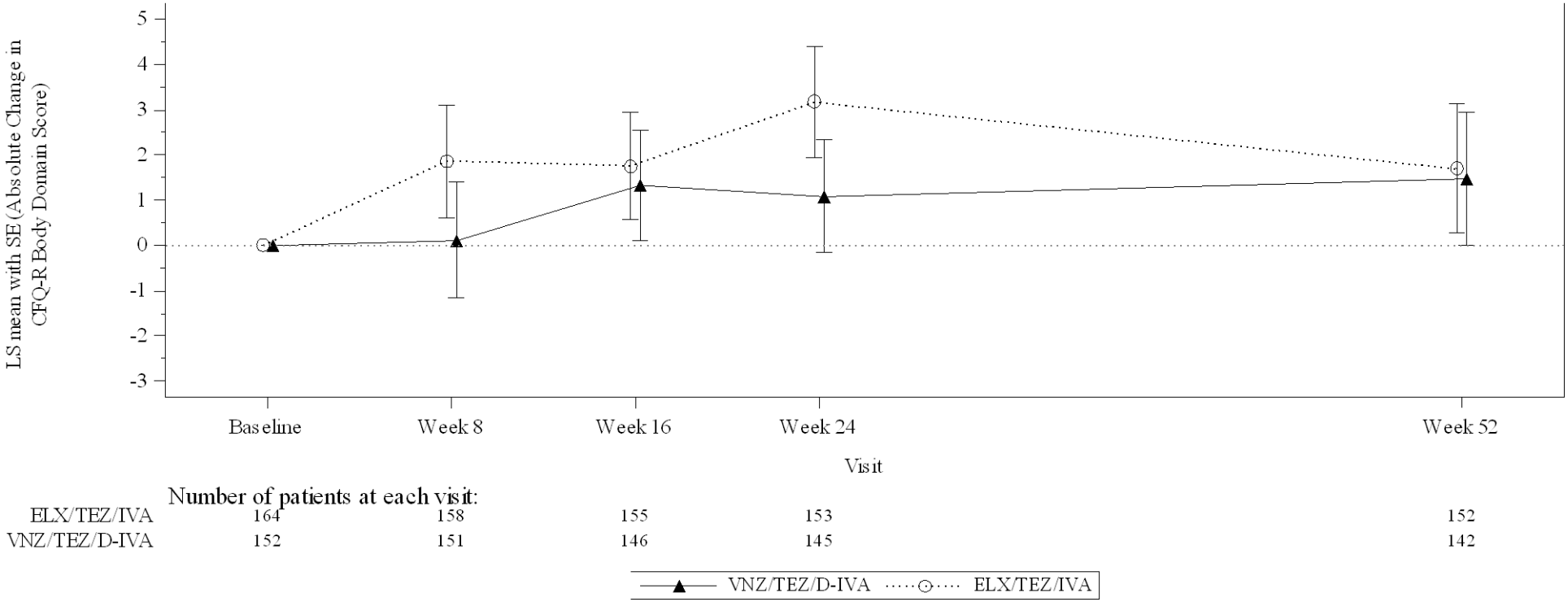
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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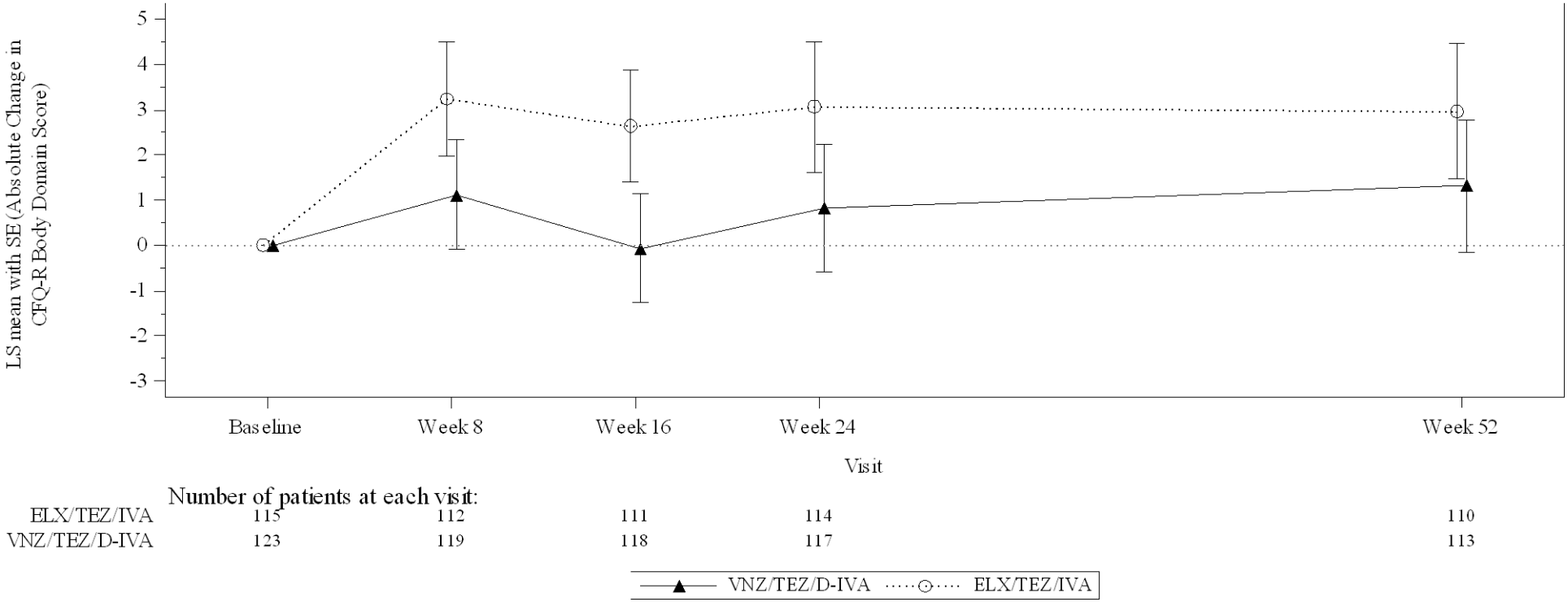
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

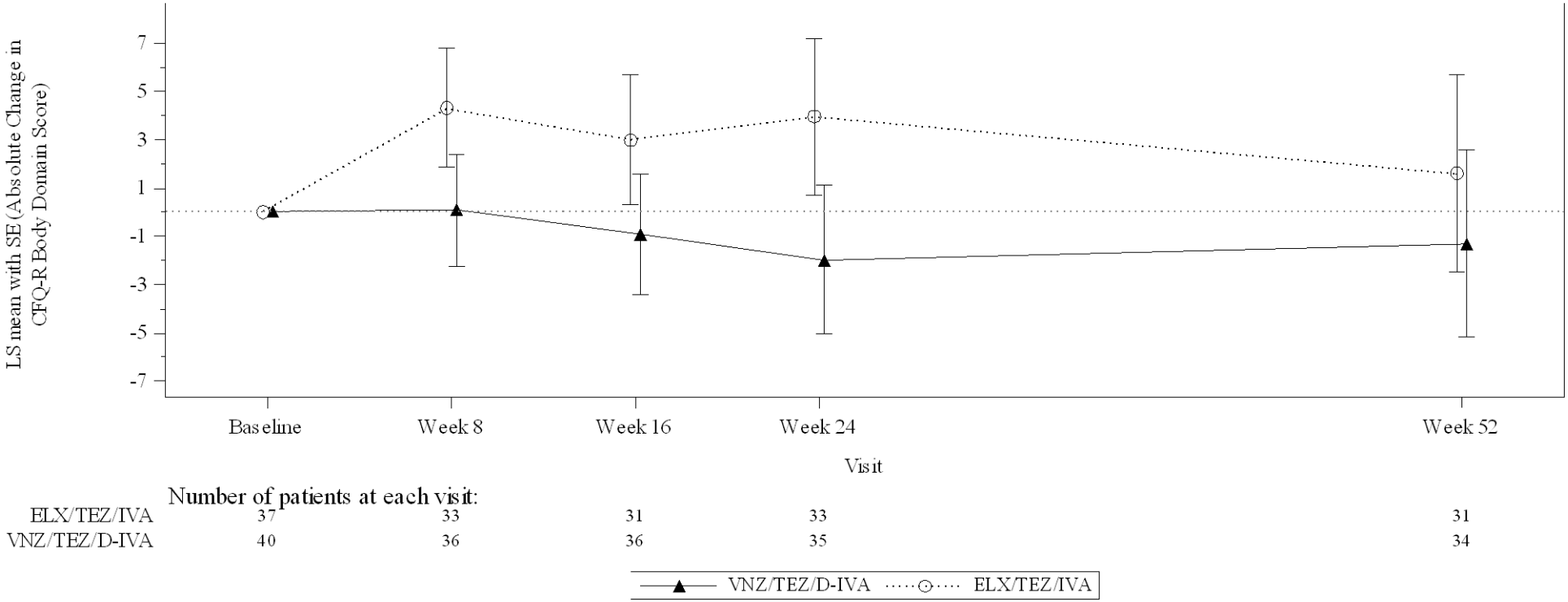
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

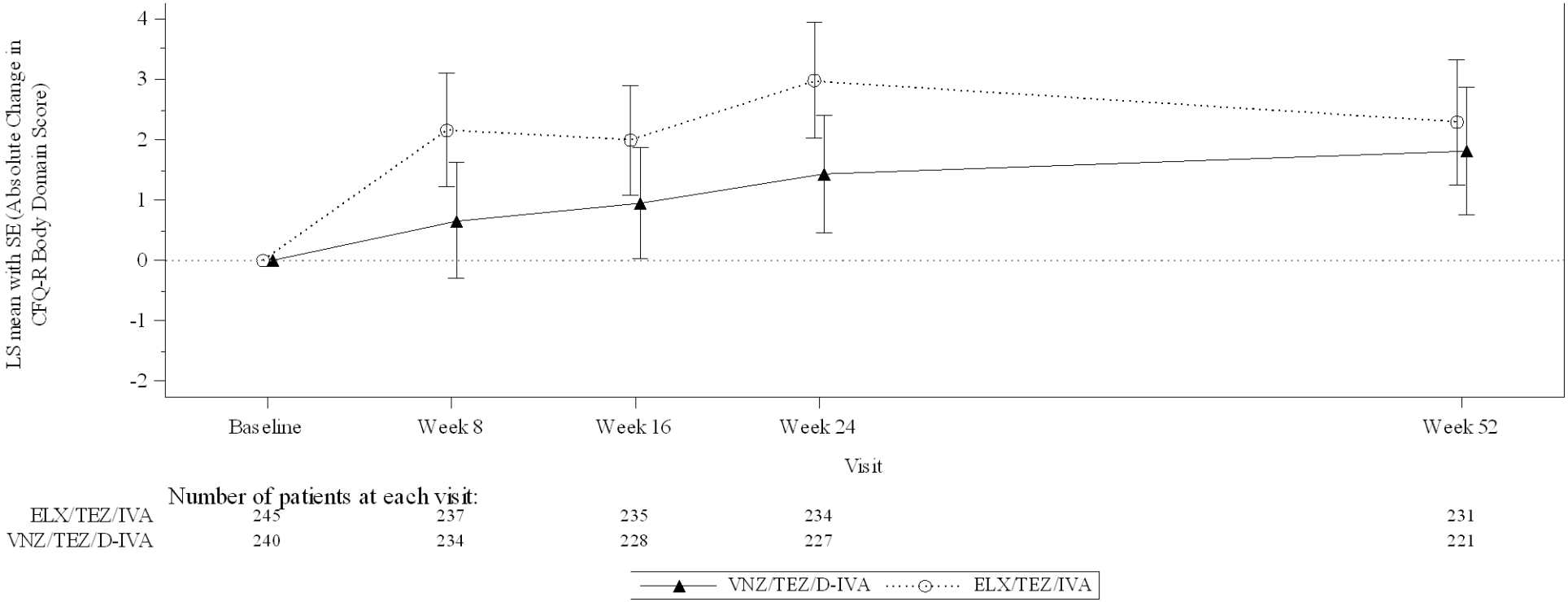
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

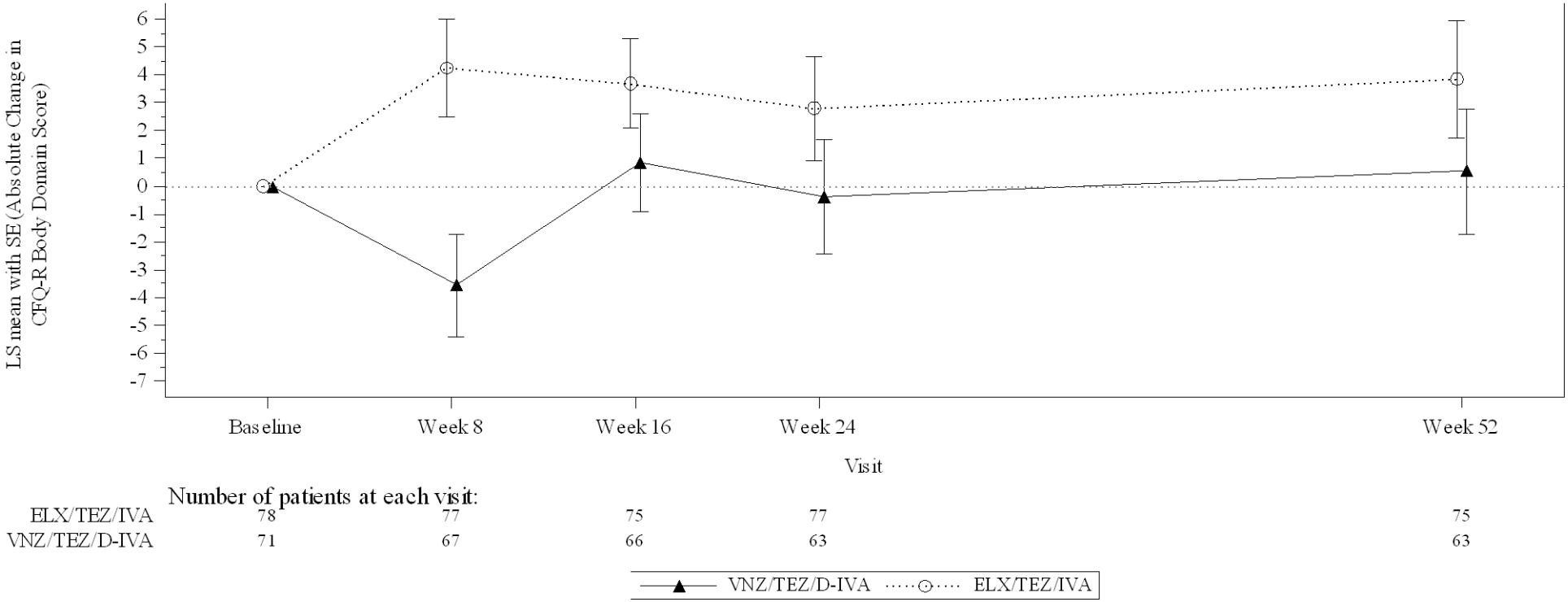
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

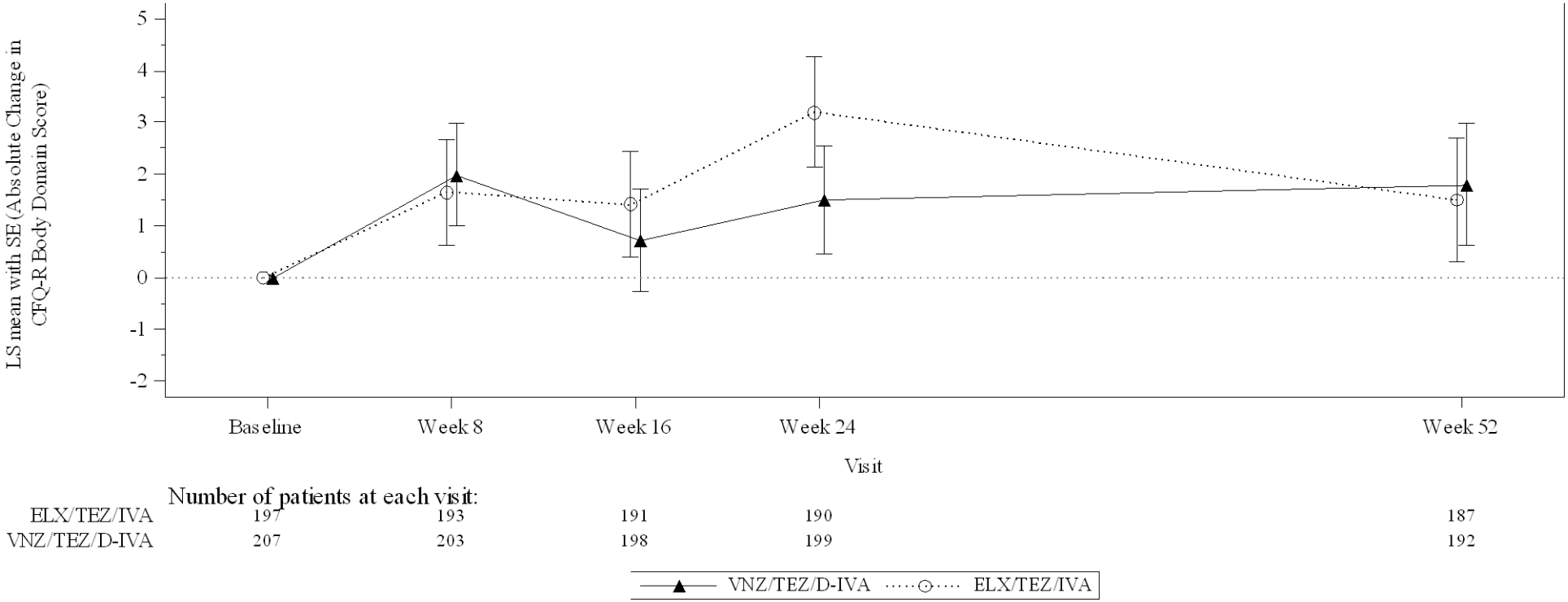
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

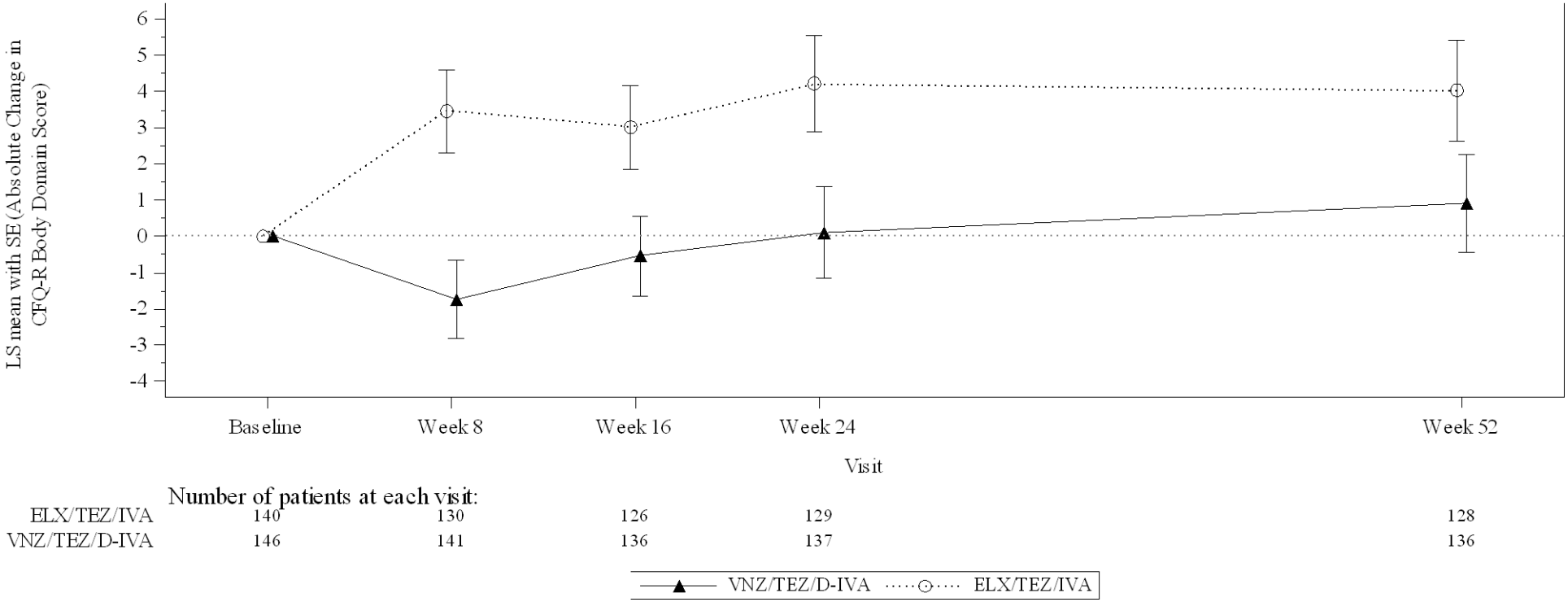
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

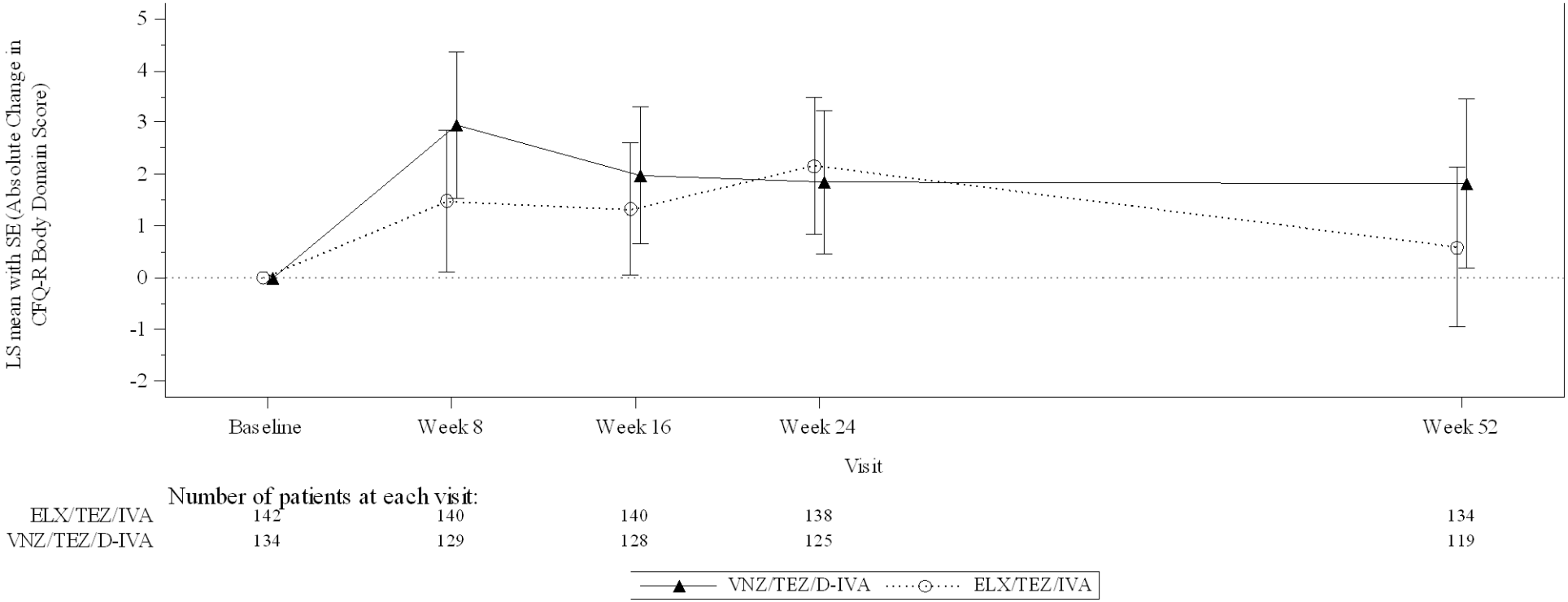
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

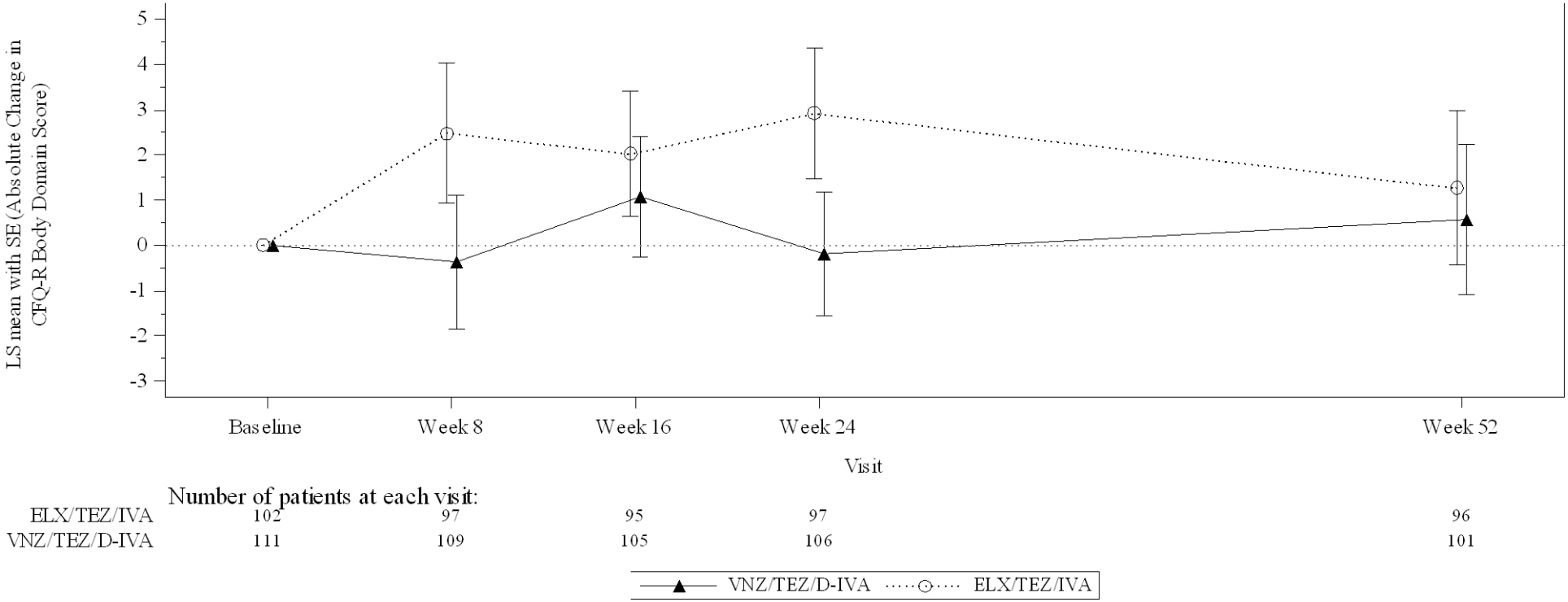
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

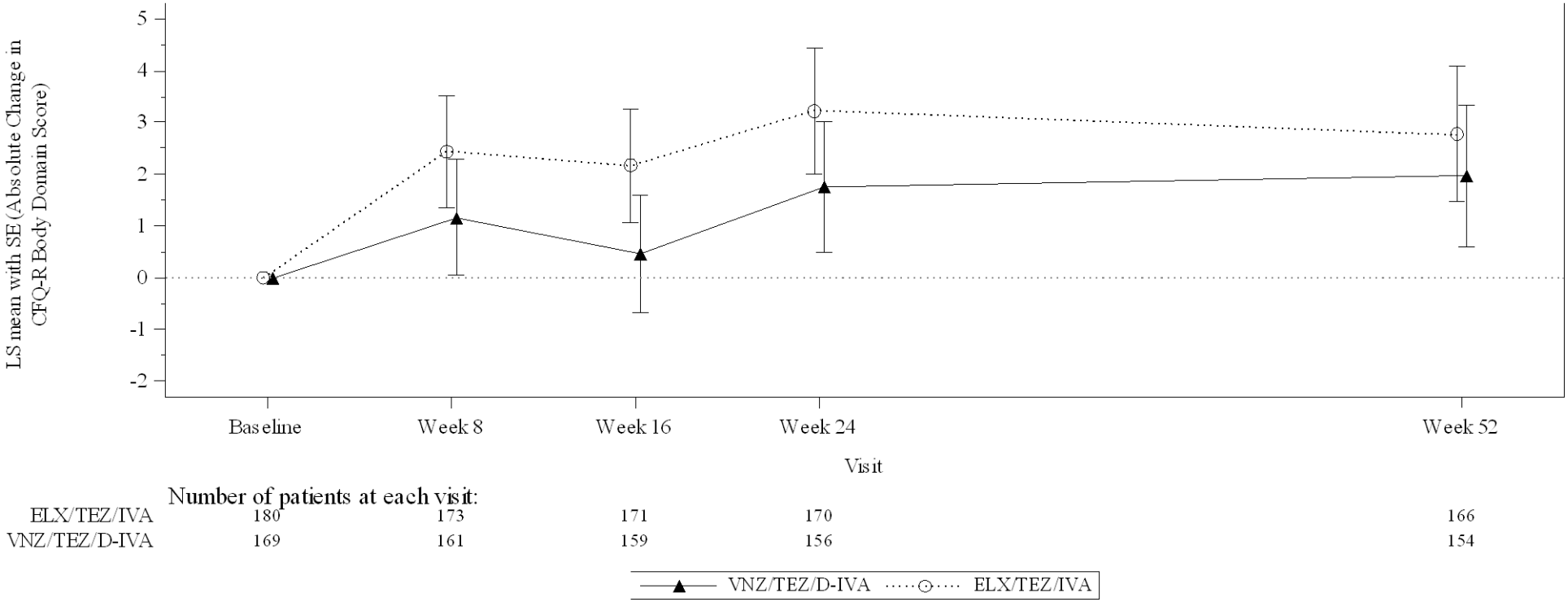
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

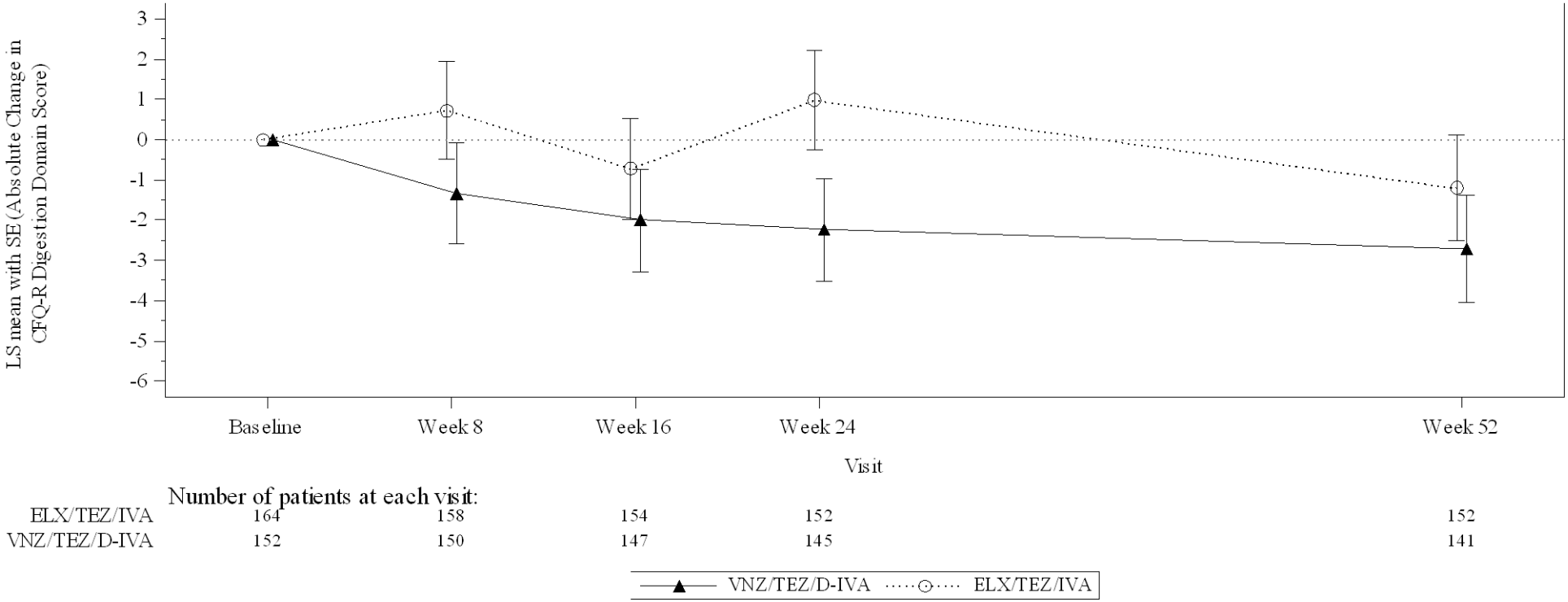
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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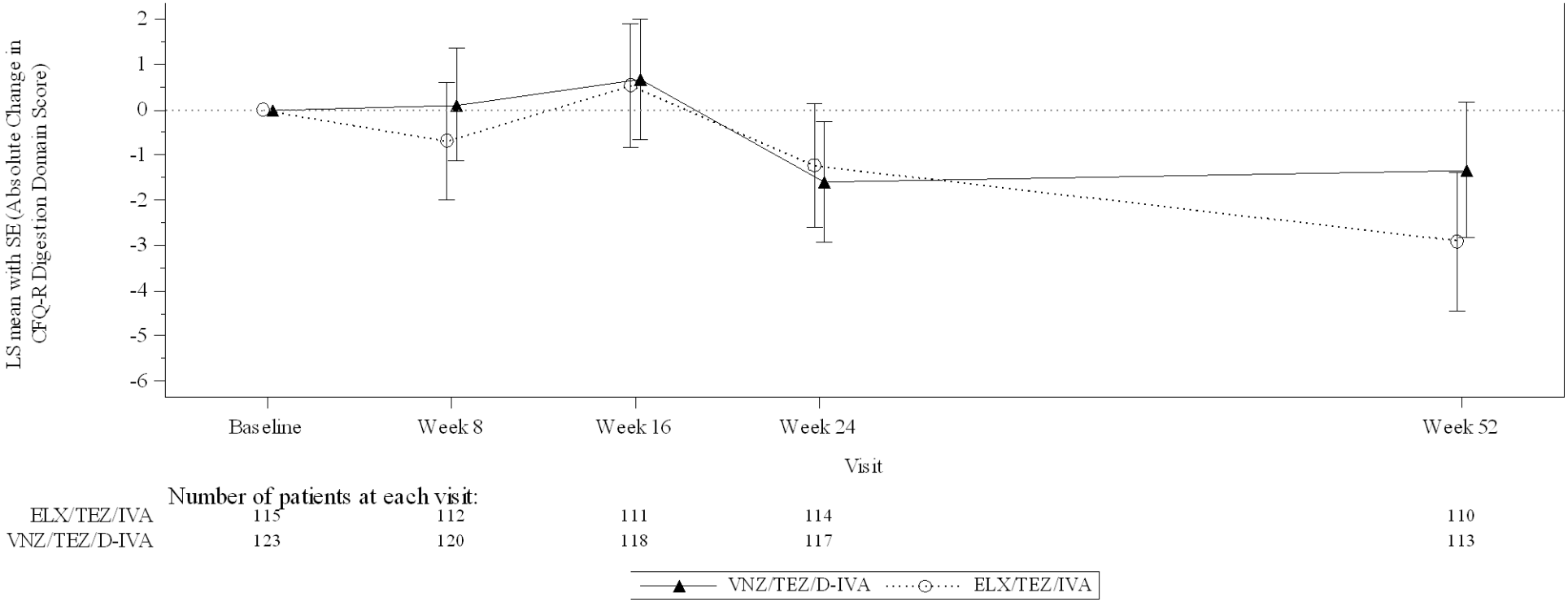
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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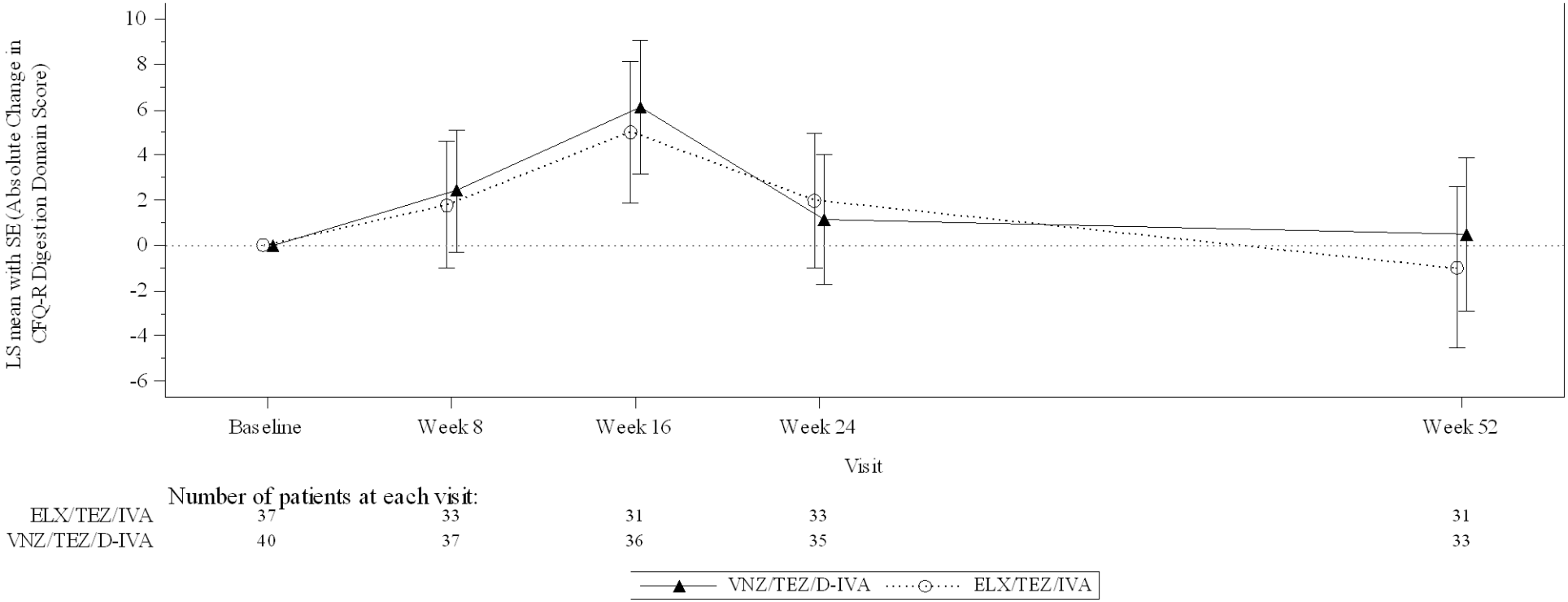
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

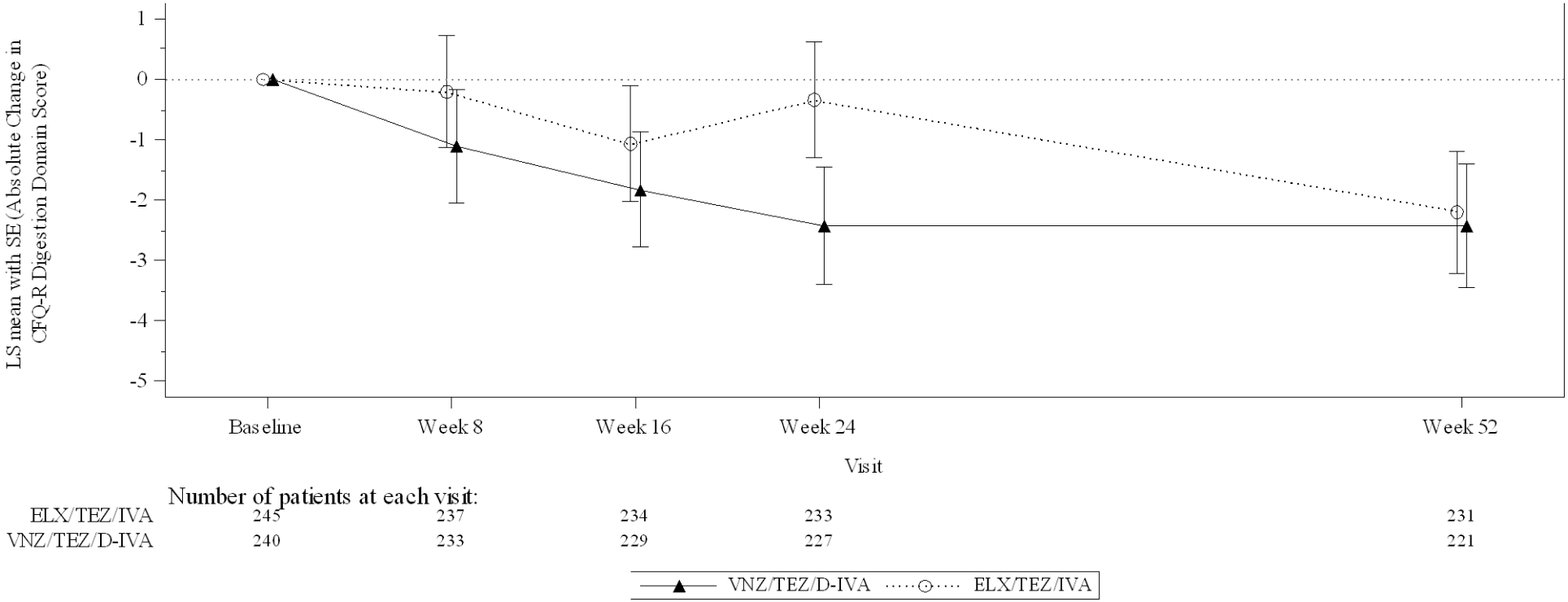
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

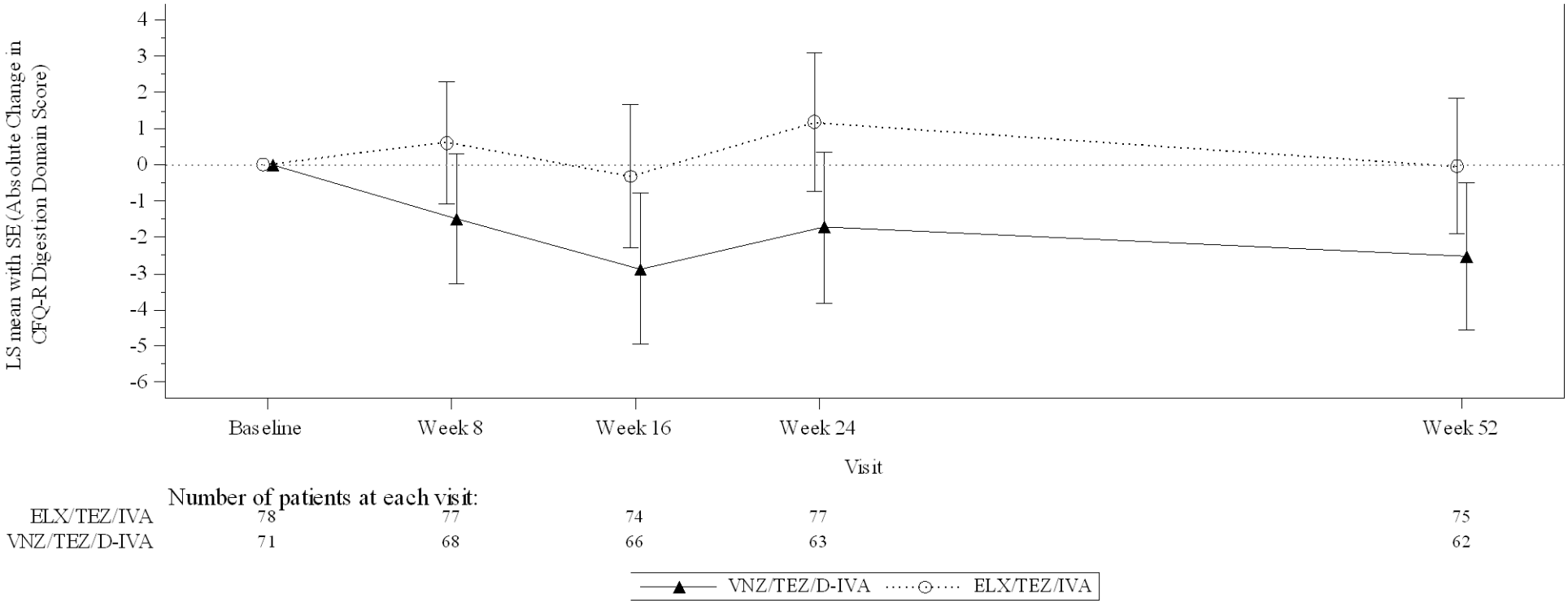
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

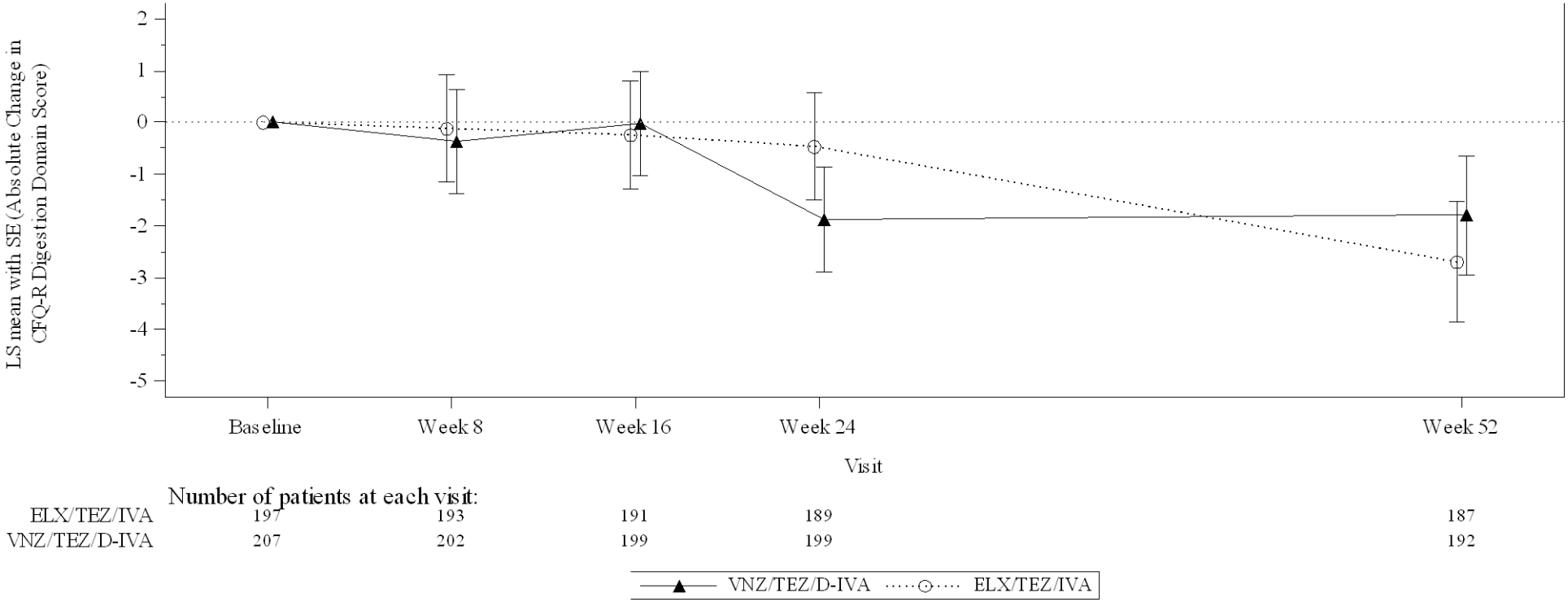
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

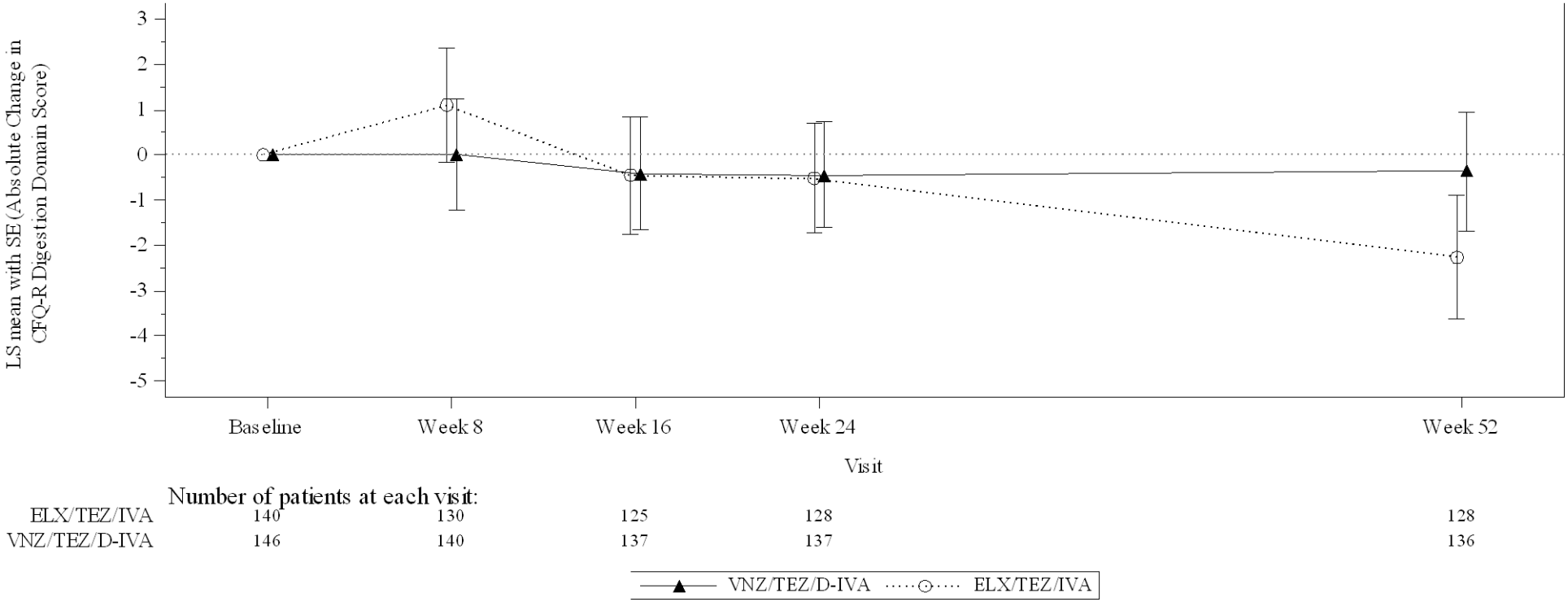
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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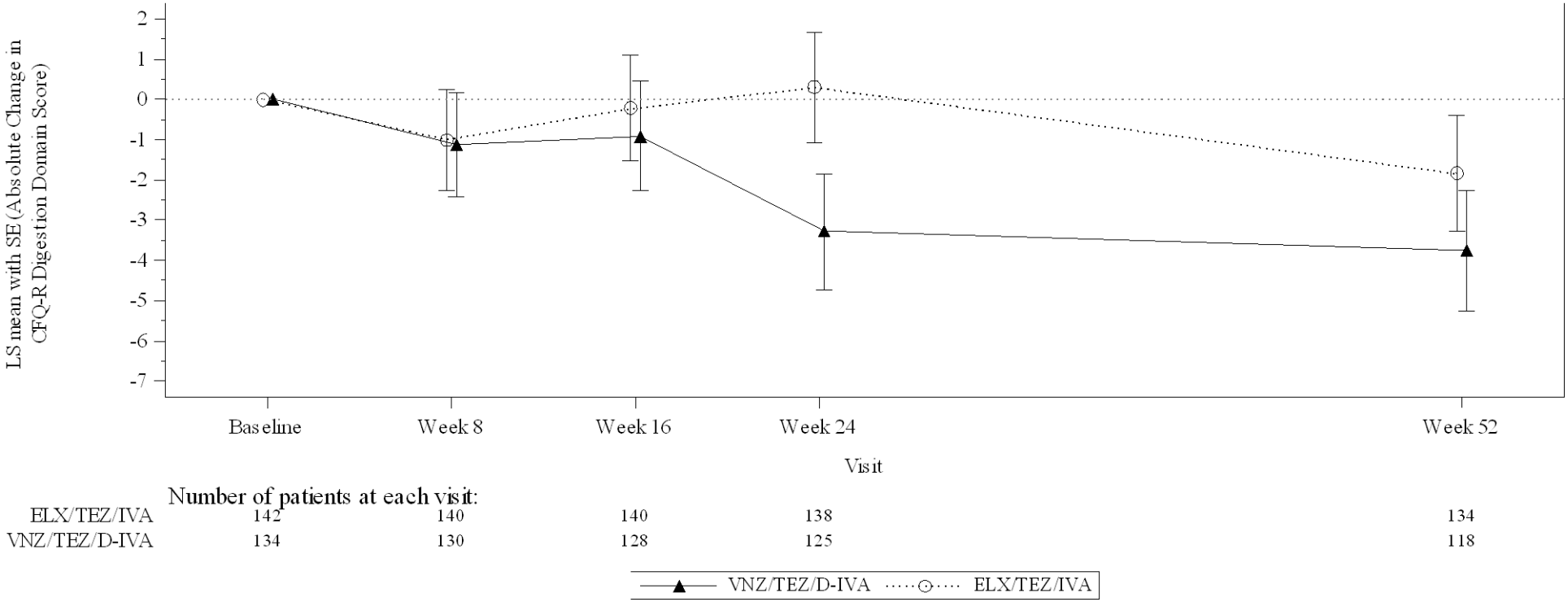
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

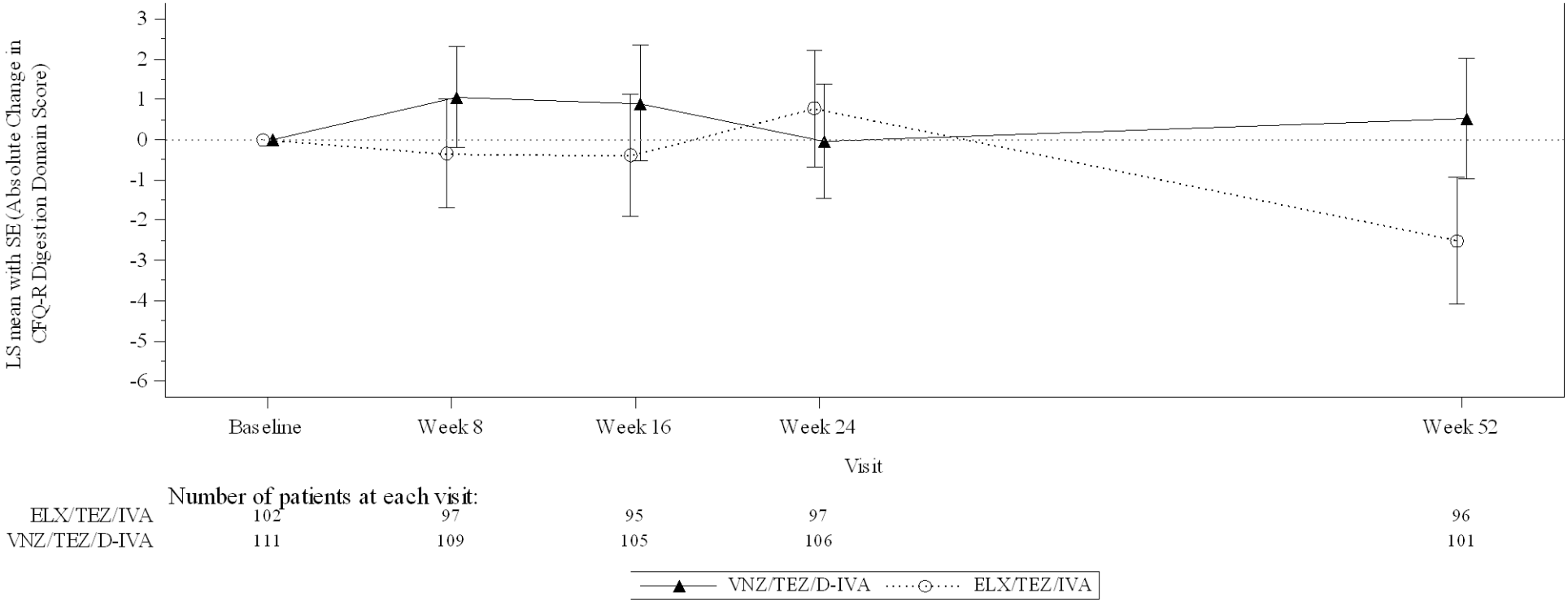
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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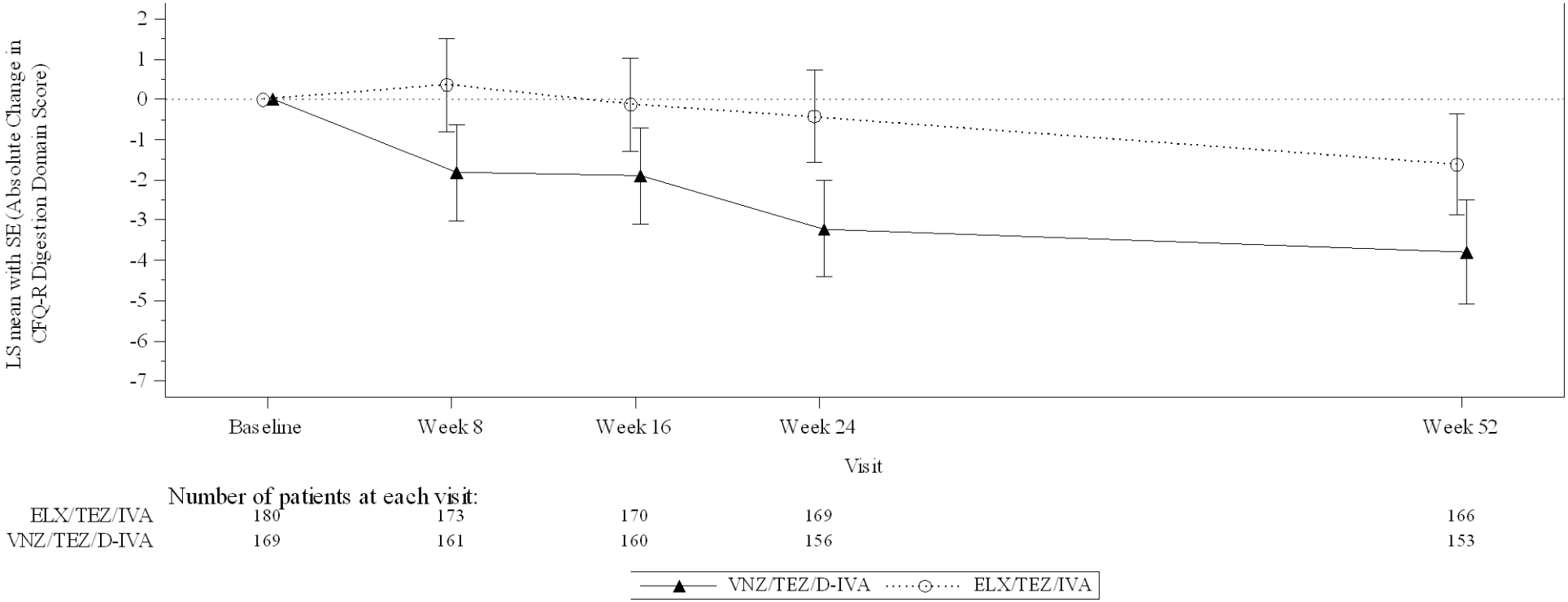
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



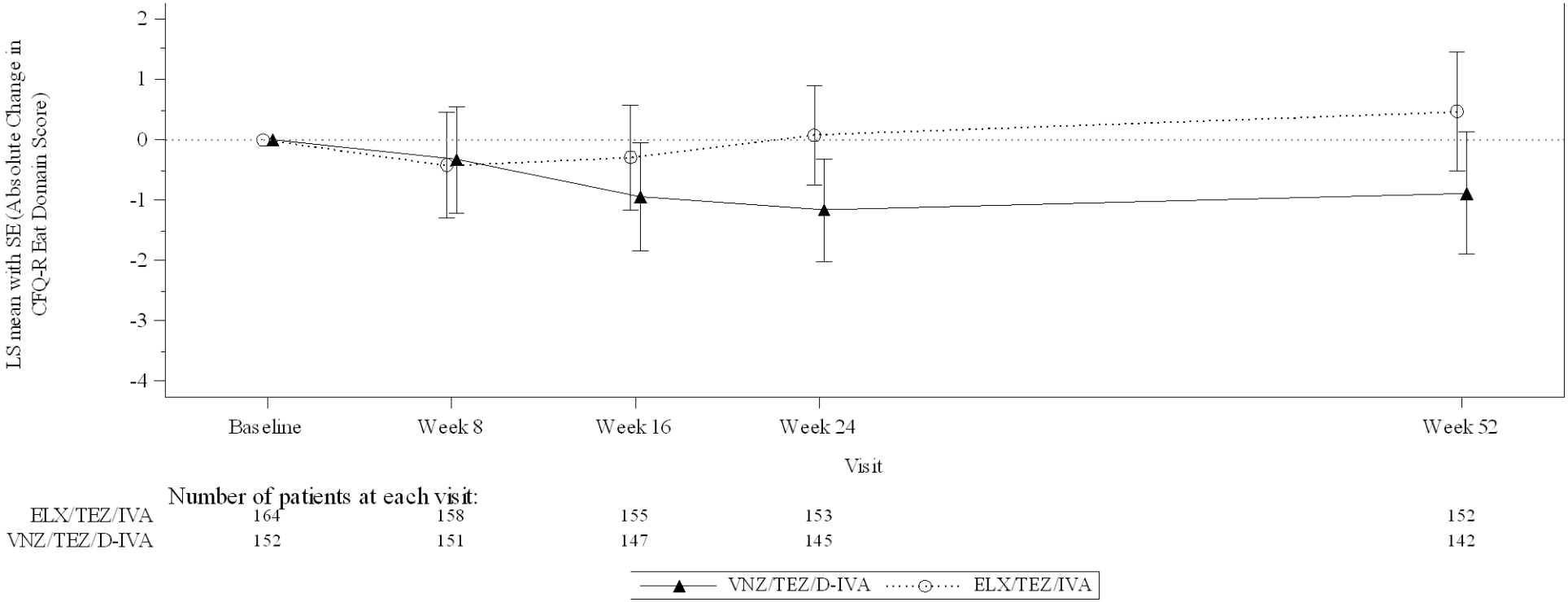
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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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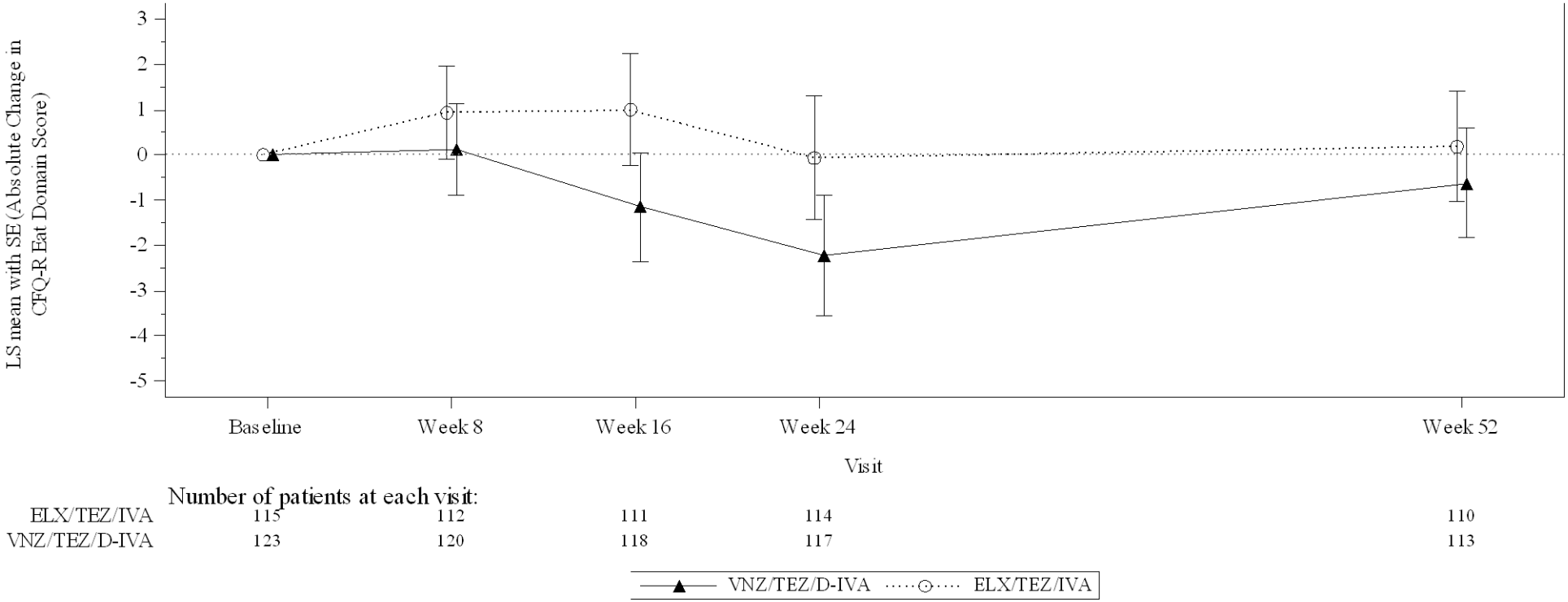
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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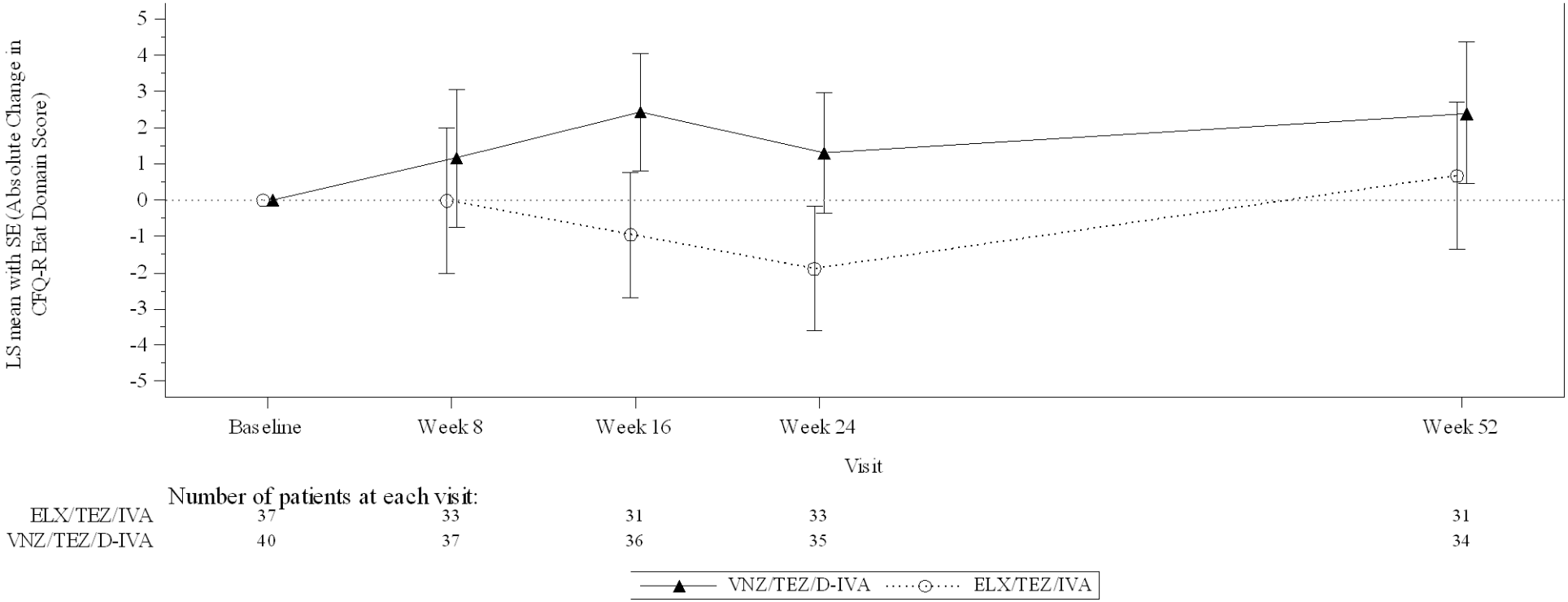
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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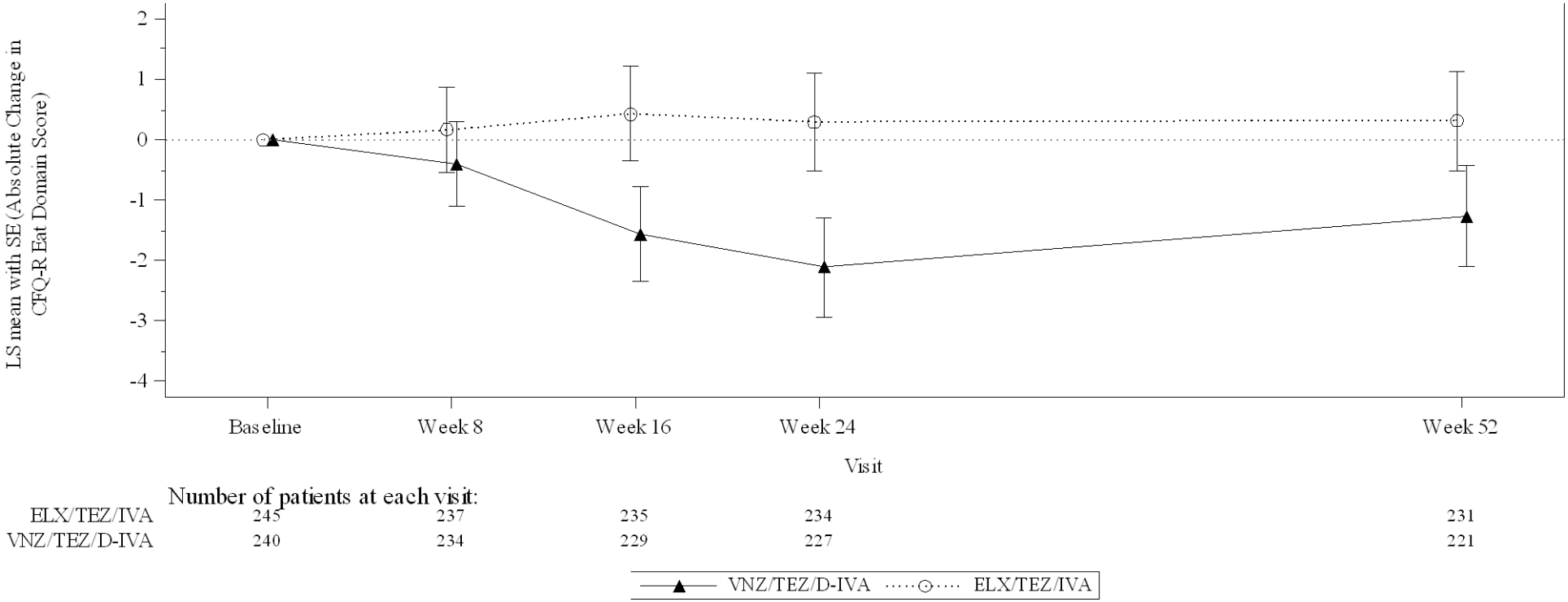
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



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- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

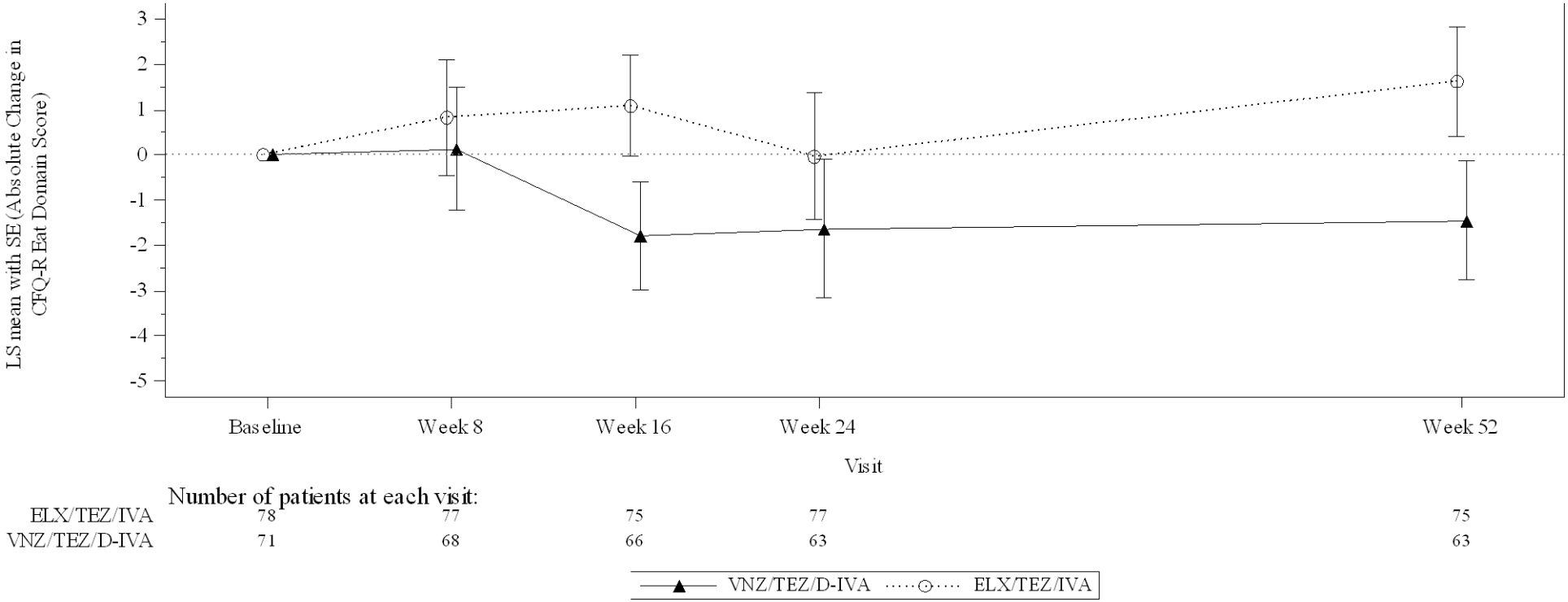
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



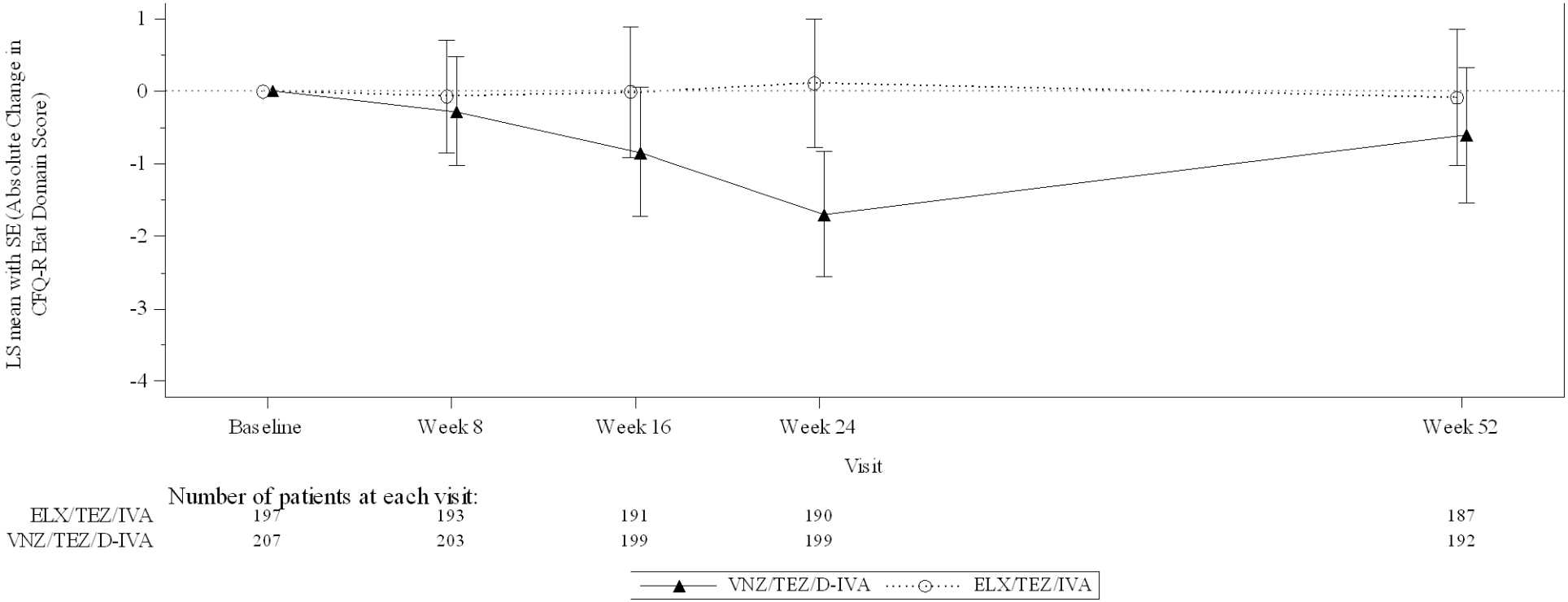
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Zusatzanalysen zur Studie VX20-121-103



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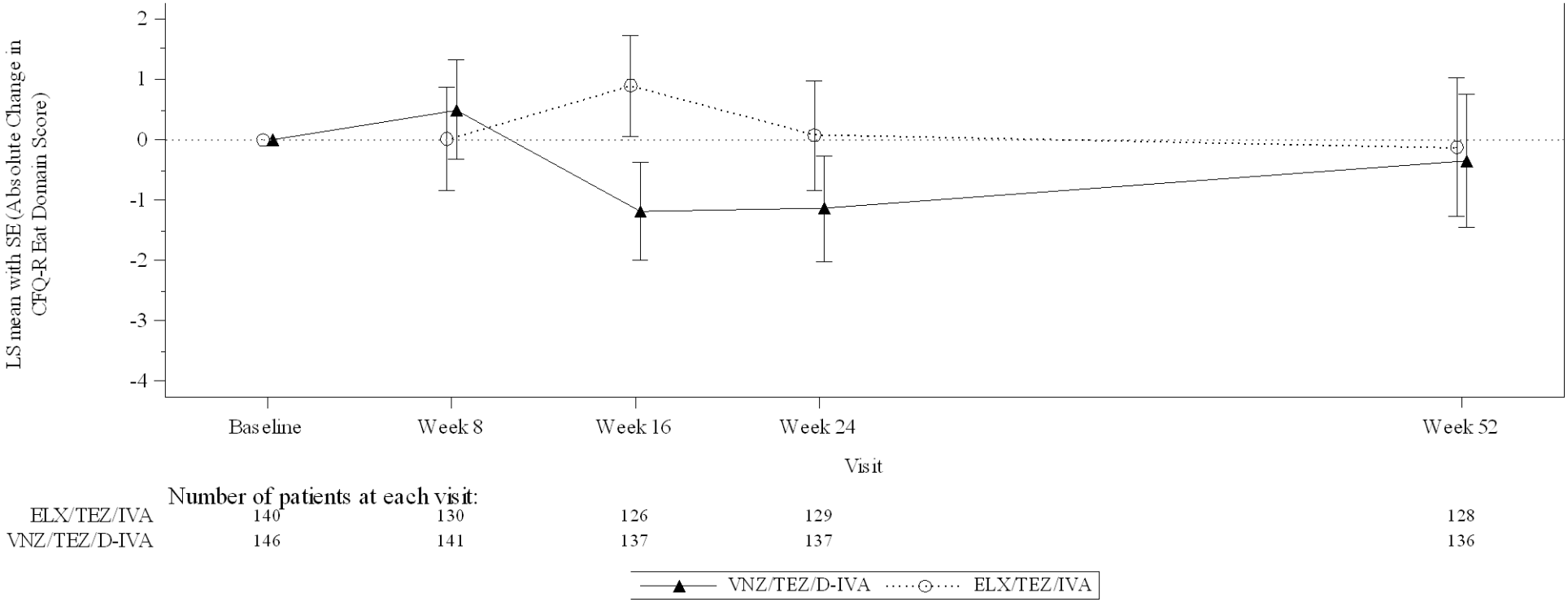
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



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- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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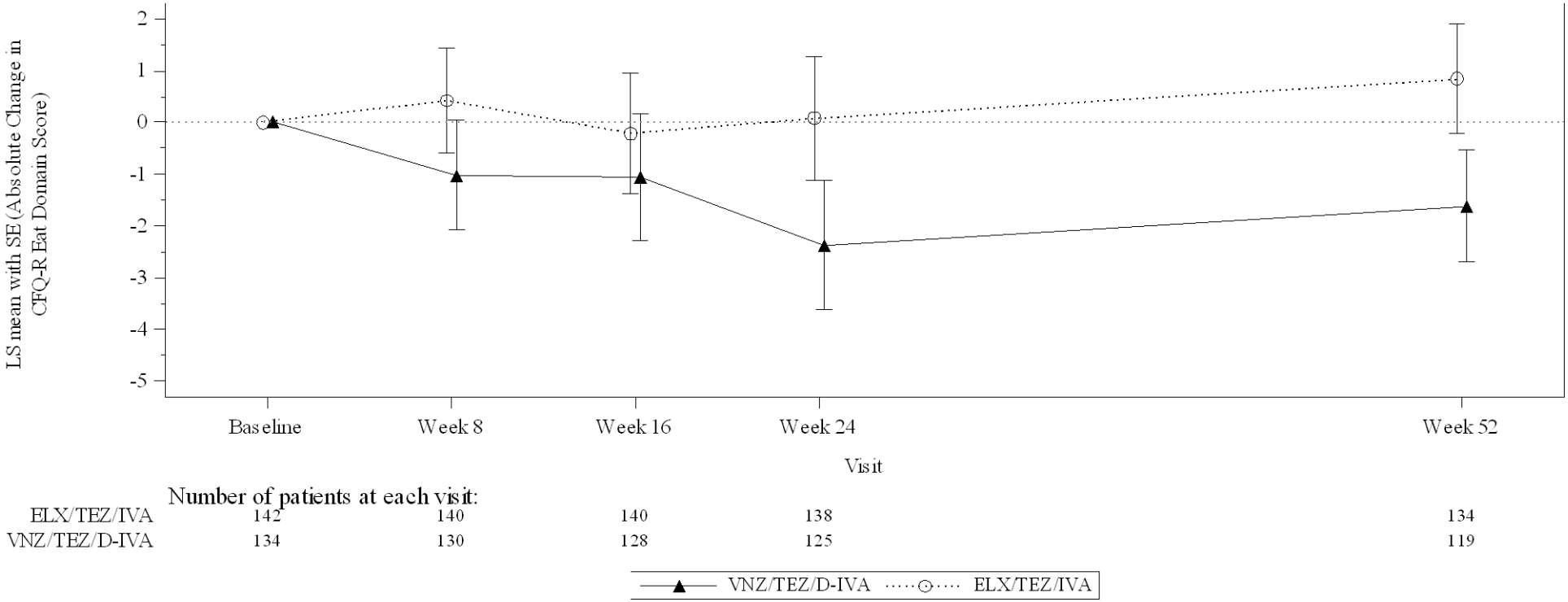
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



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- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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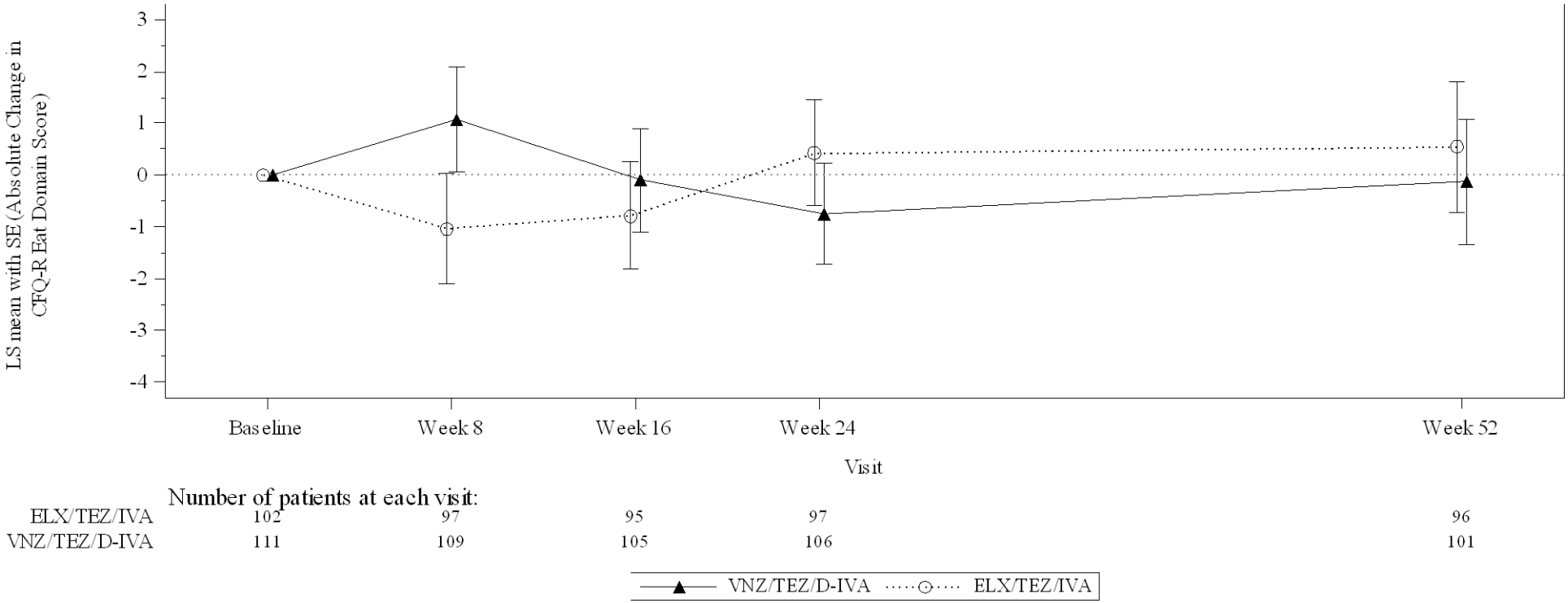
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Zusatzanalysen zur Studie VX20-121-103



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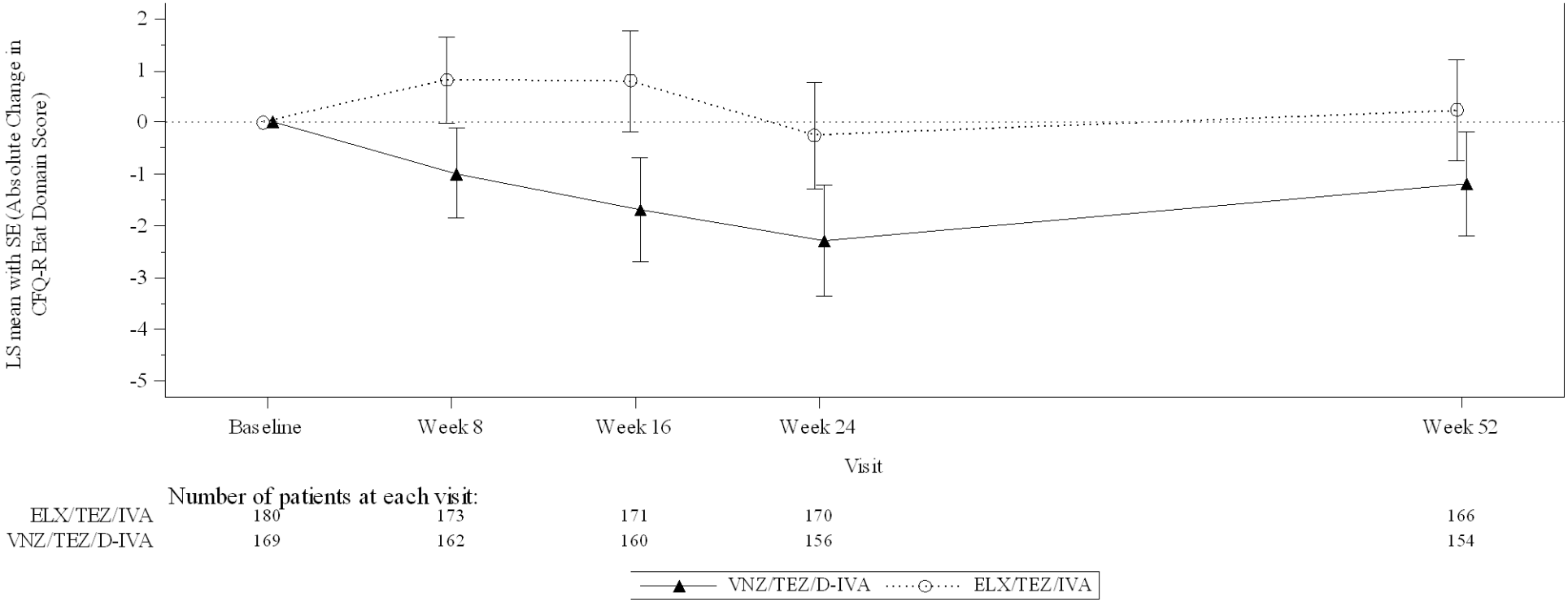
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



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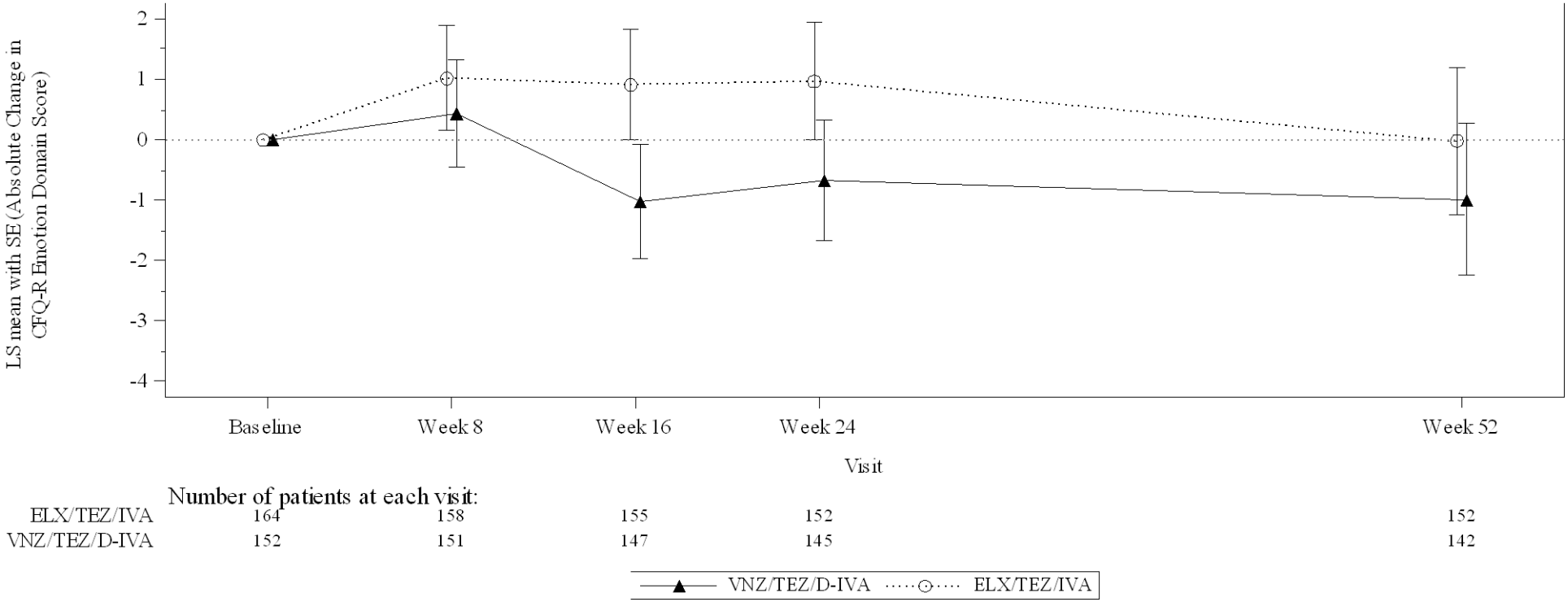
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Zusatzanalysen zur Studie VX20-121-103



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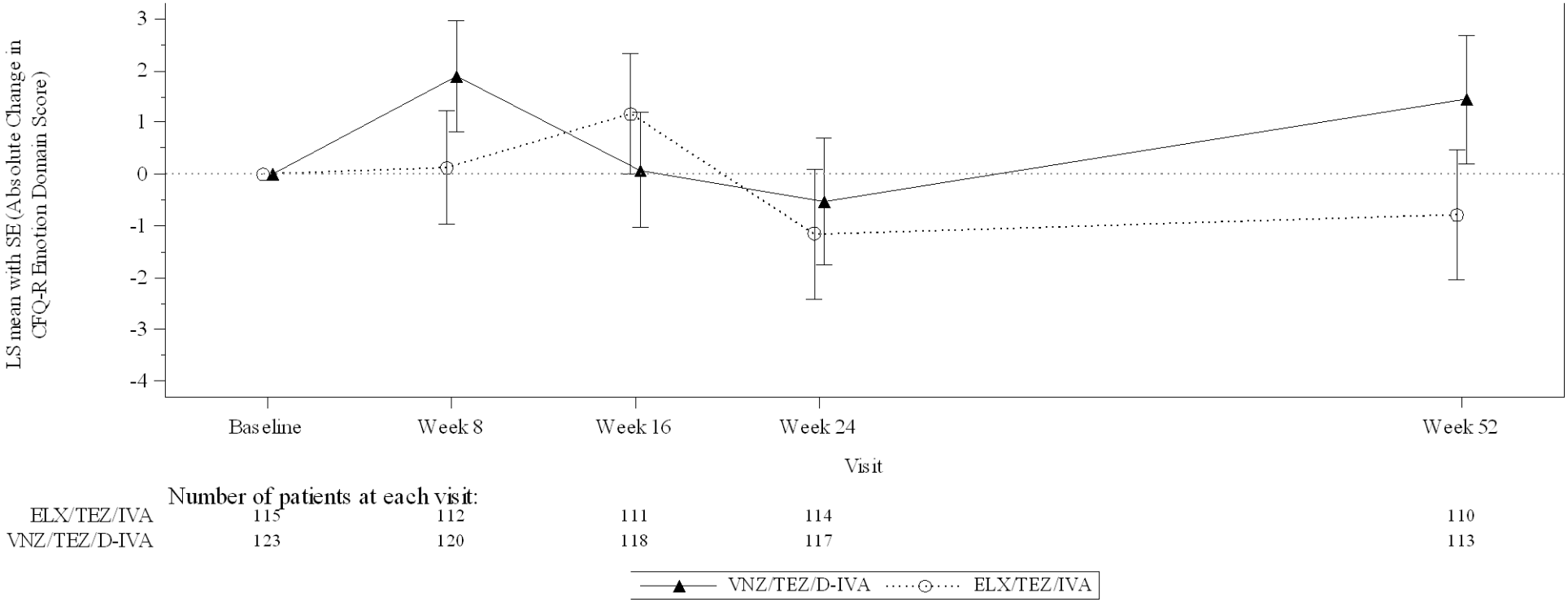
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Zusatzanalysen zur Studie VX20-121-103



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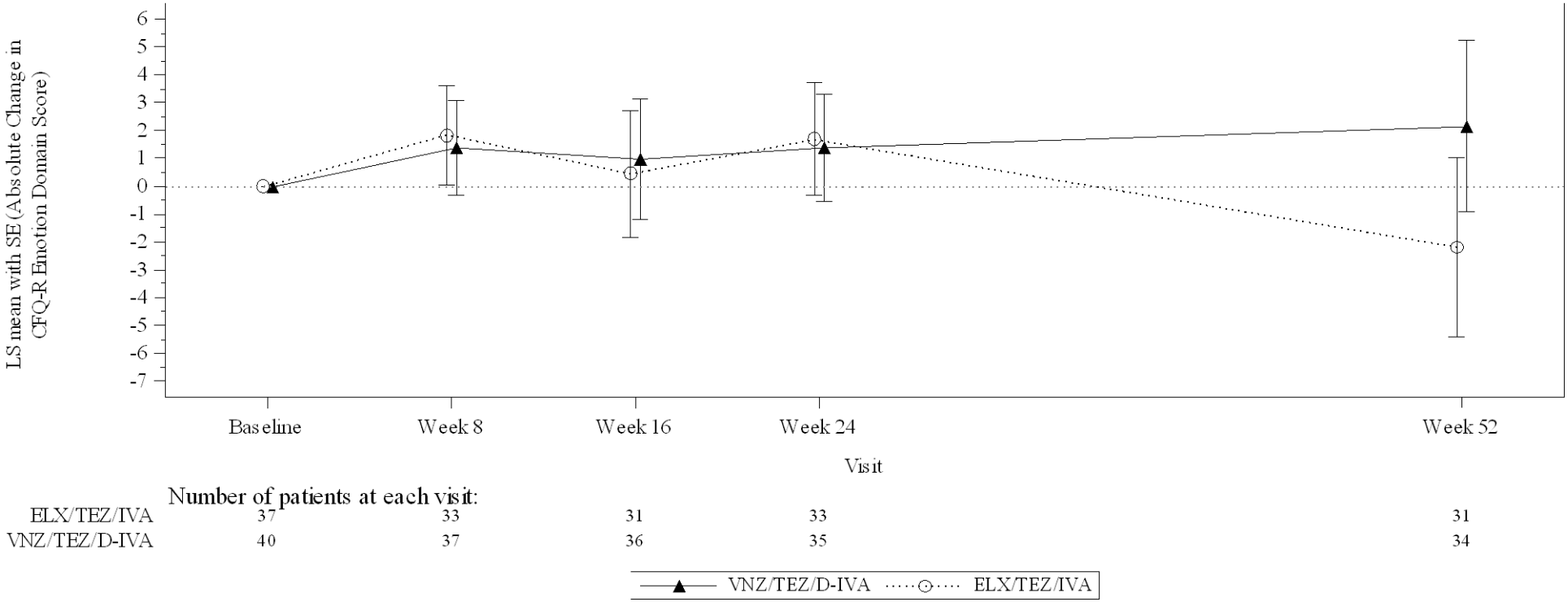
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Zusatzanalysen zur Studie VX20-121-103



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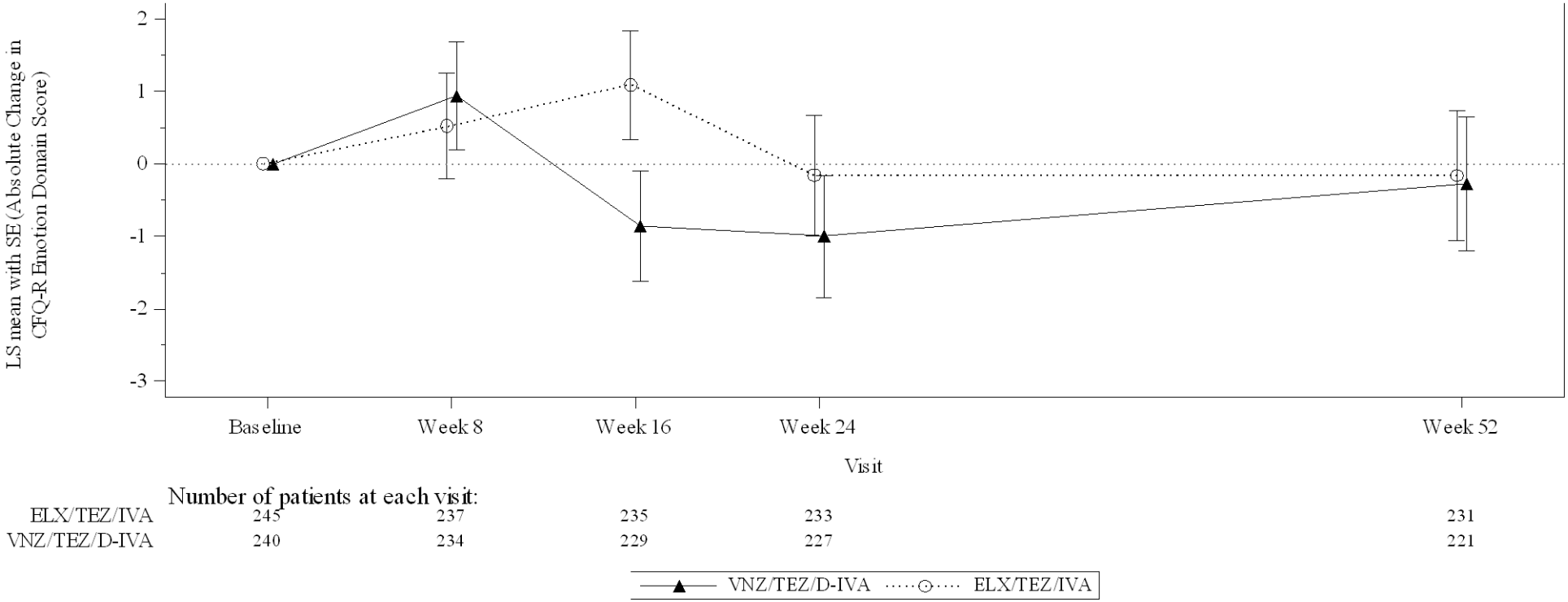
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Zusatzanalysen zur Studie VX20-121-103



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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

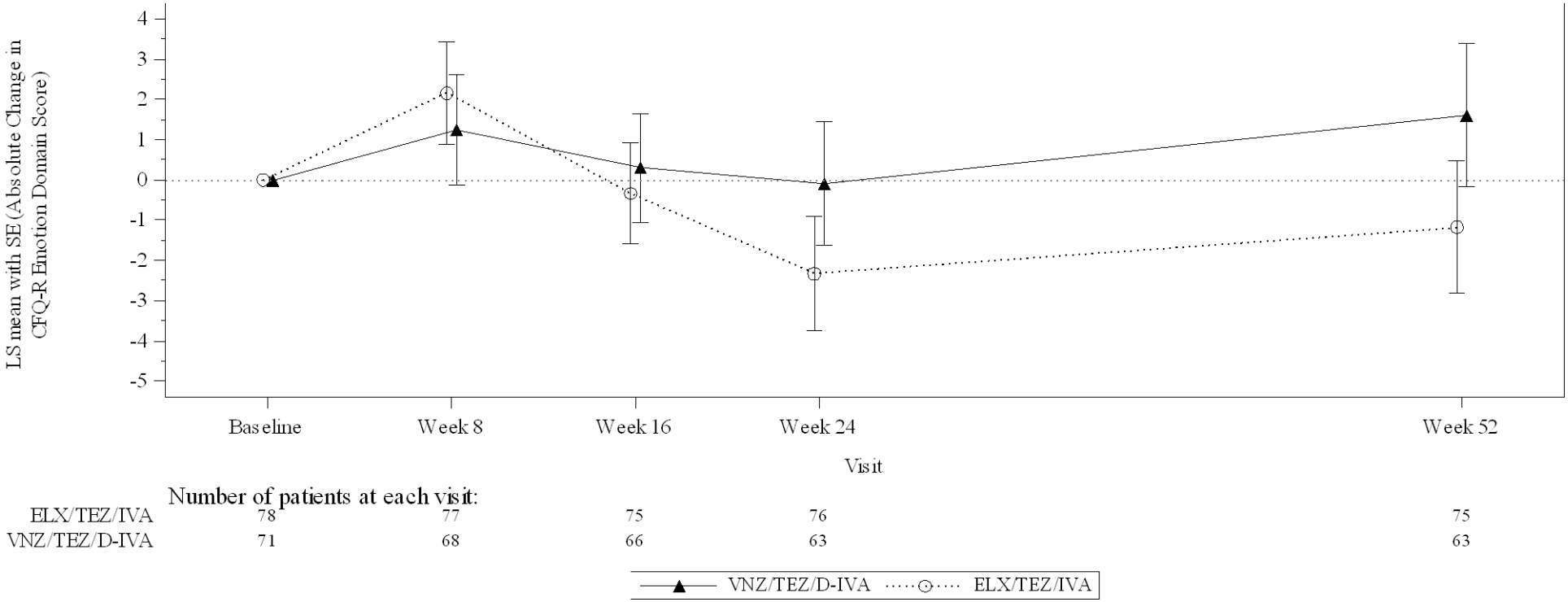
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

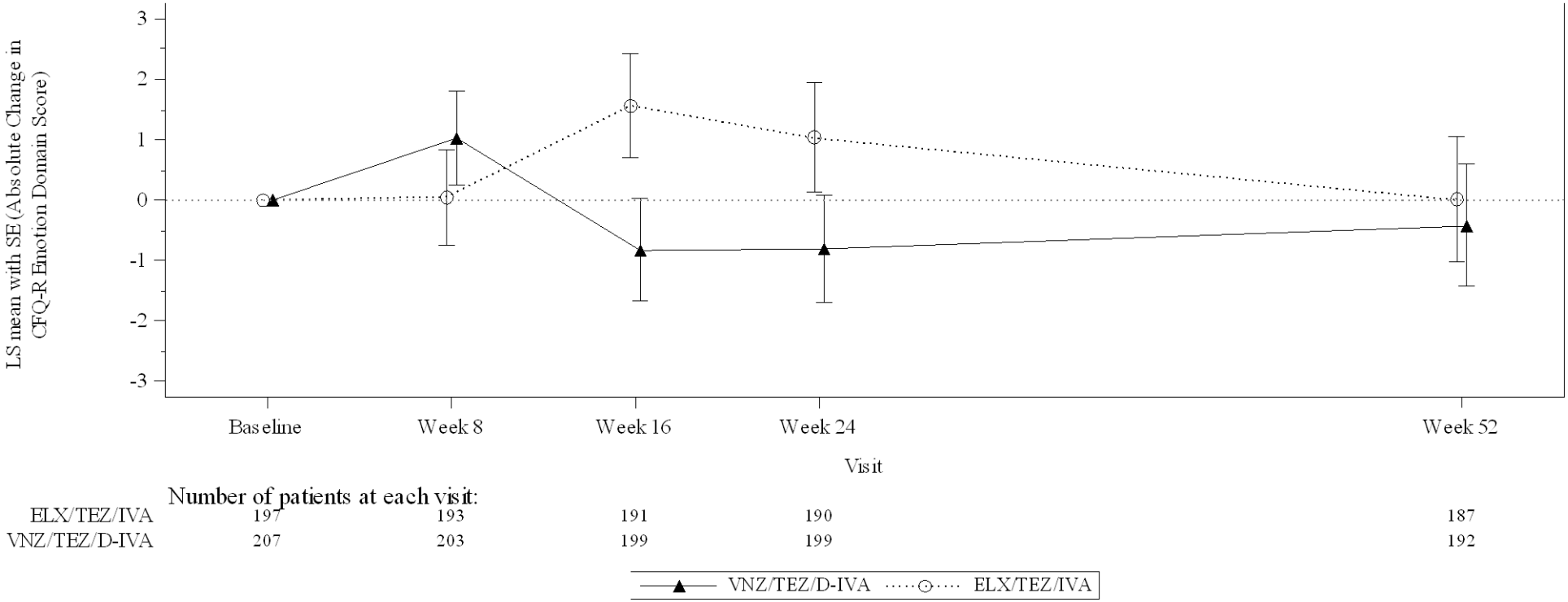
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

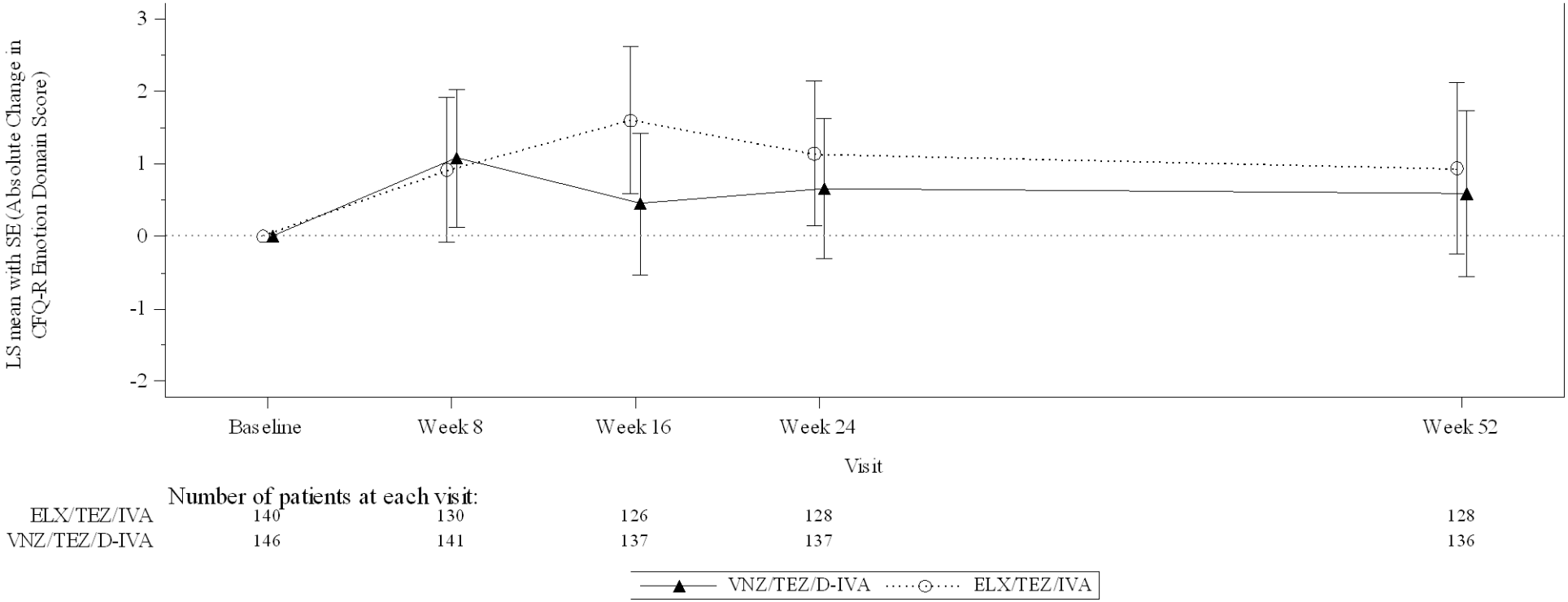
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

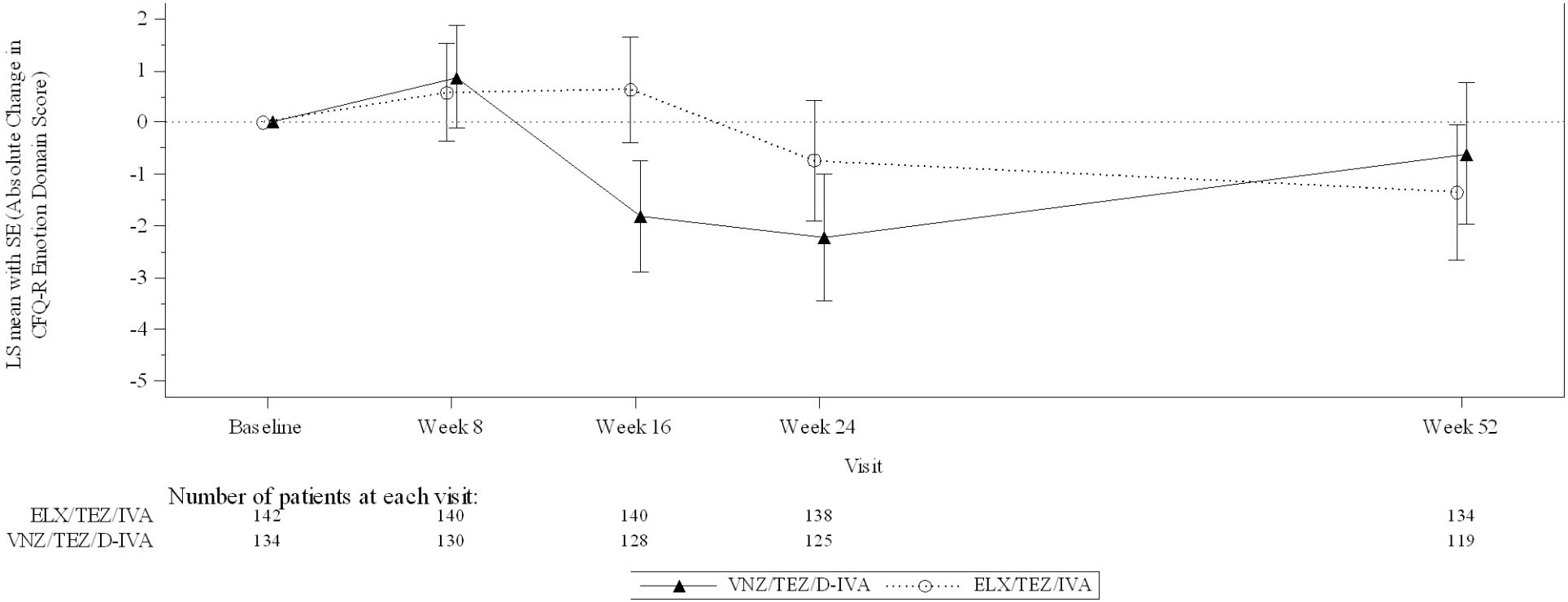
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

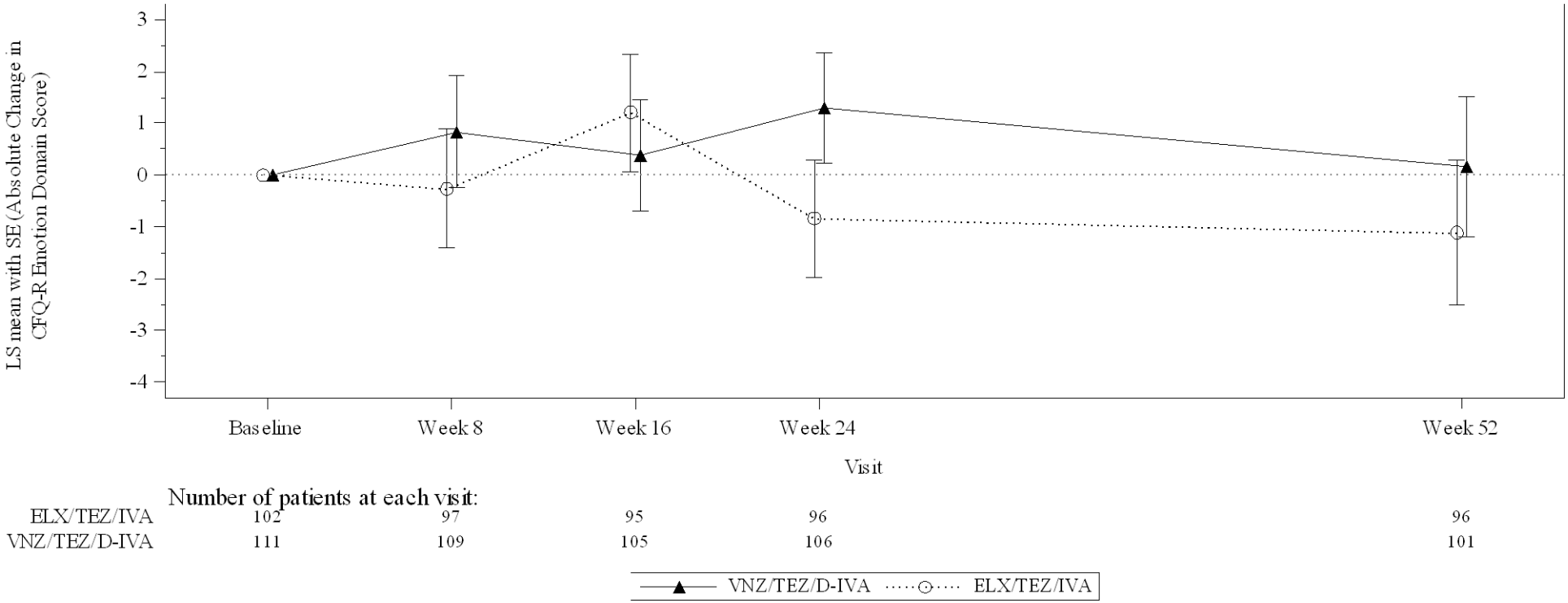
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

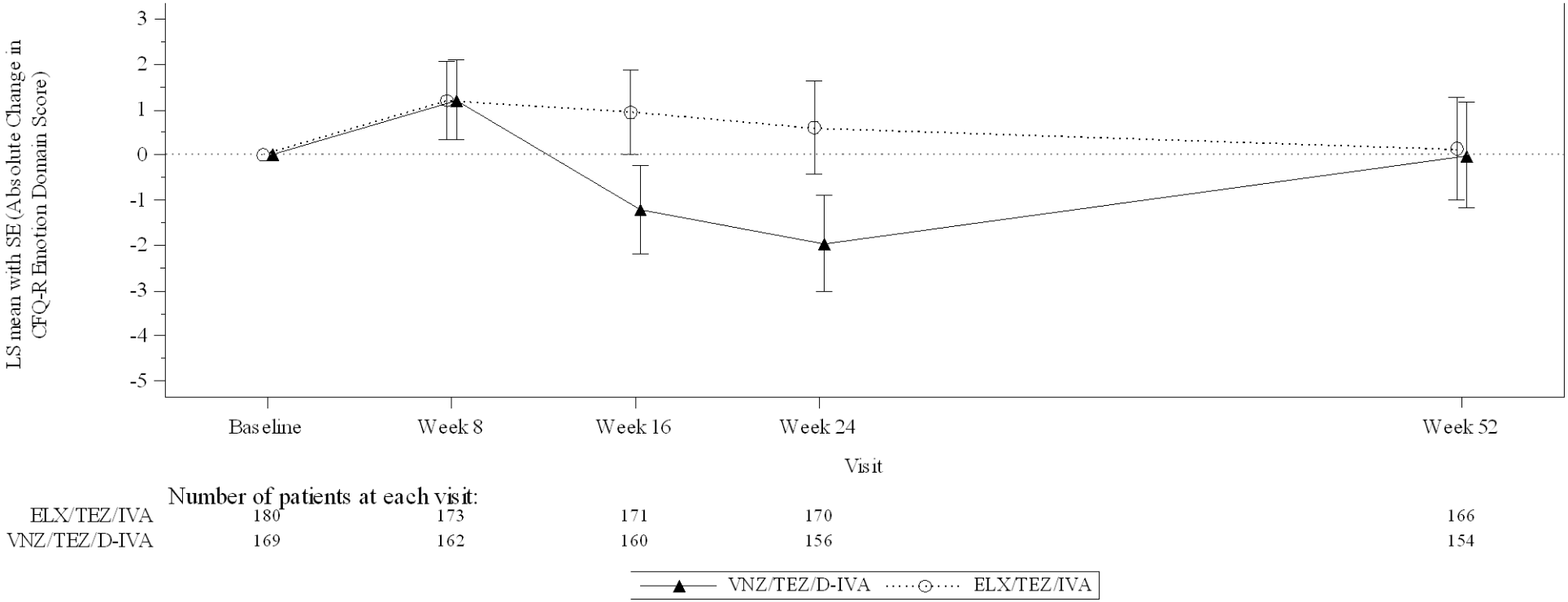
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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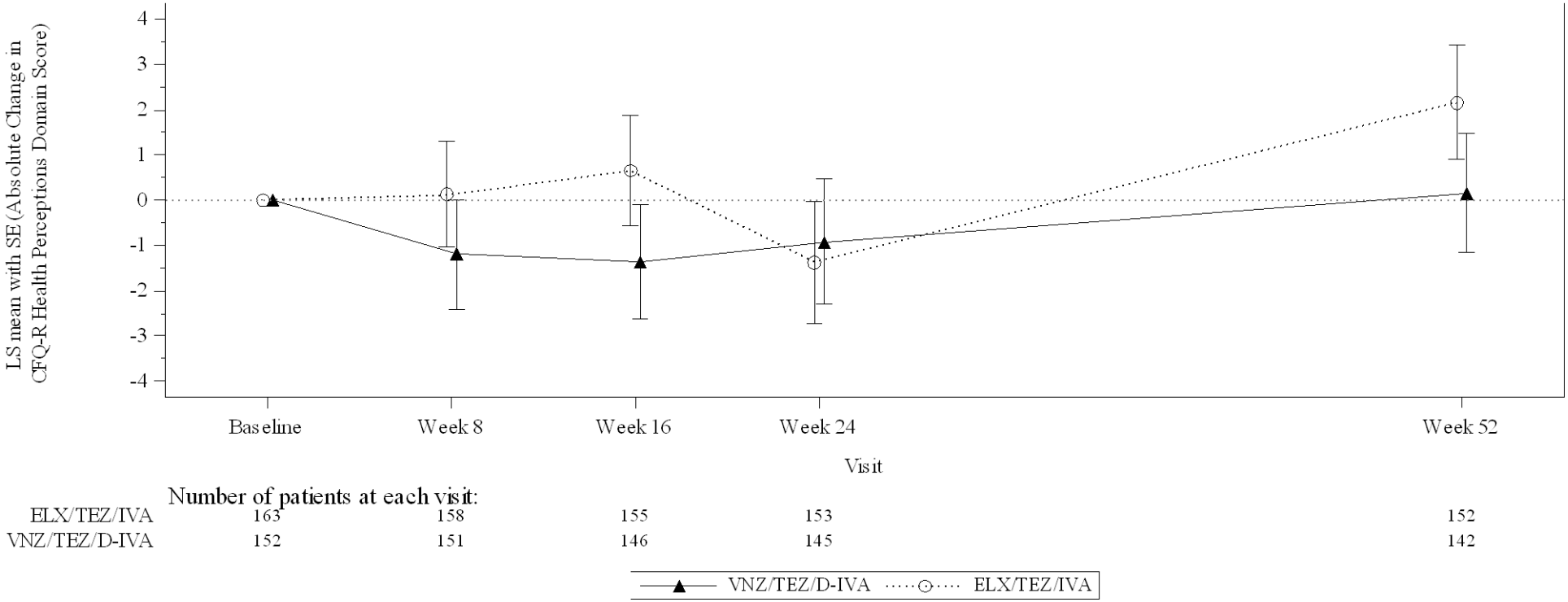
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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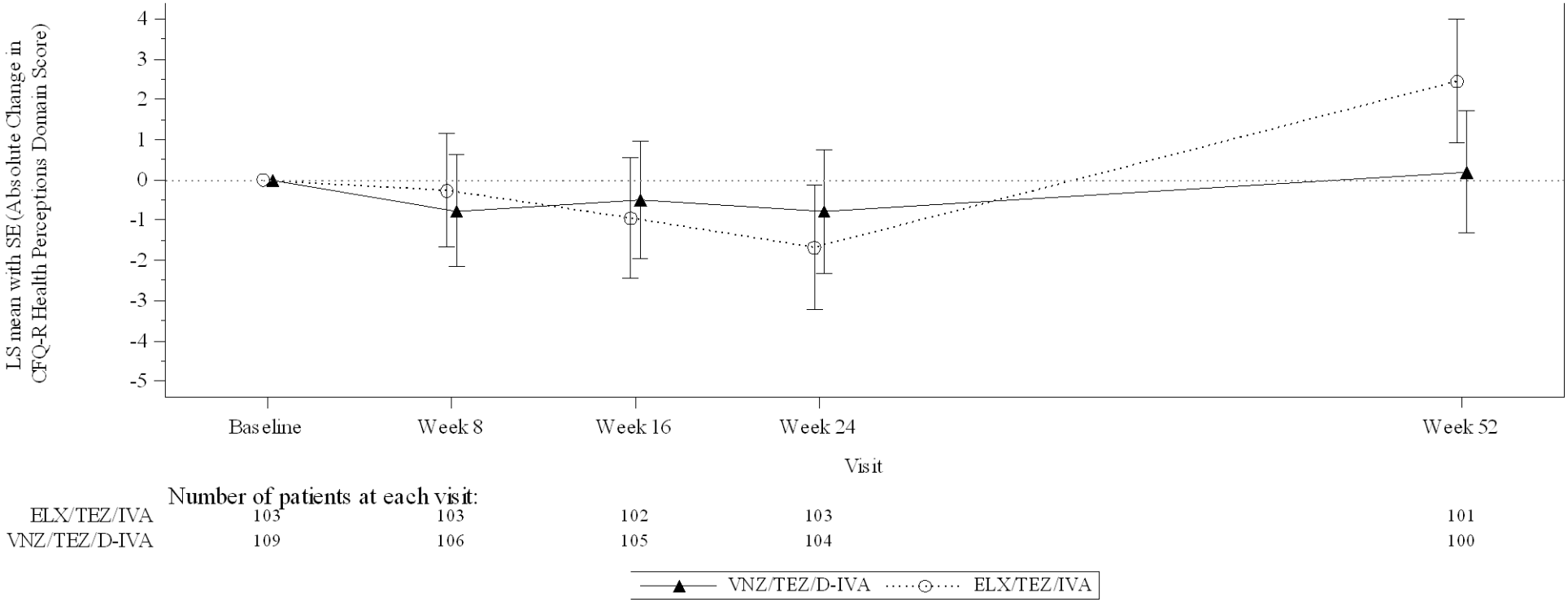
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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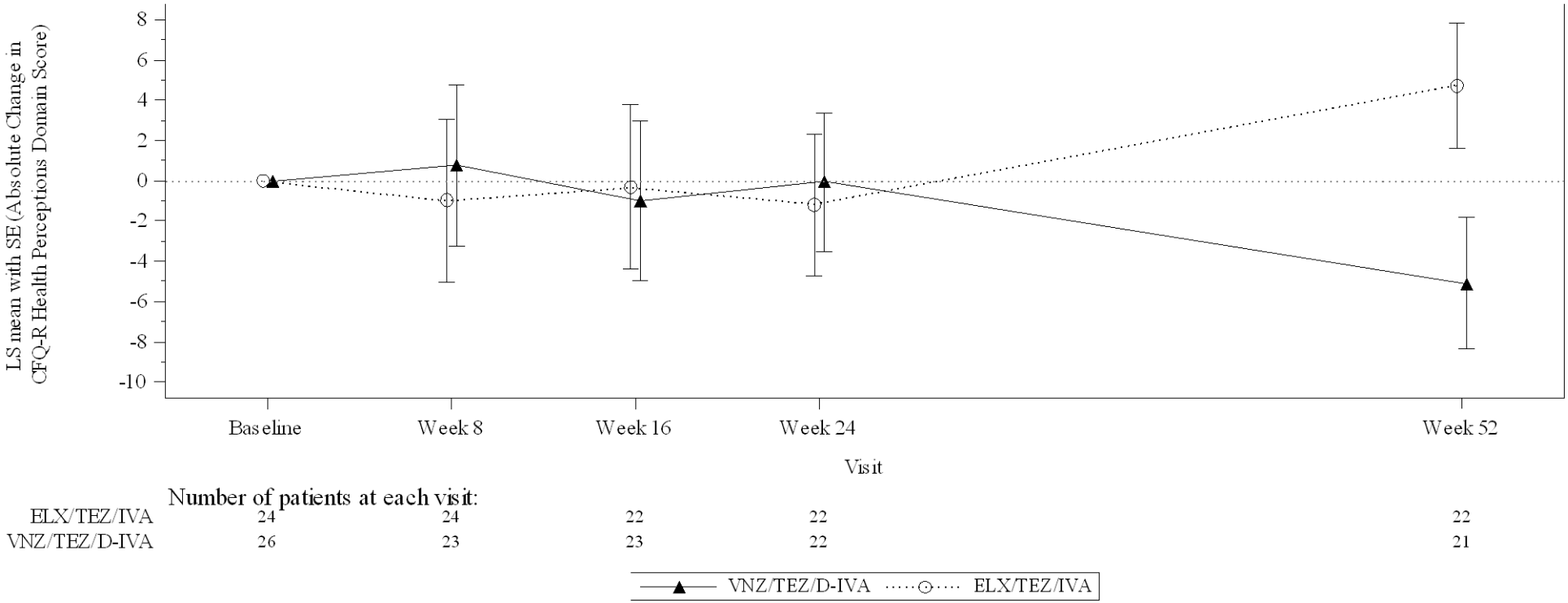
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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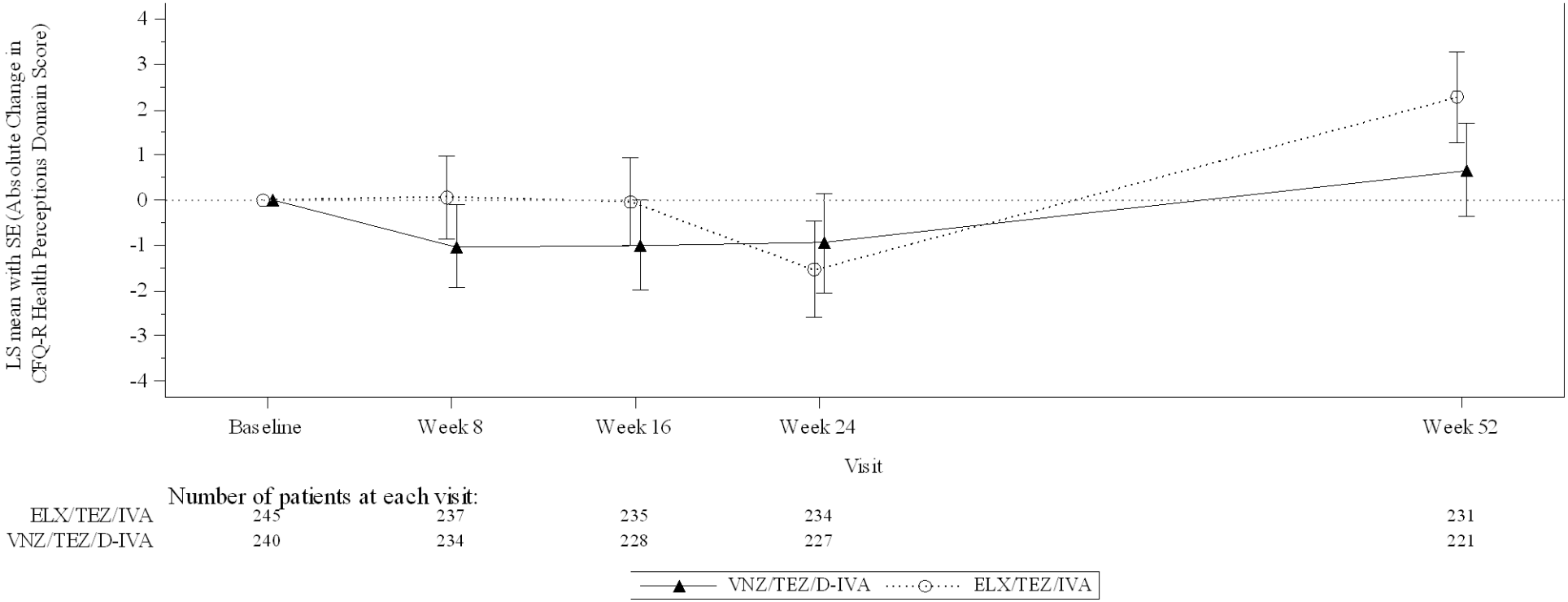
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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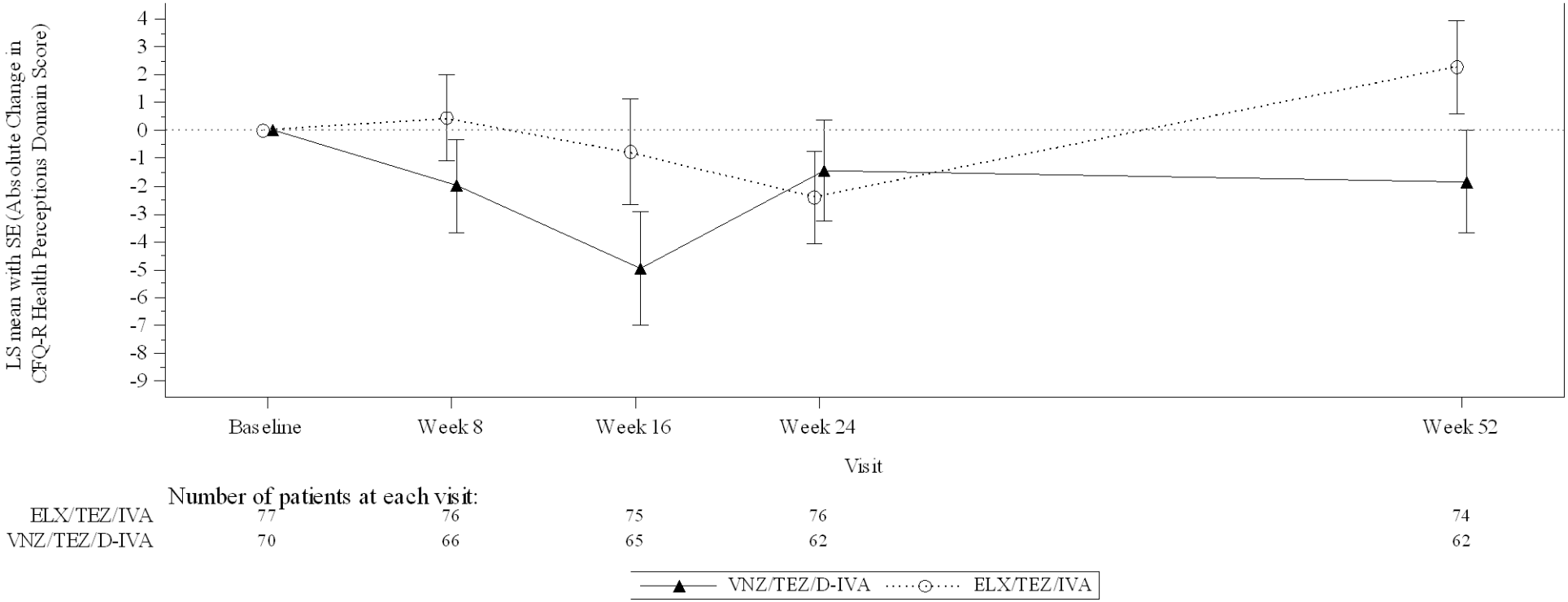
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

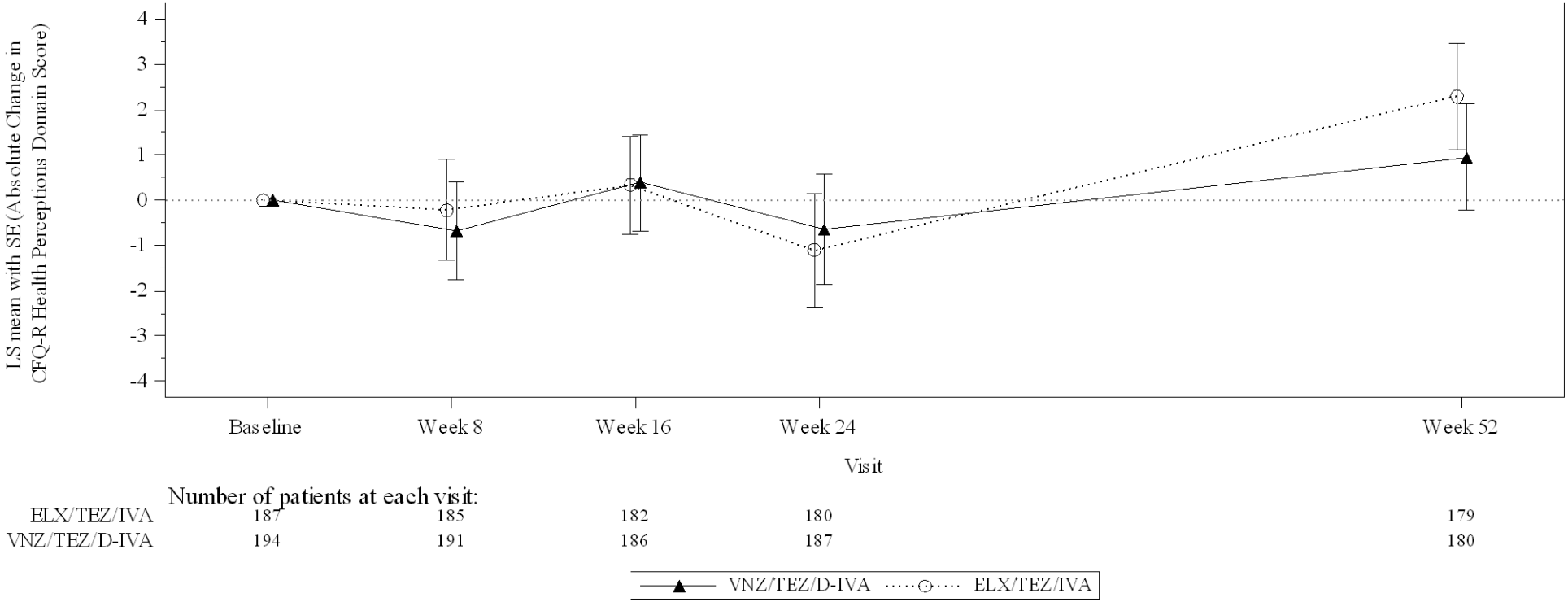
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

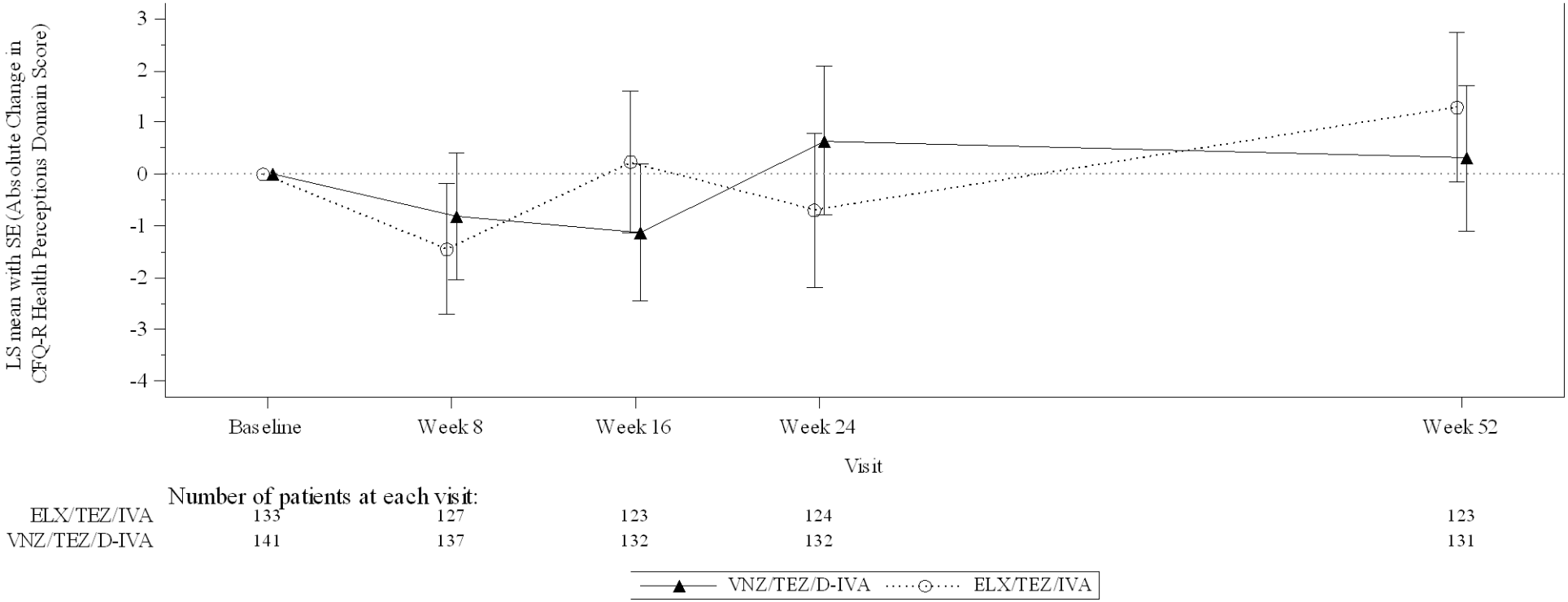
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

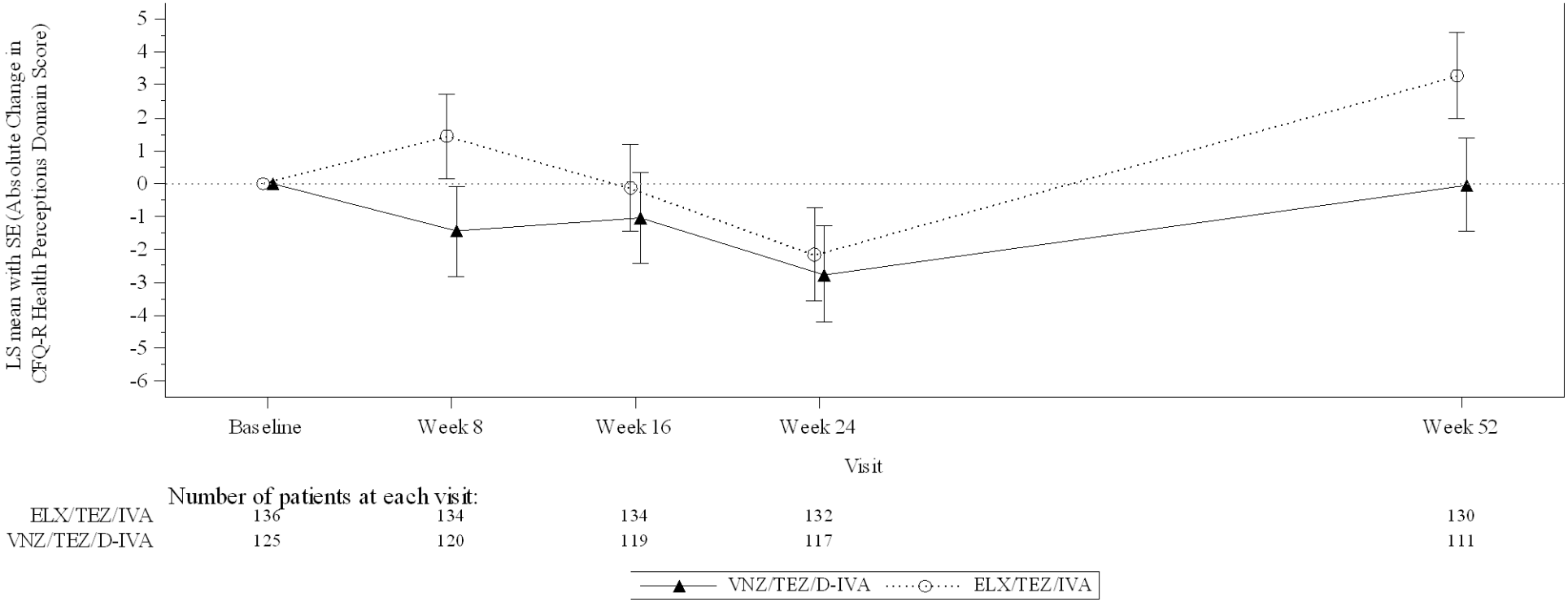
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

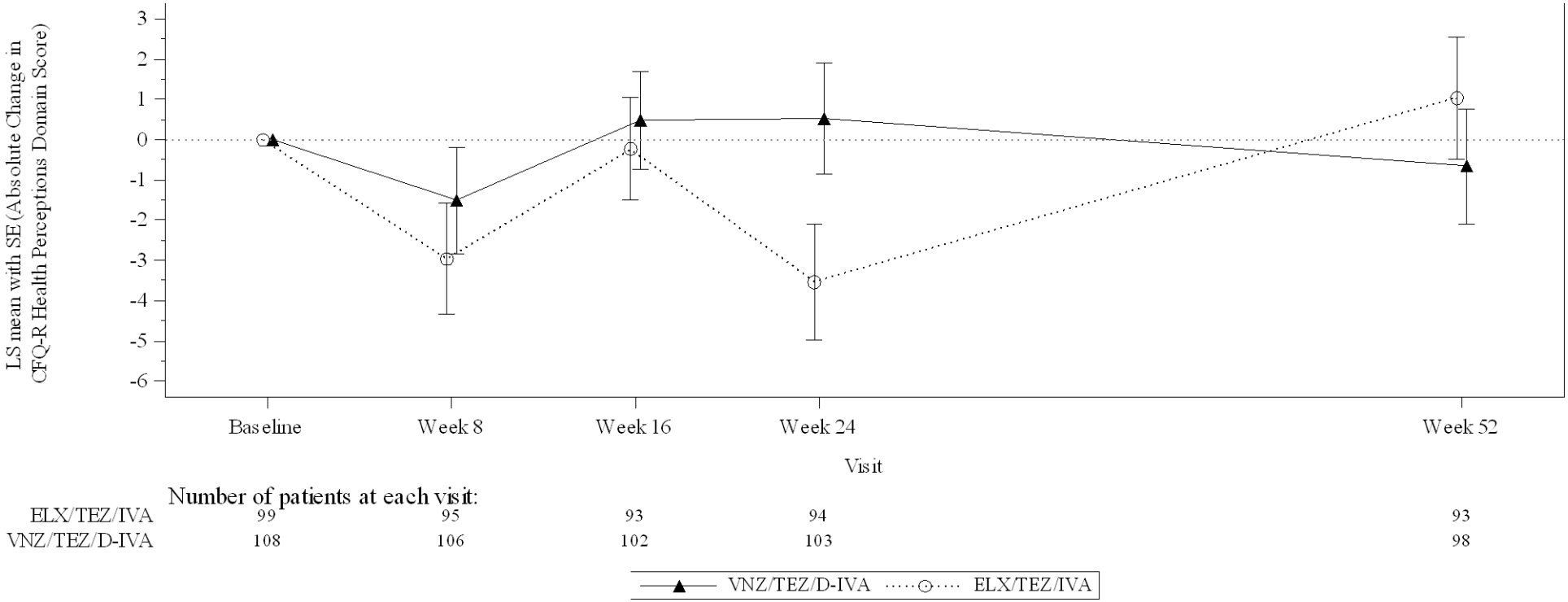
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

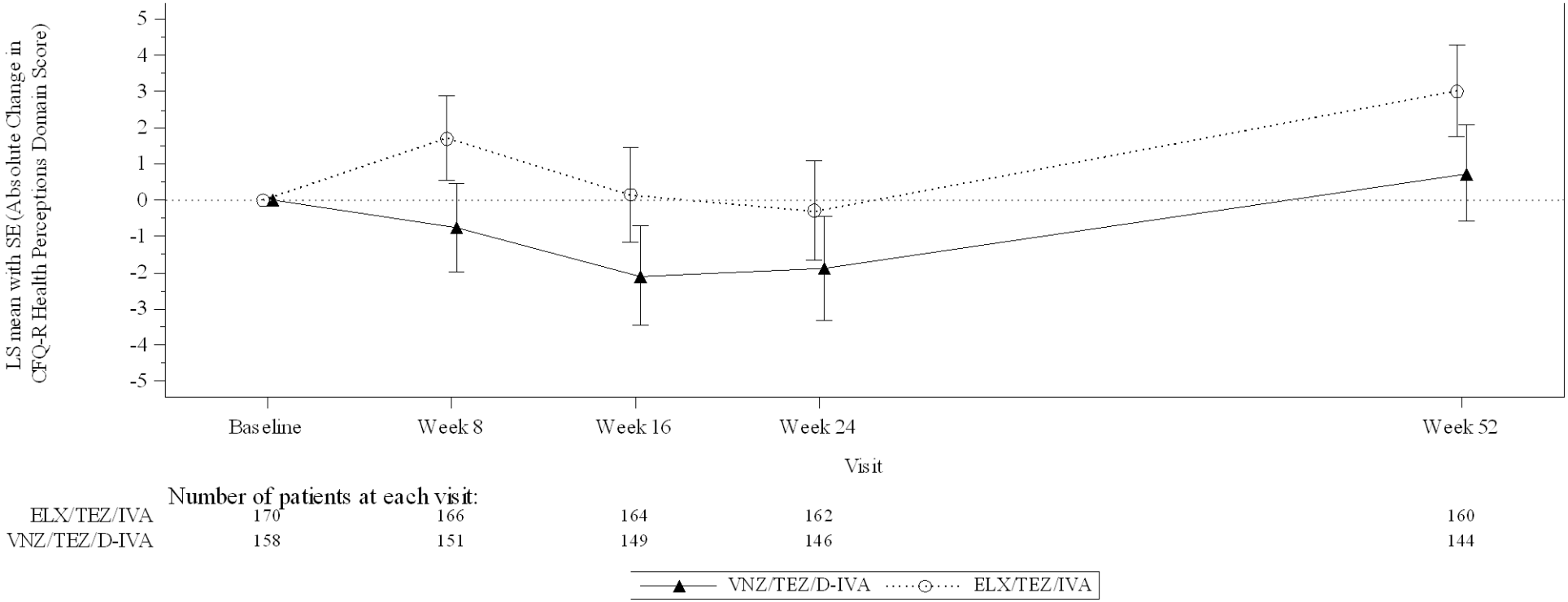
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

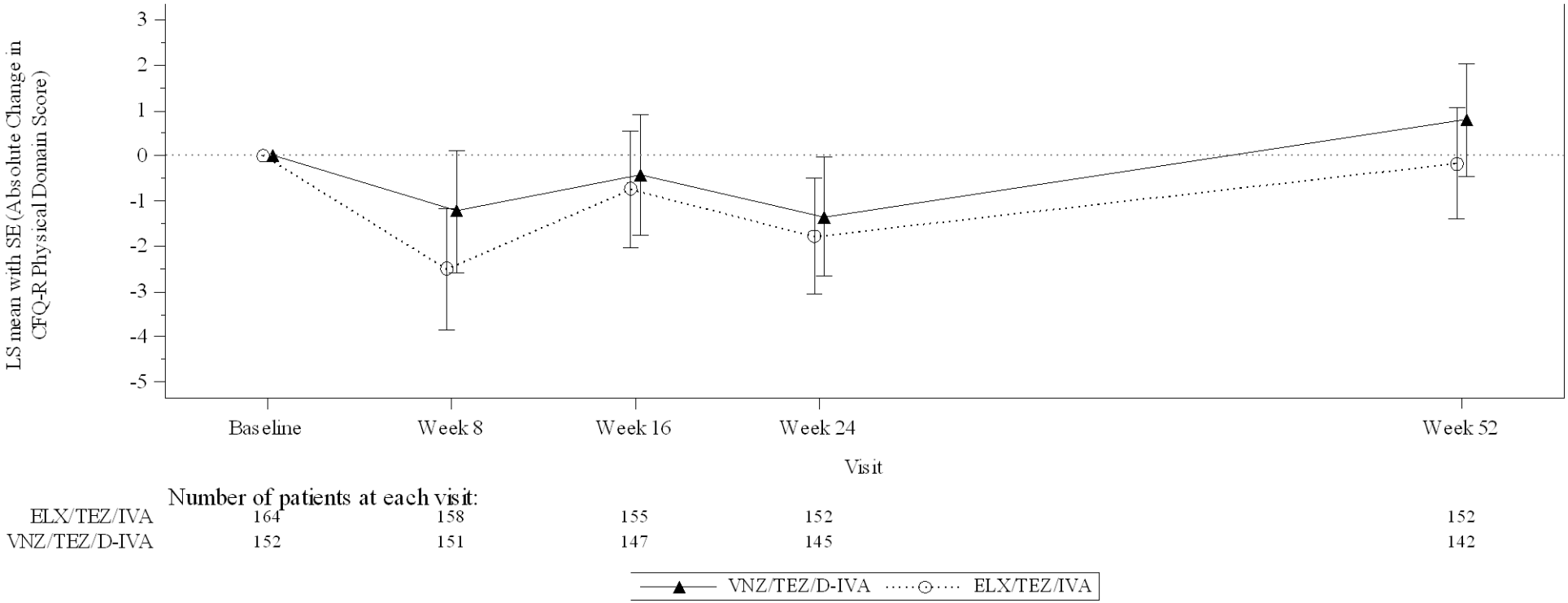
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

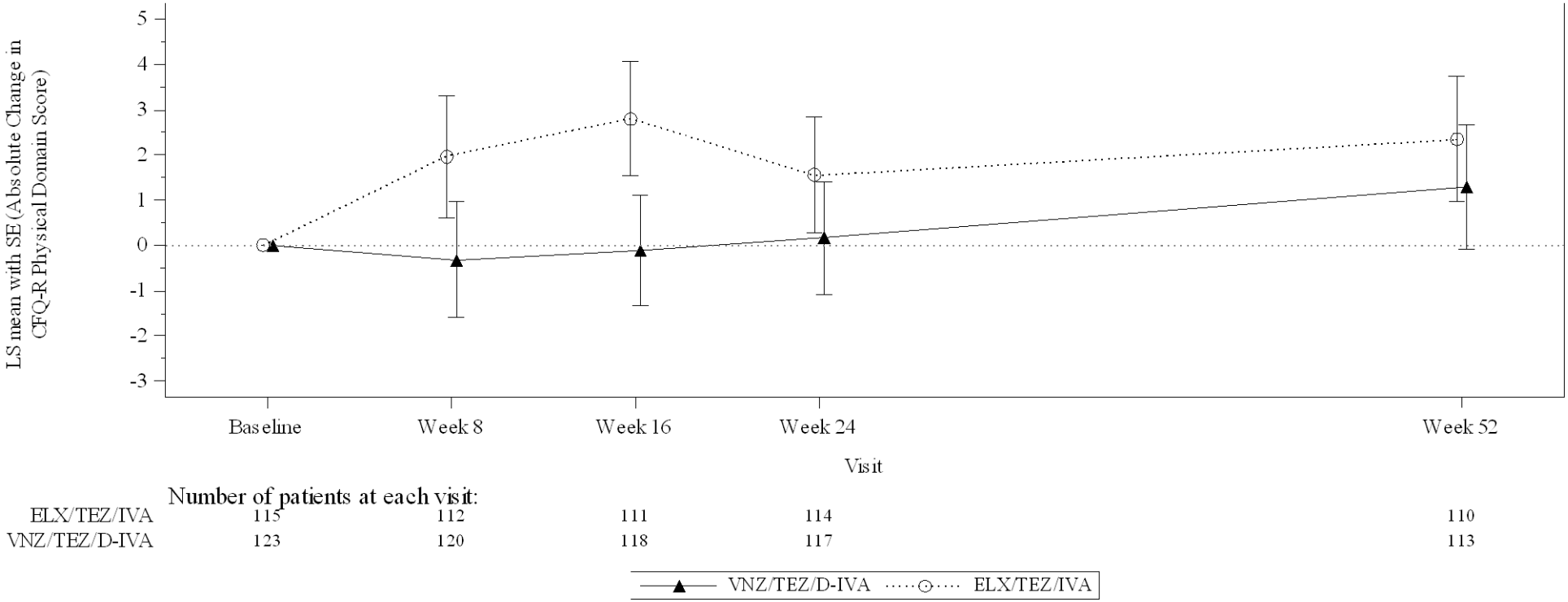
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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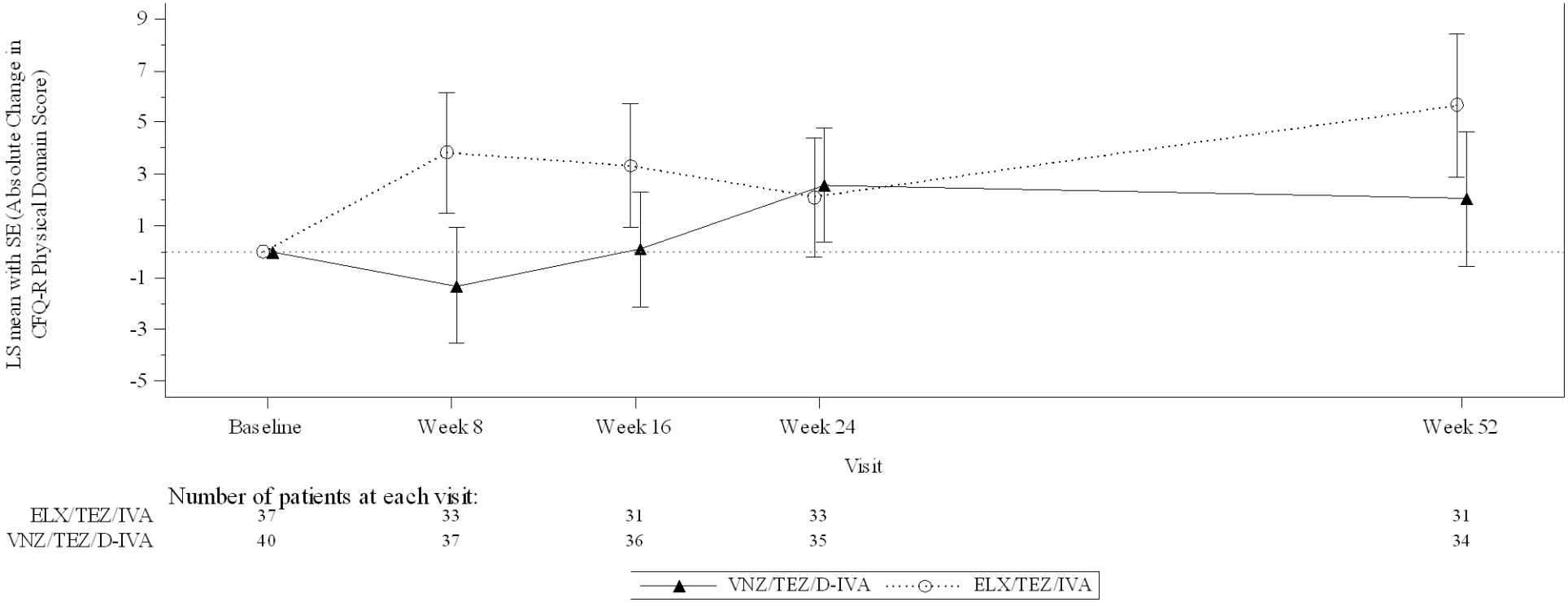
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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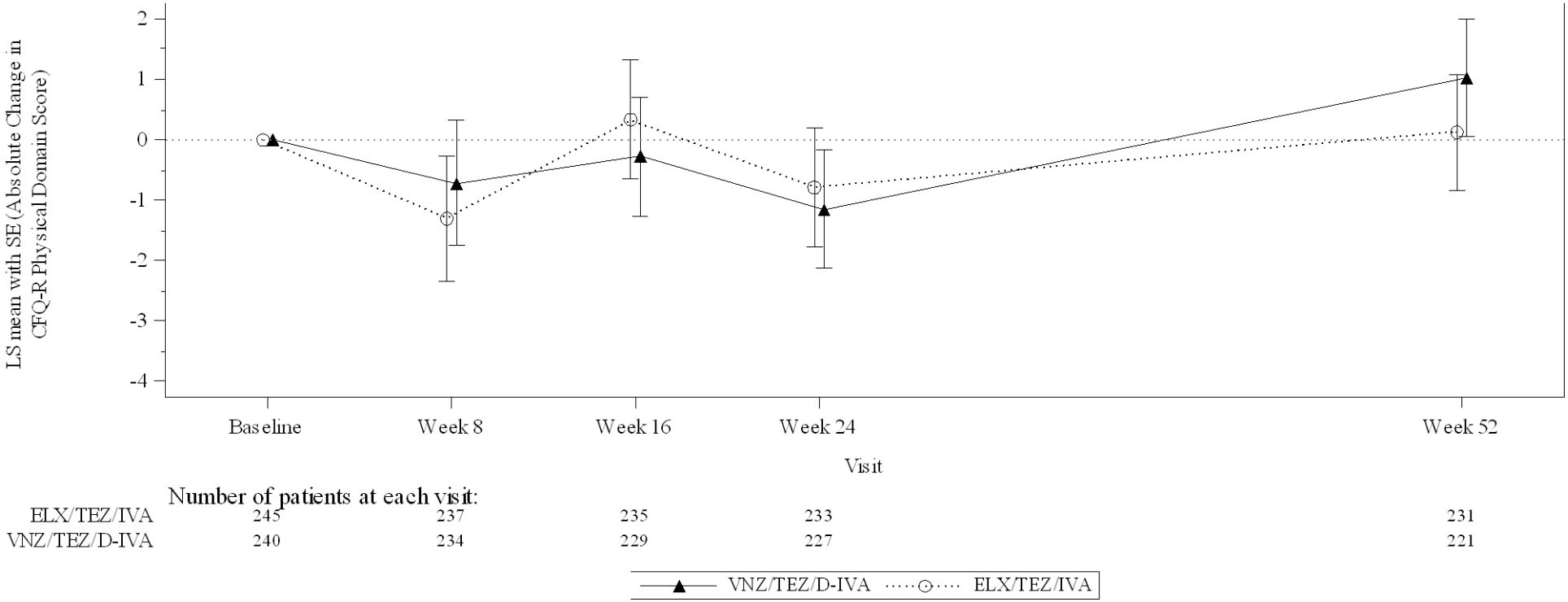
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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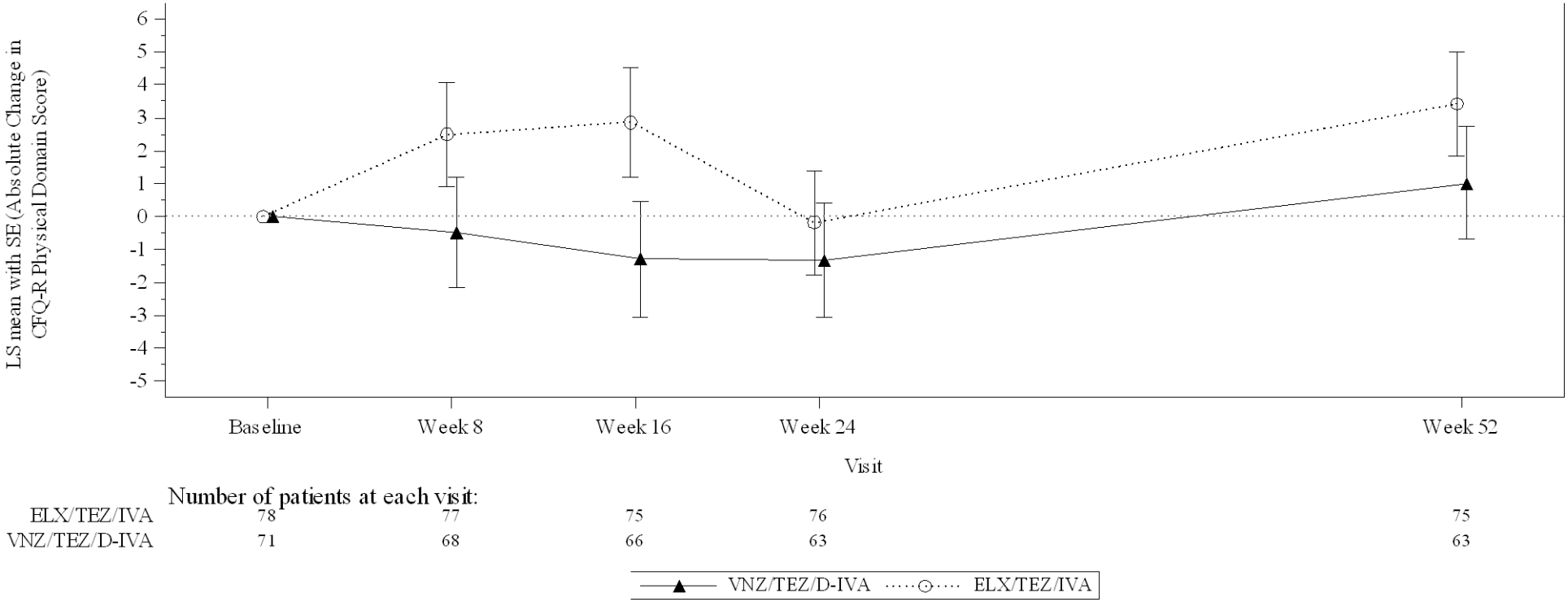
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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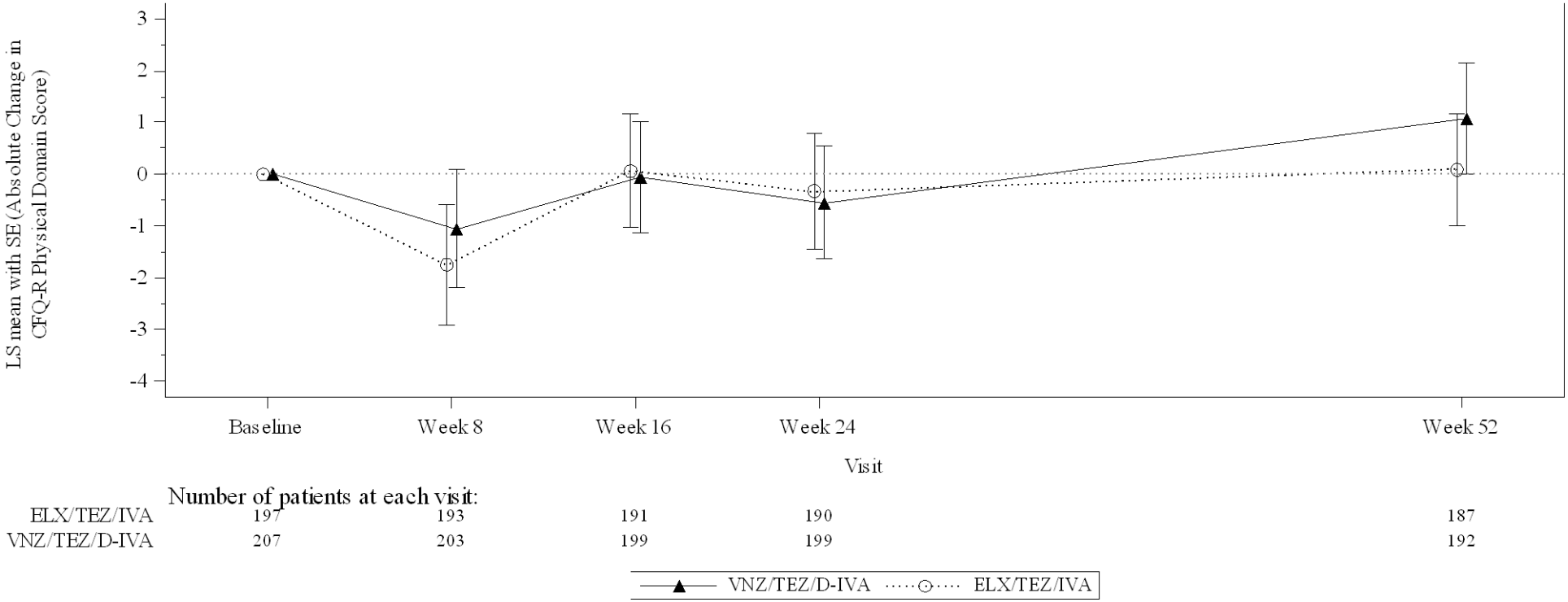
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

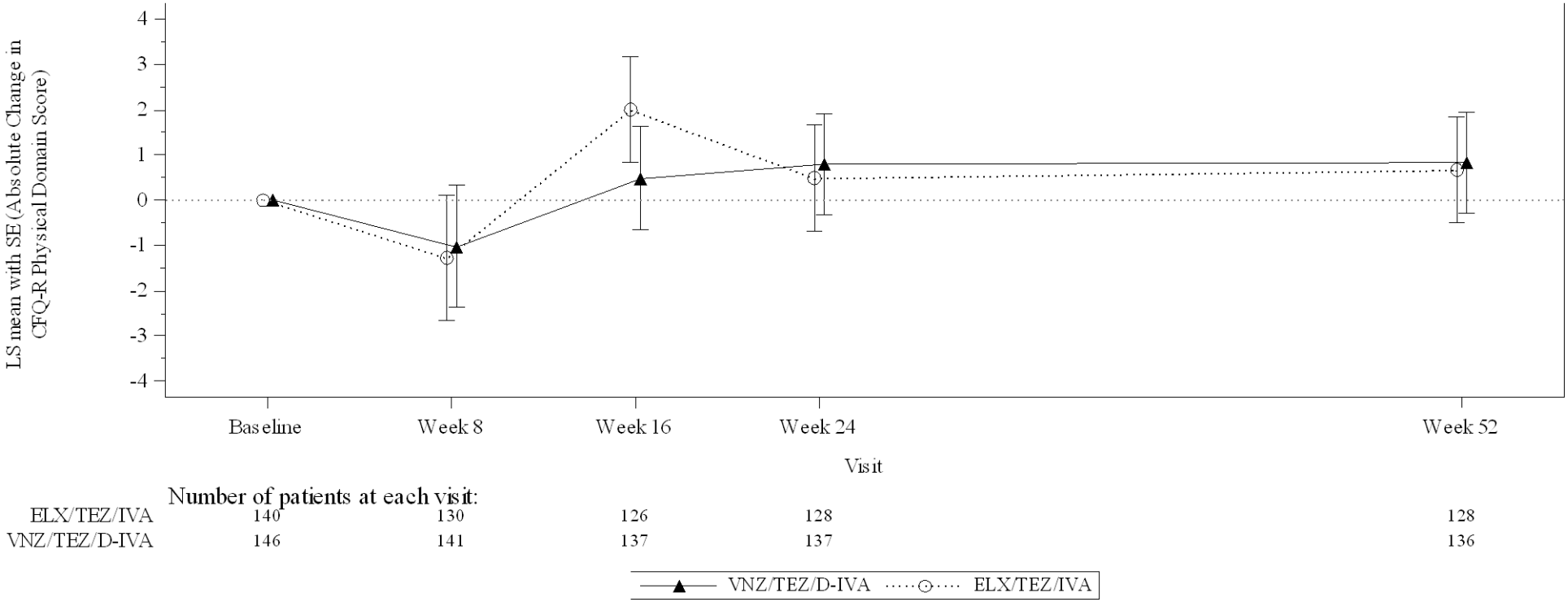
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

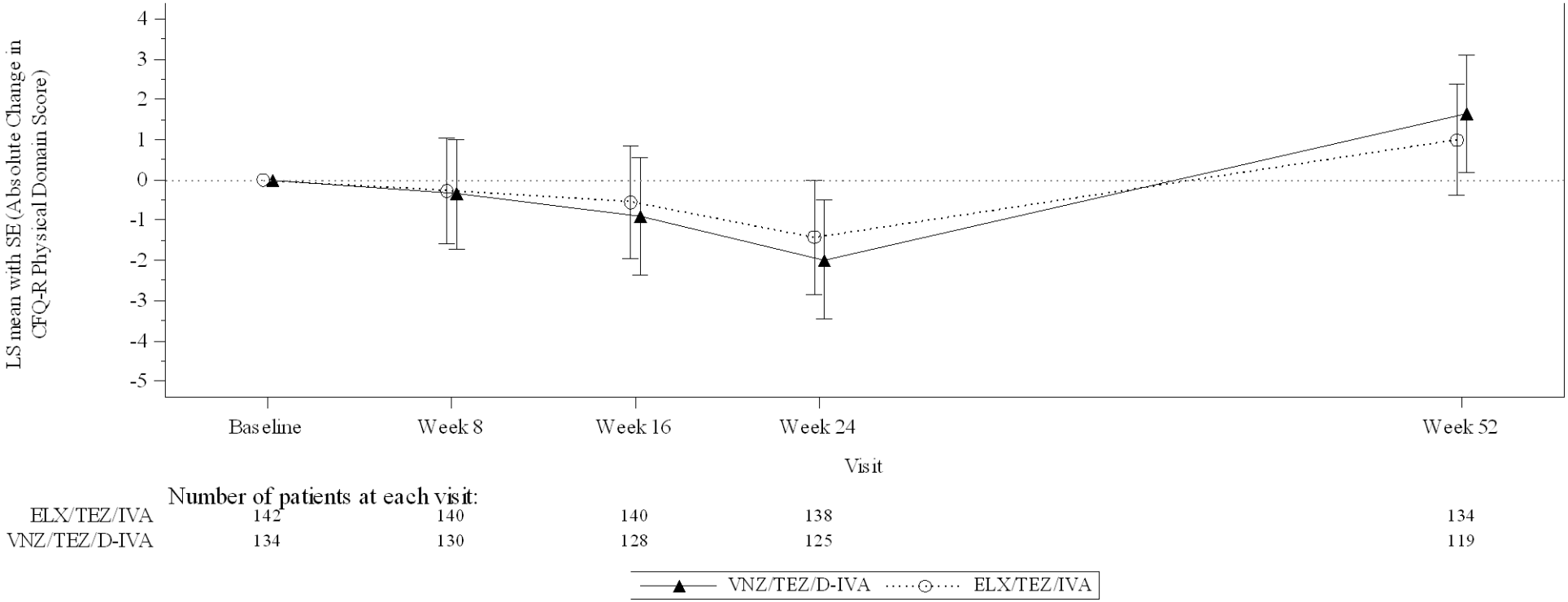
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

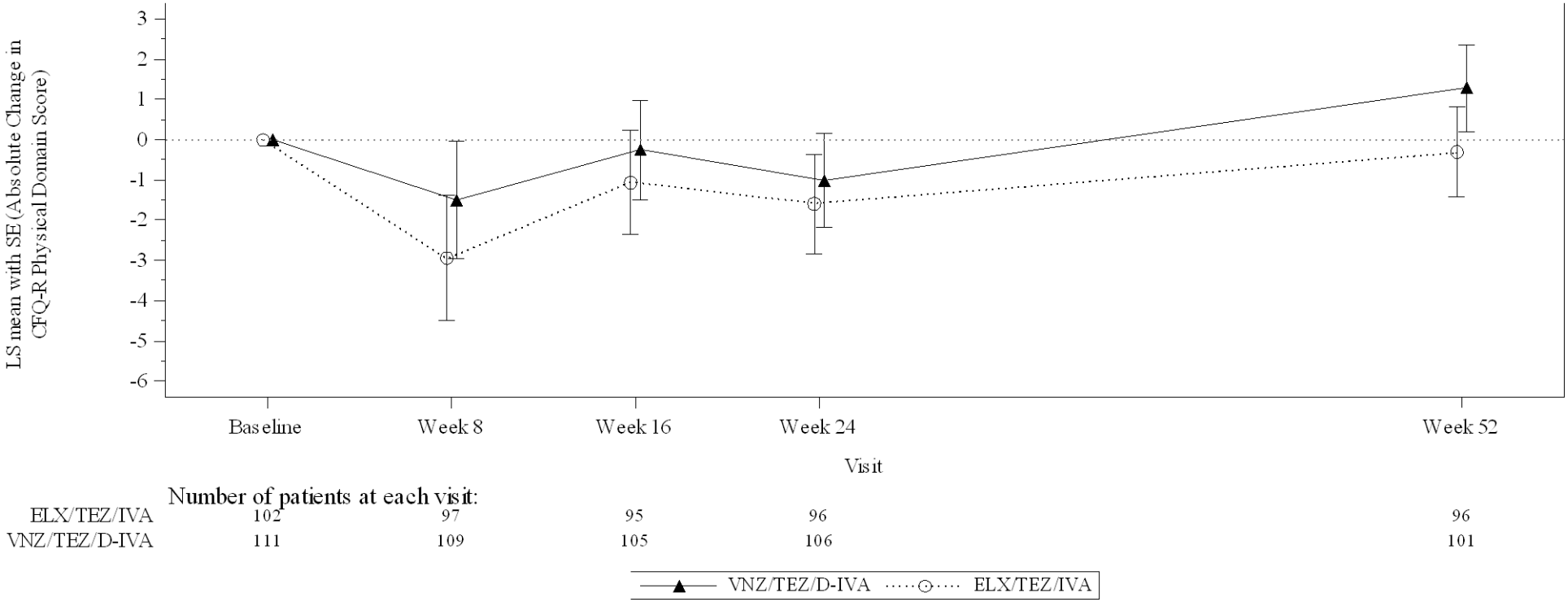
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

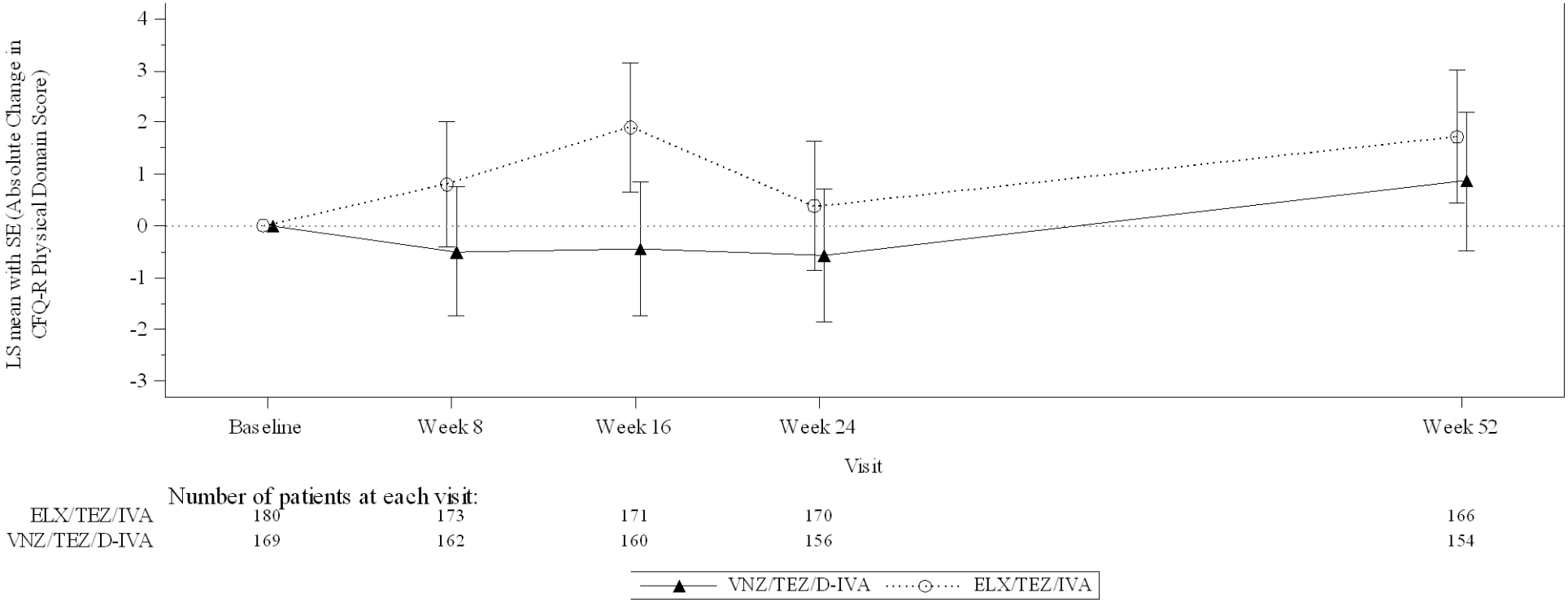
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

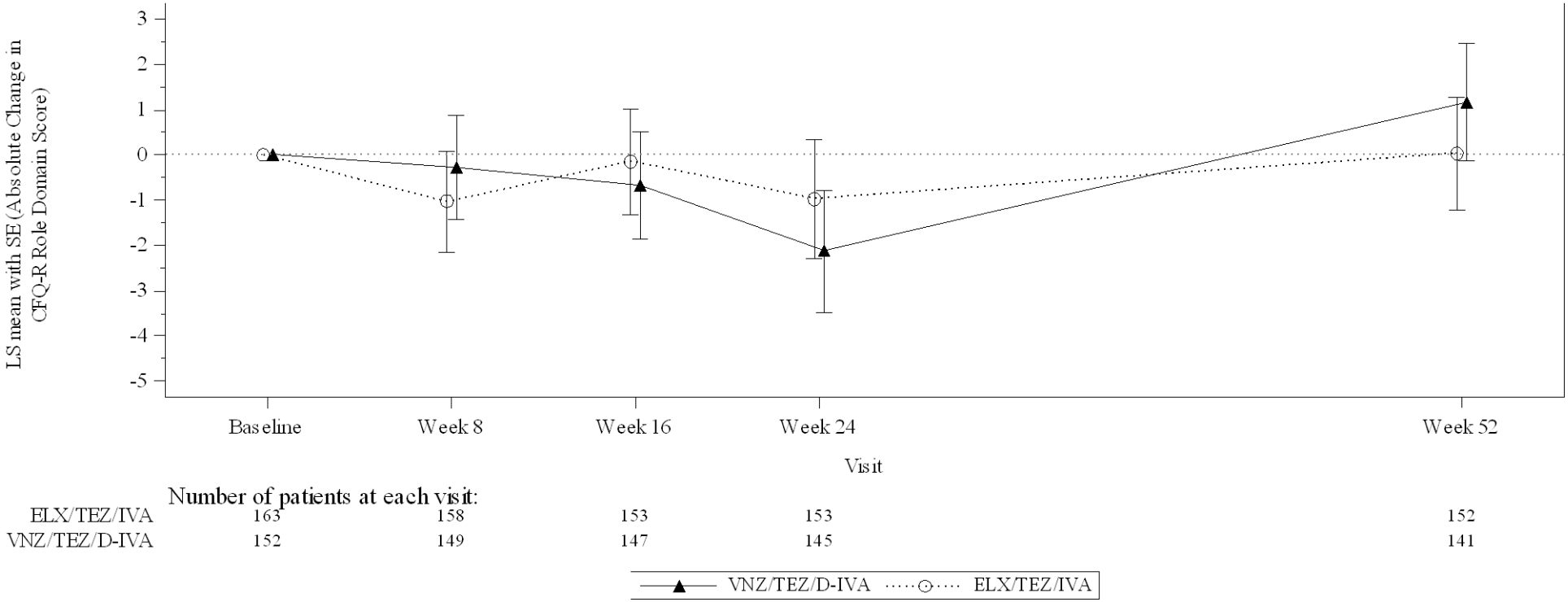
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

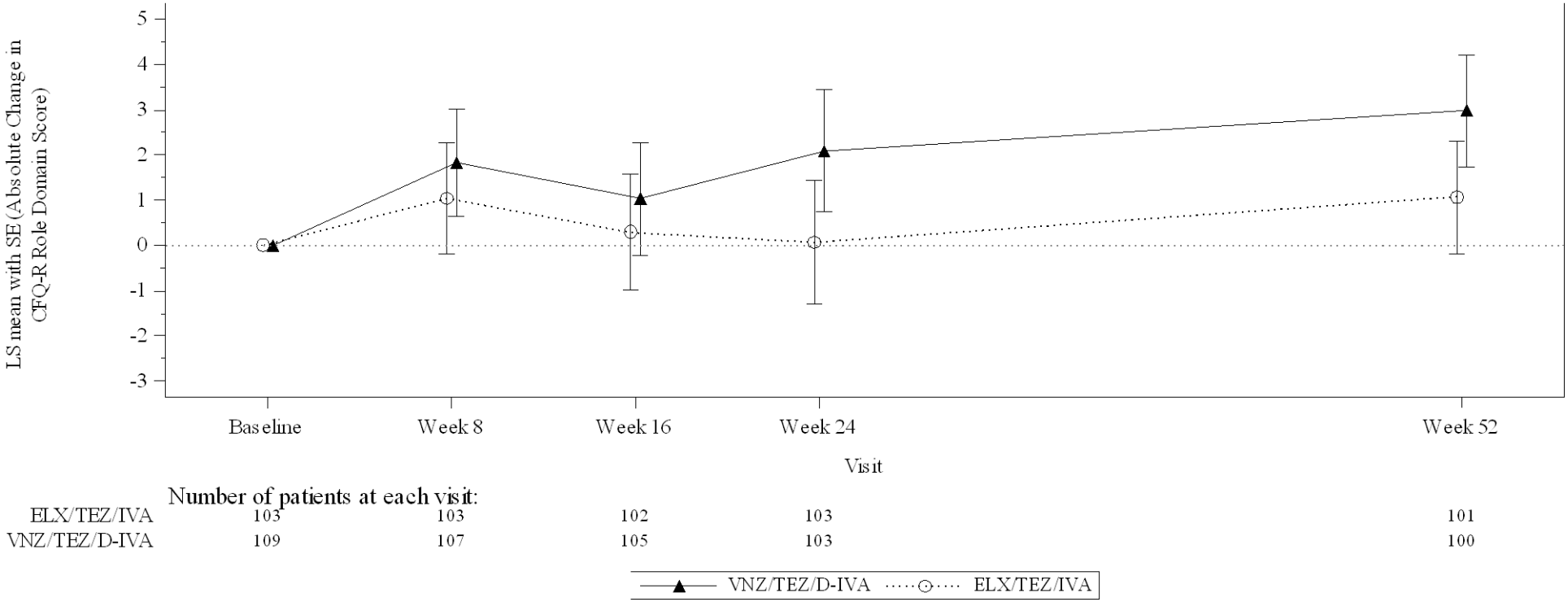
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

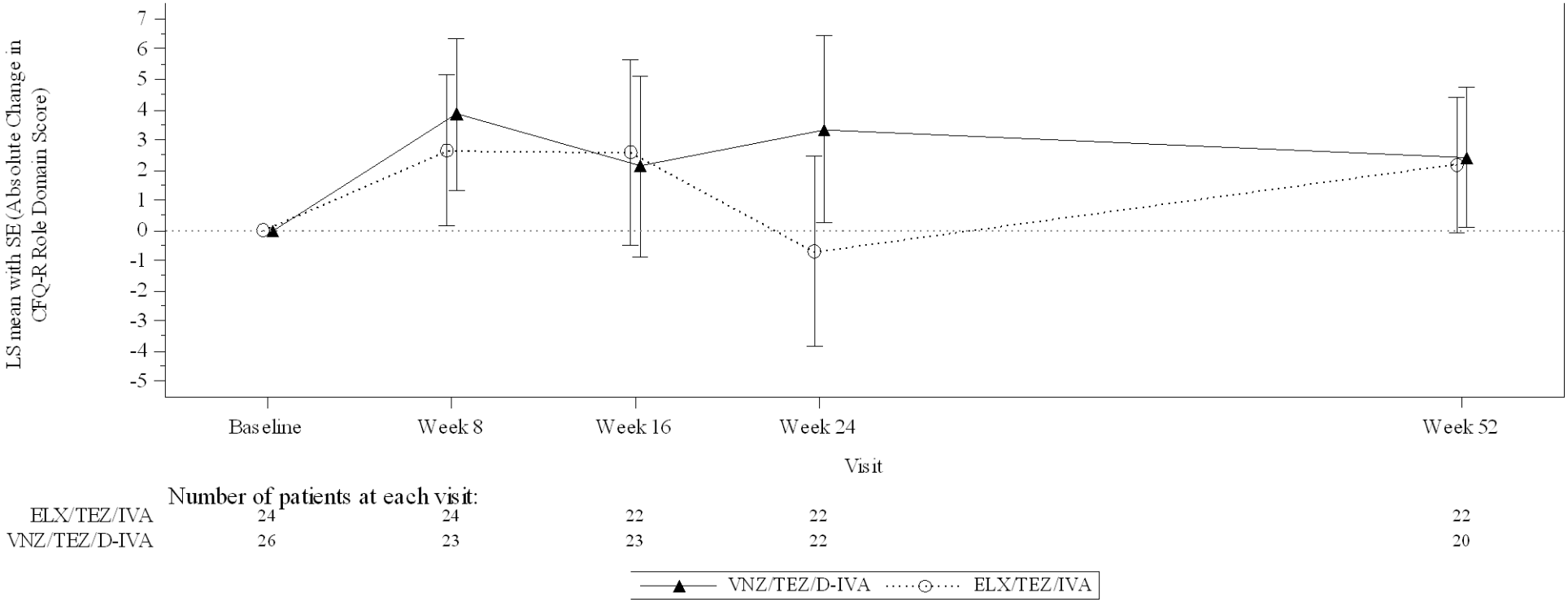
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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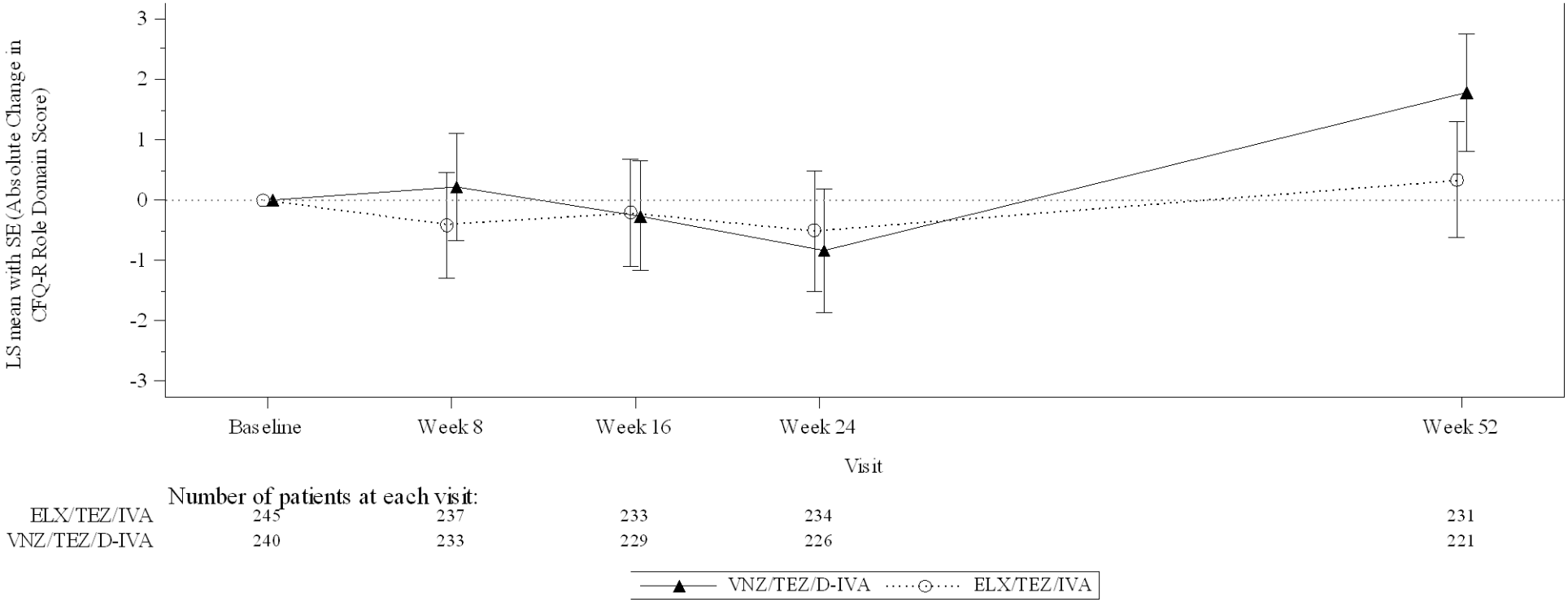
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

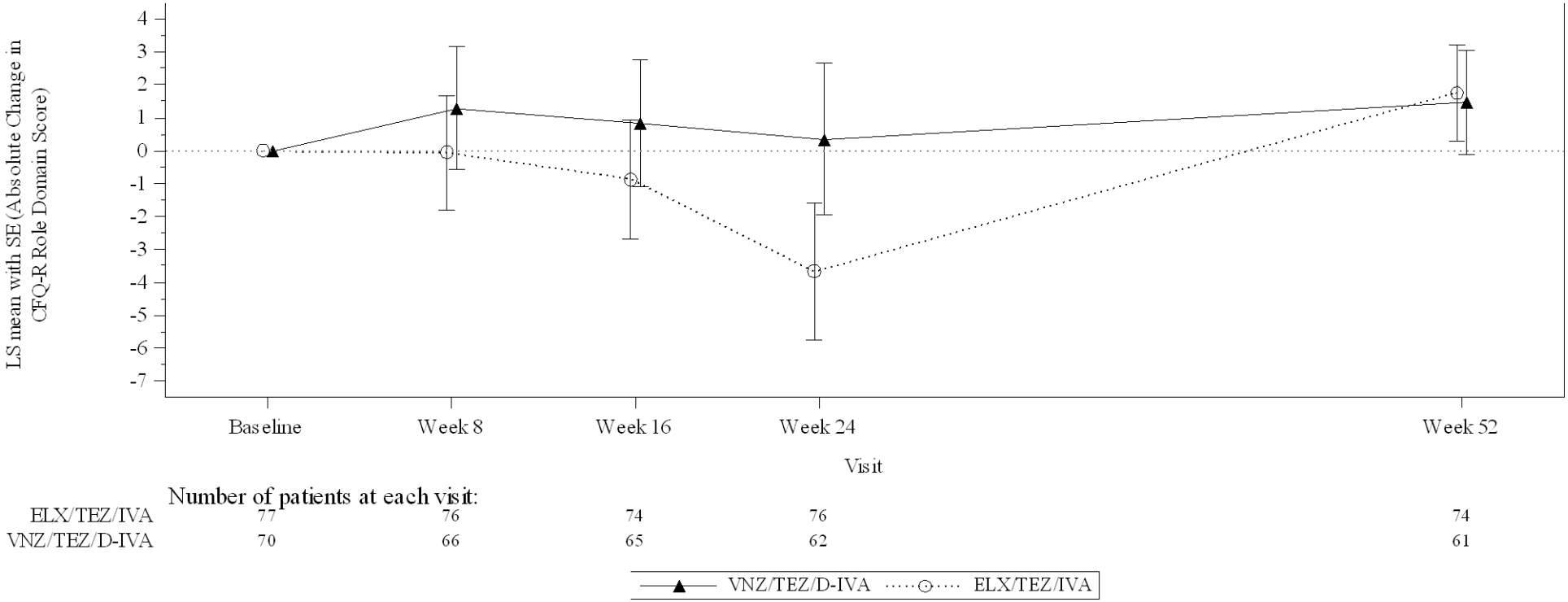
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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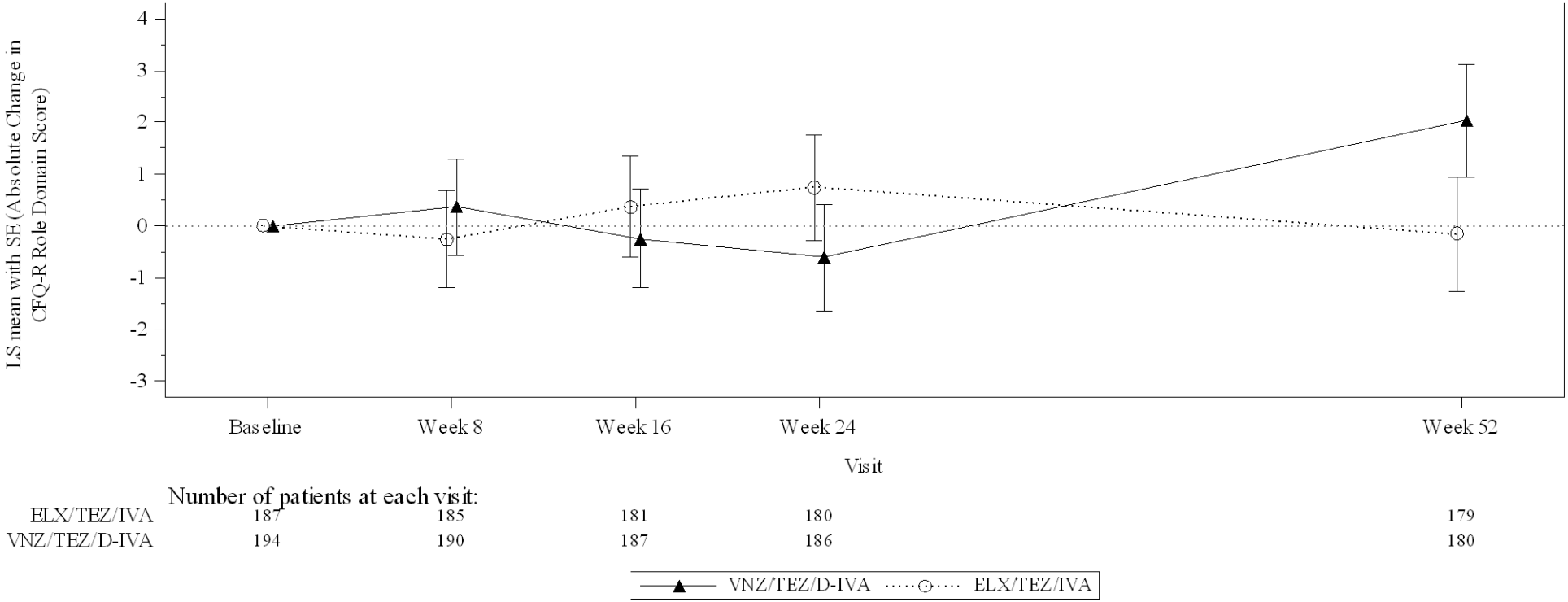
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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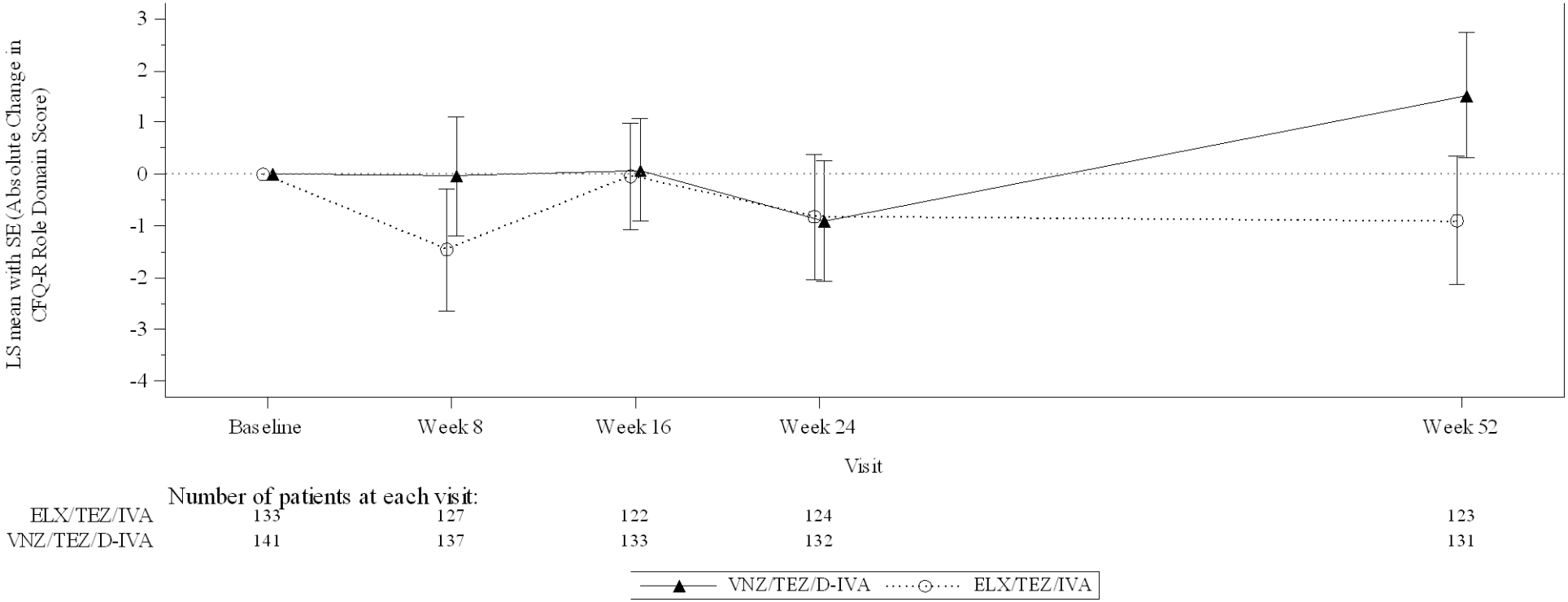
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

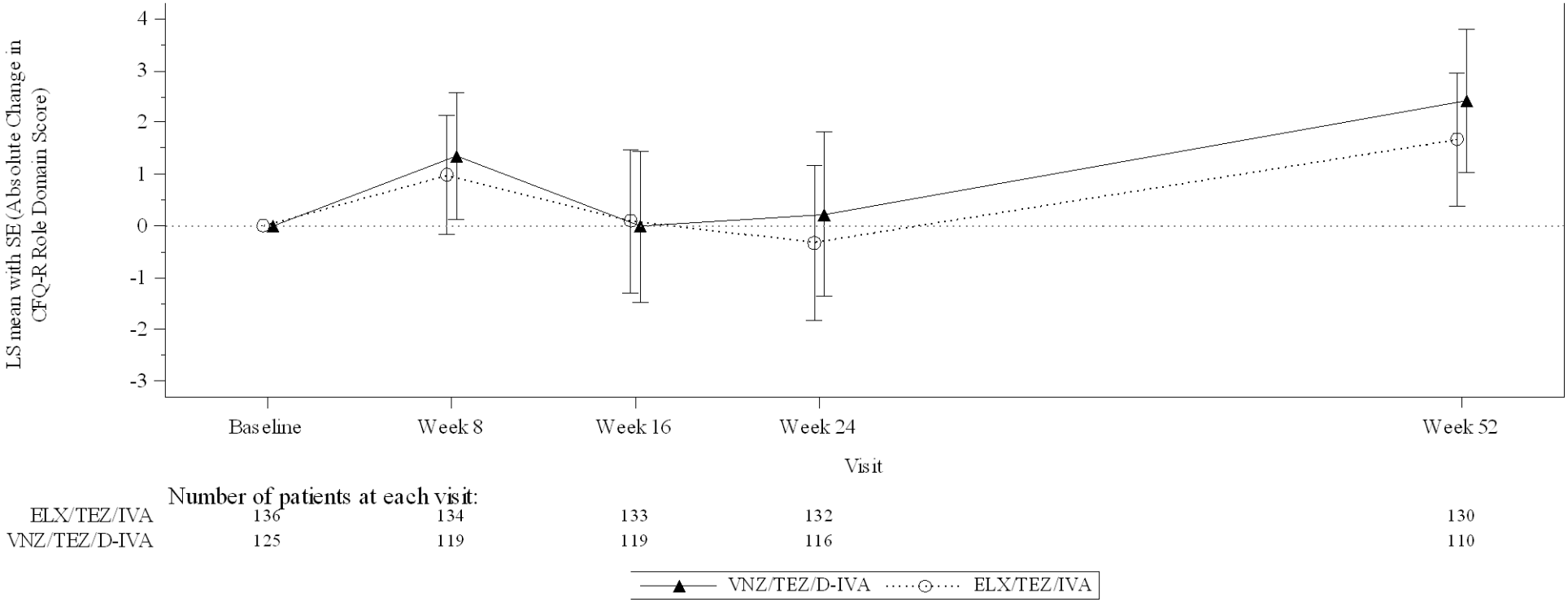
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

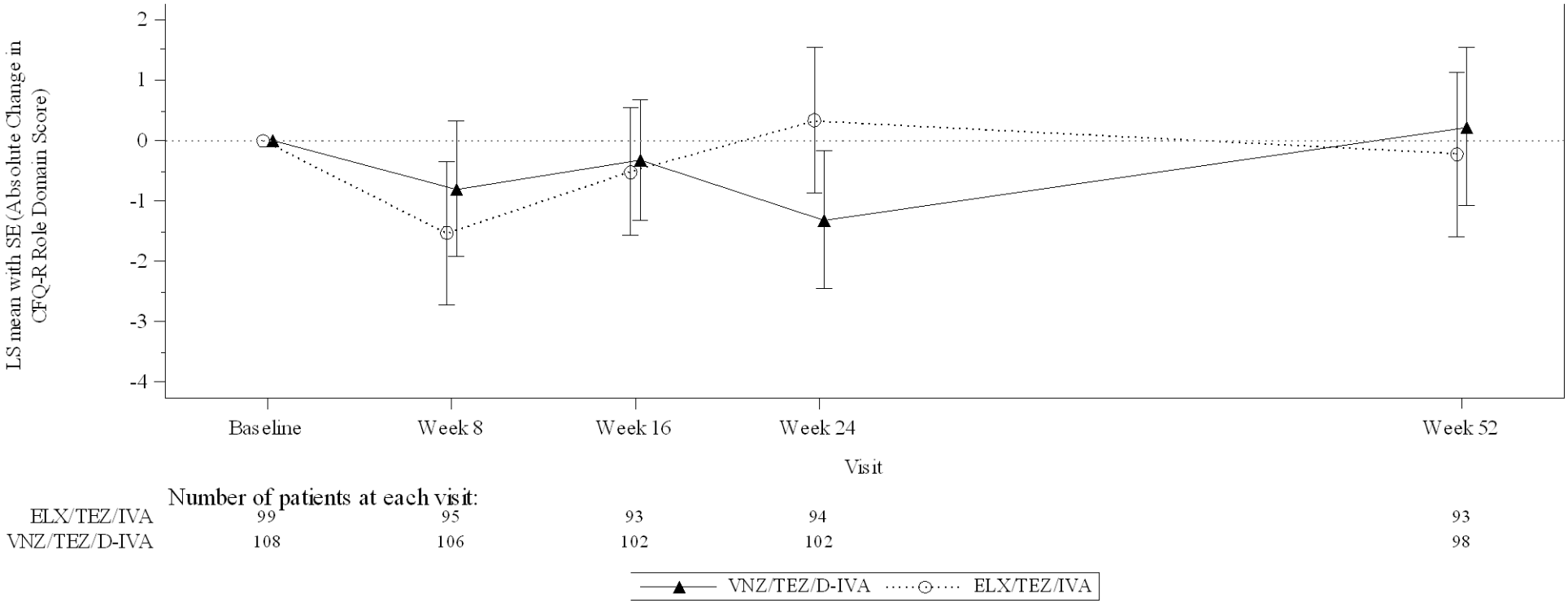
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

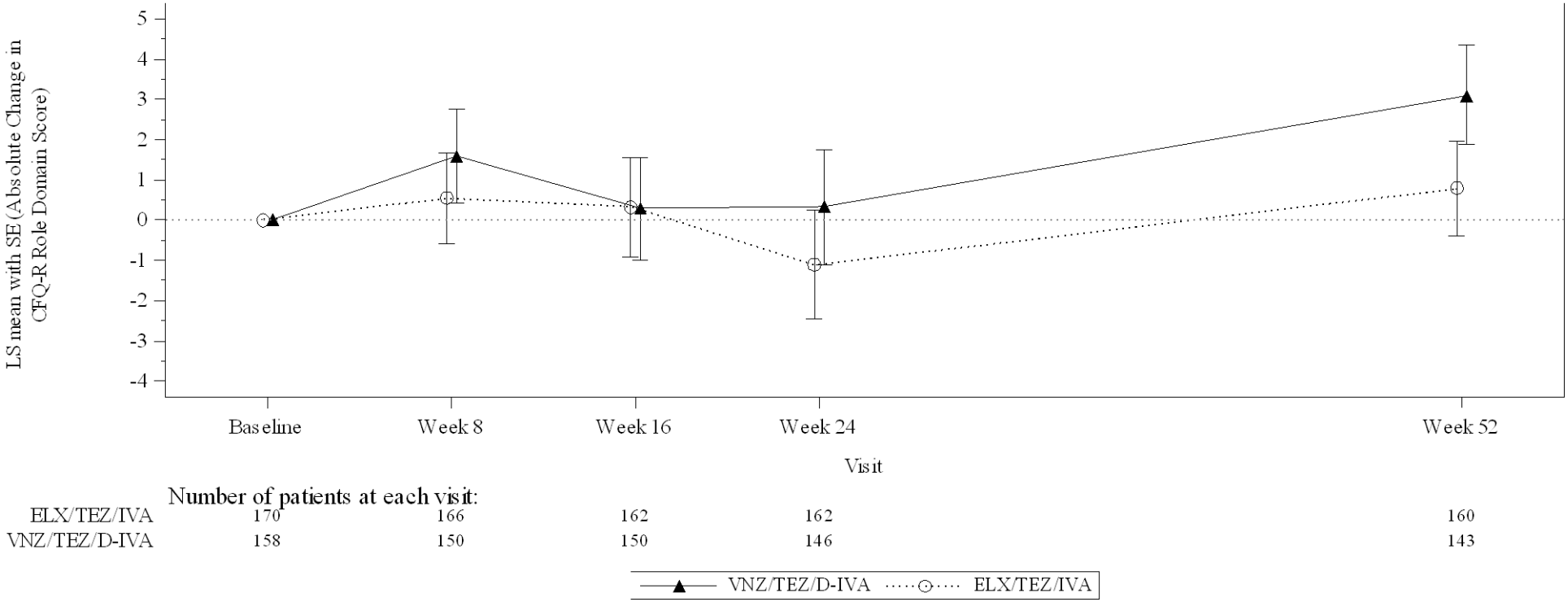
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

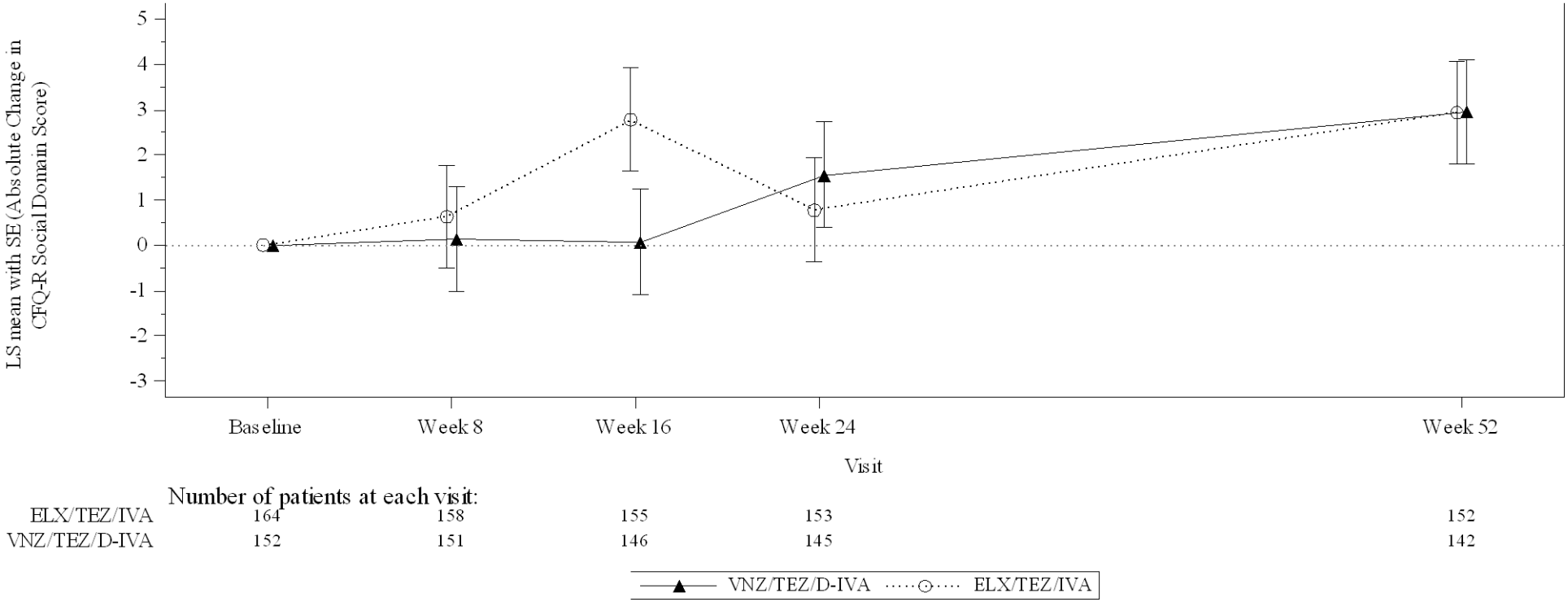
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

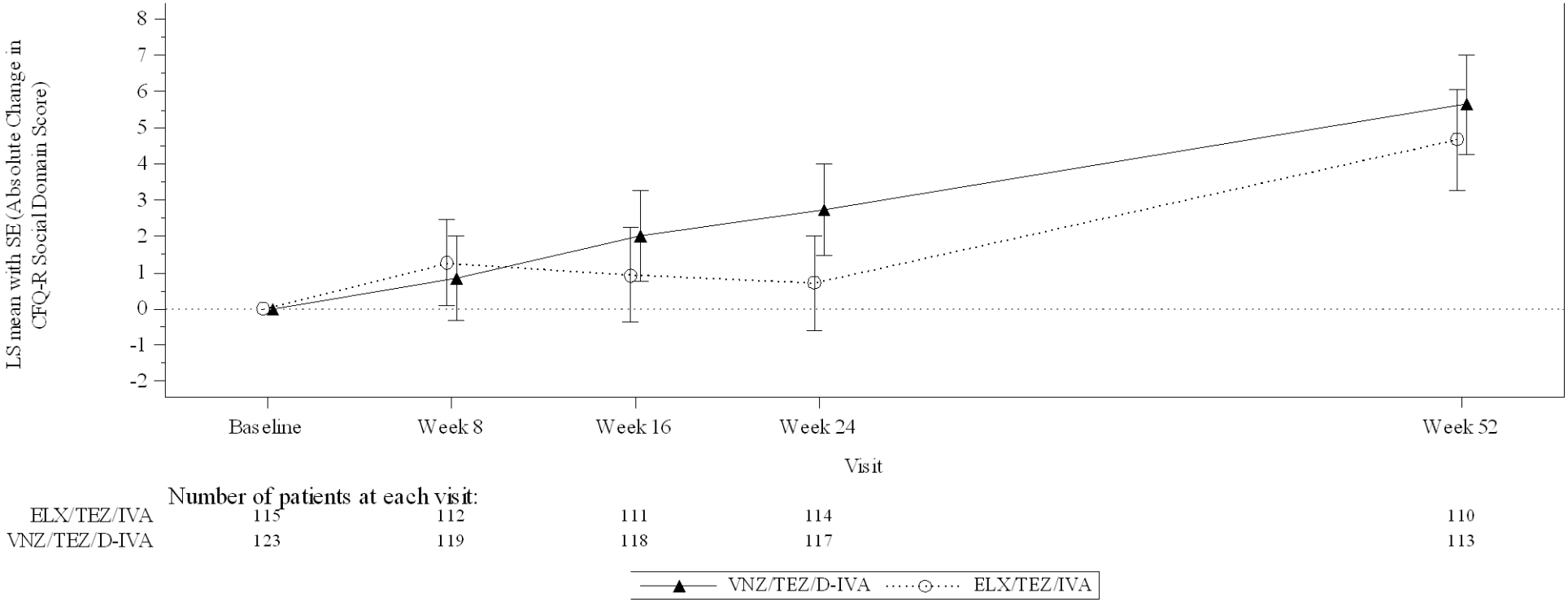
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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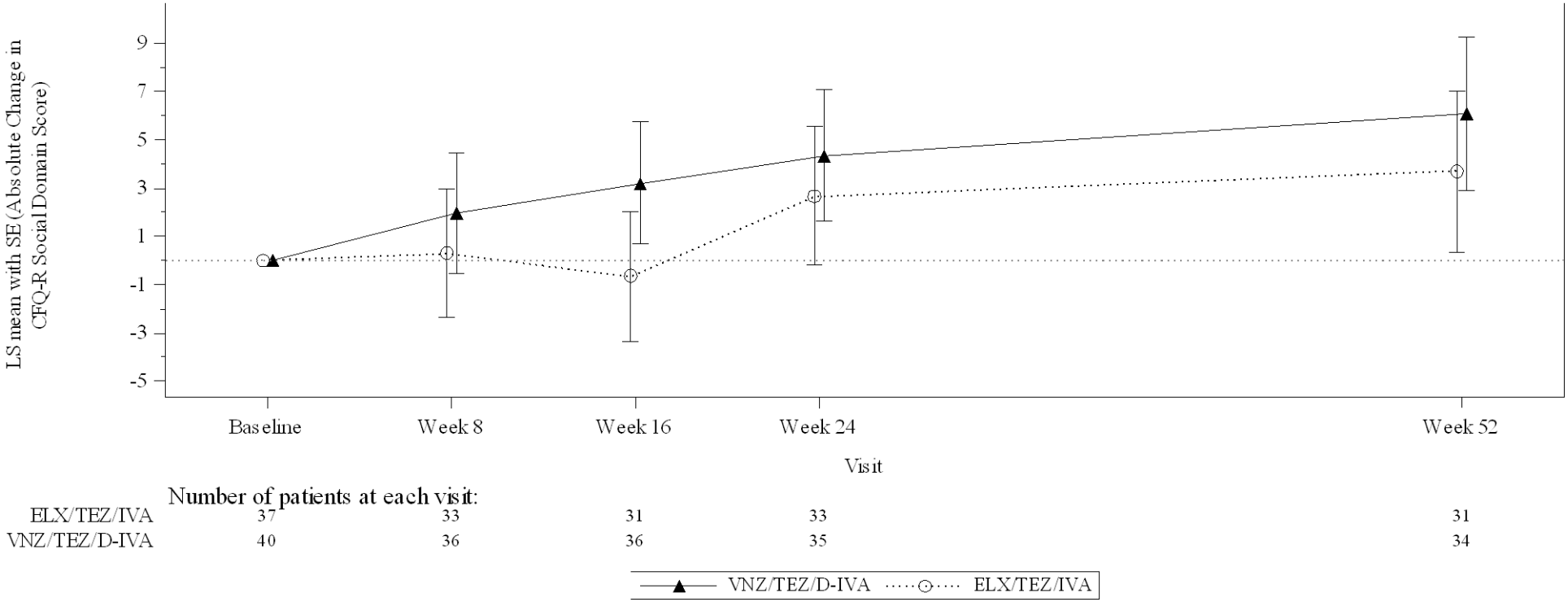
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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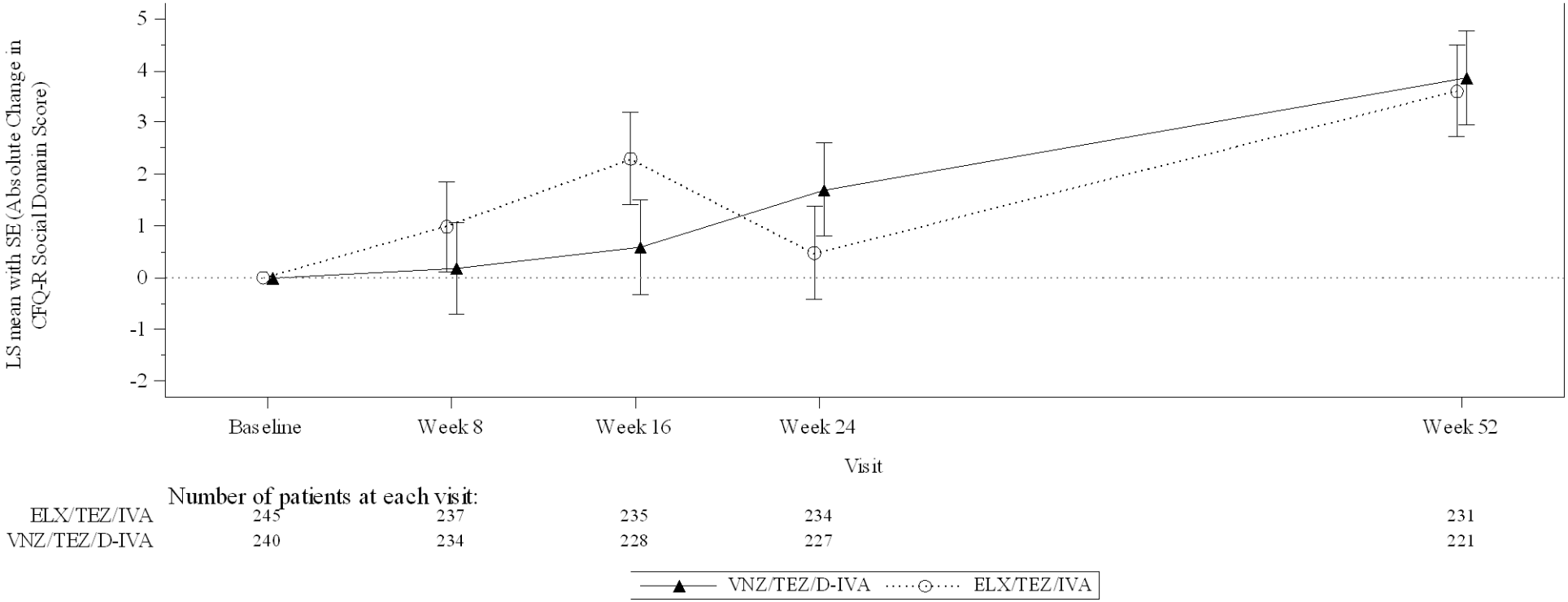
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

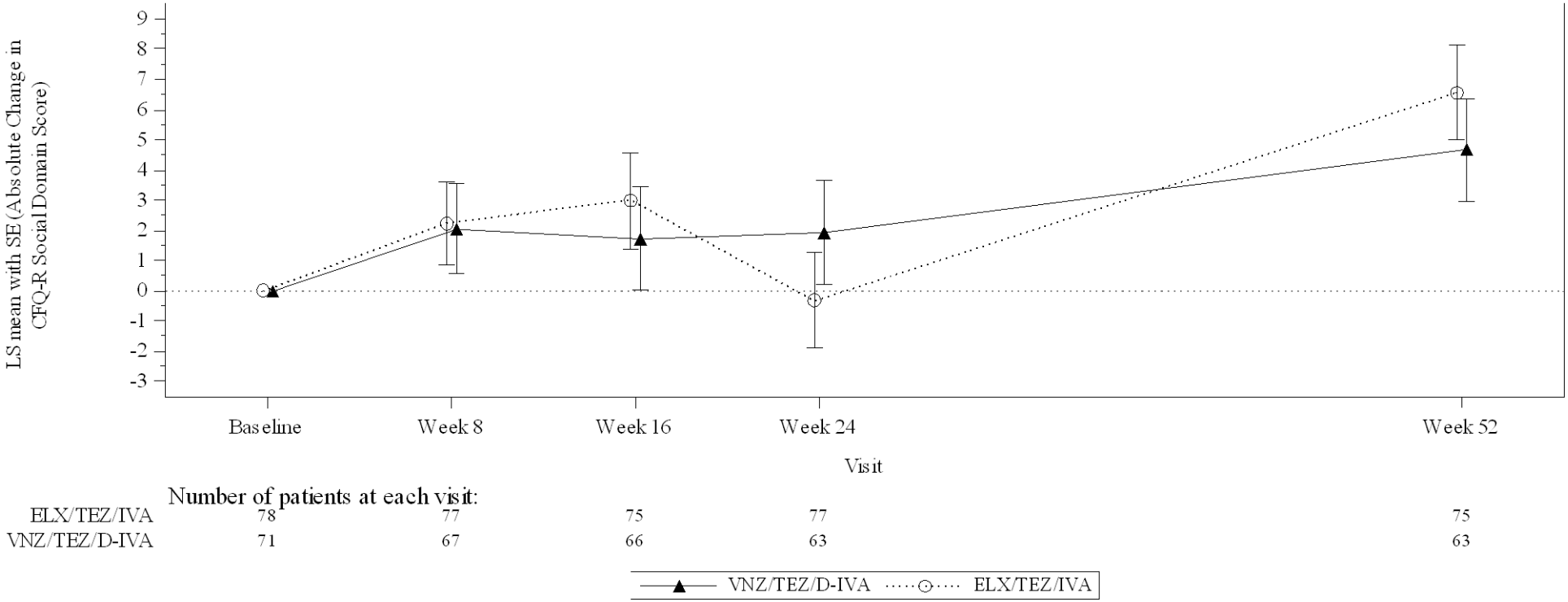
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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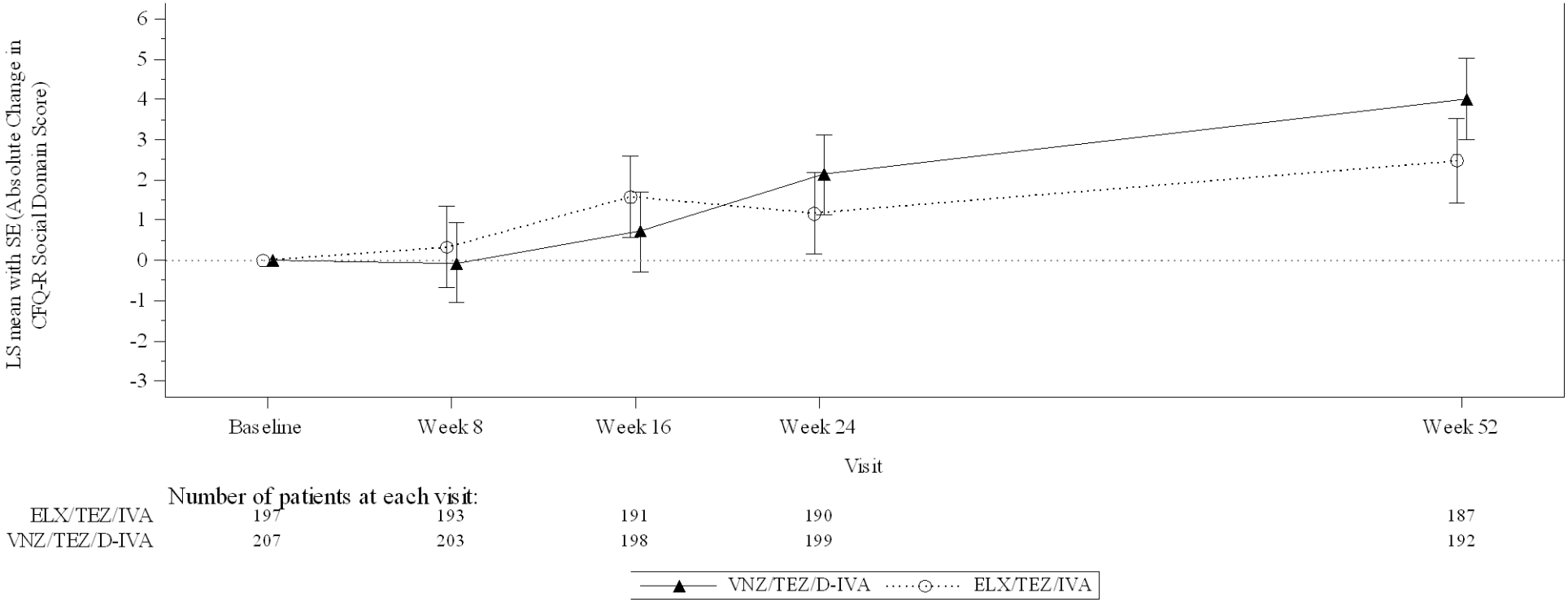
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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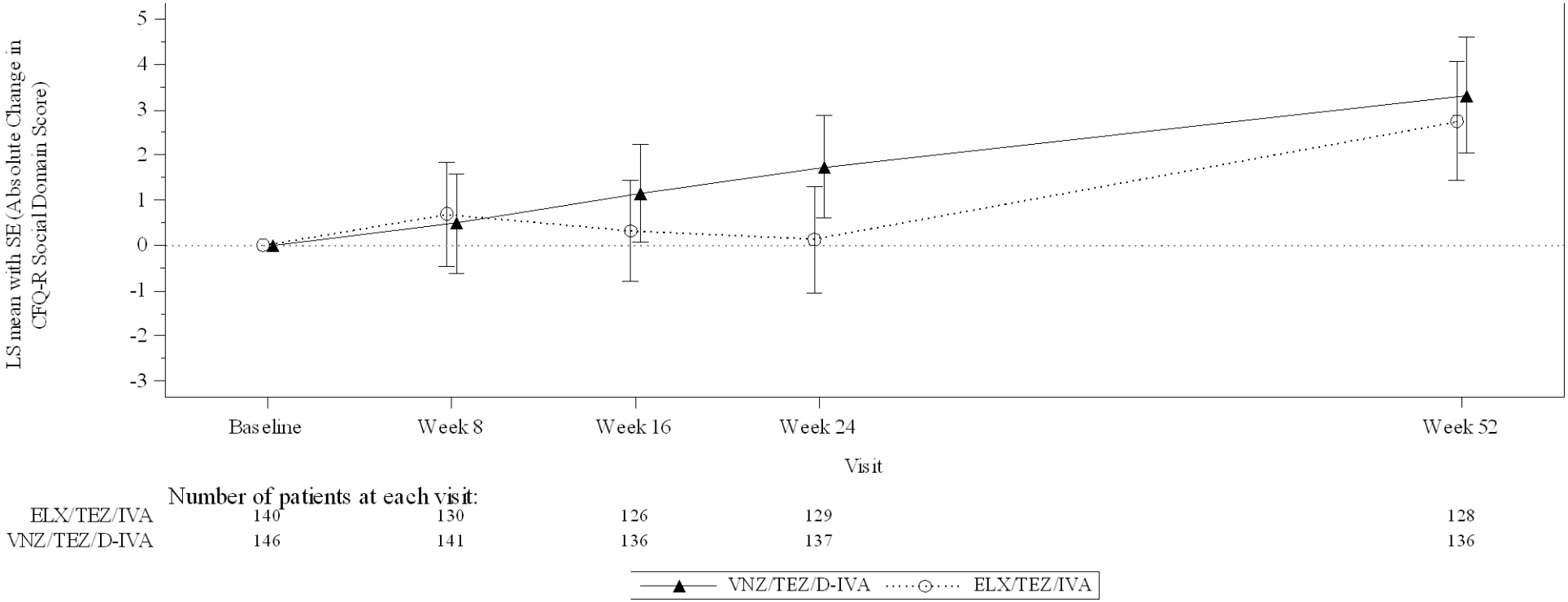
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

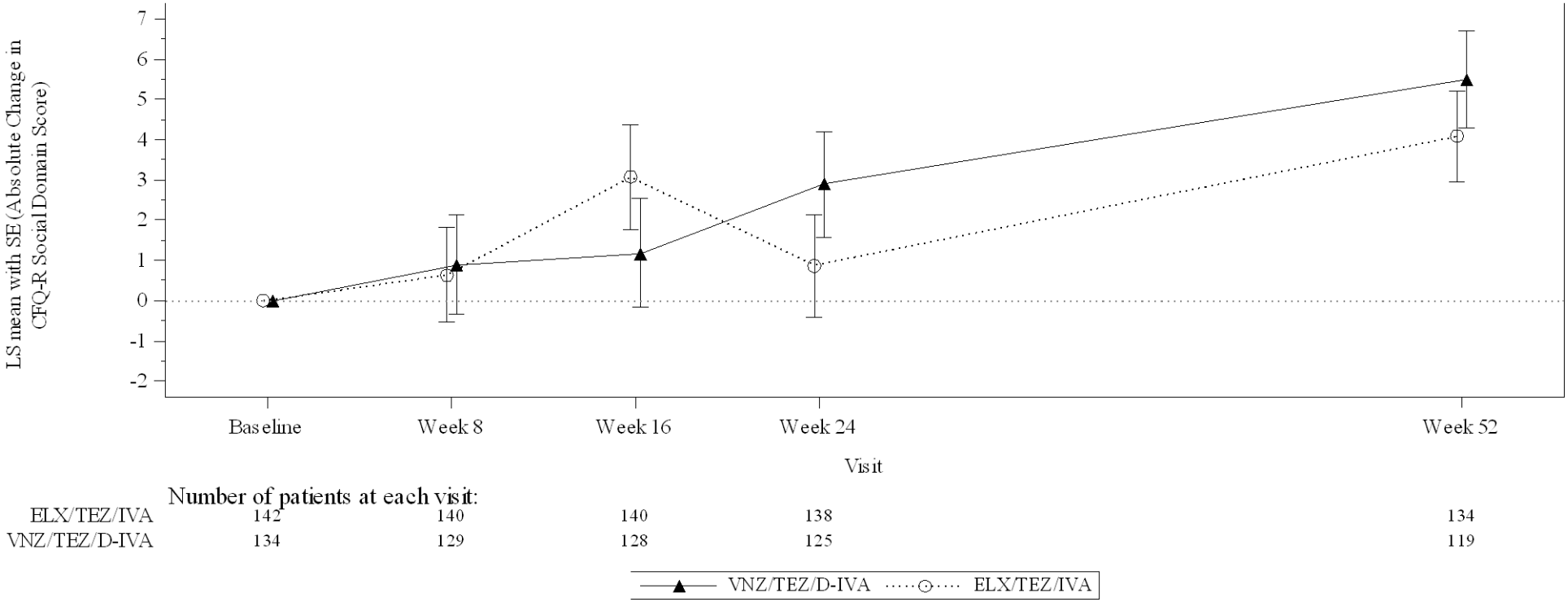
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

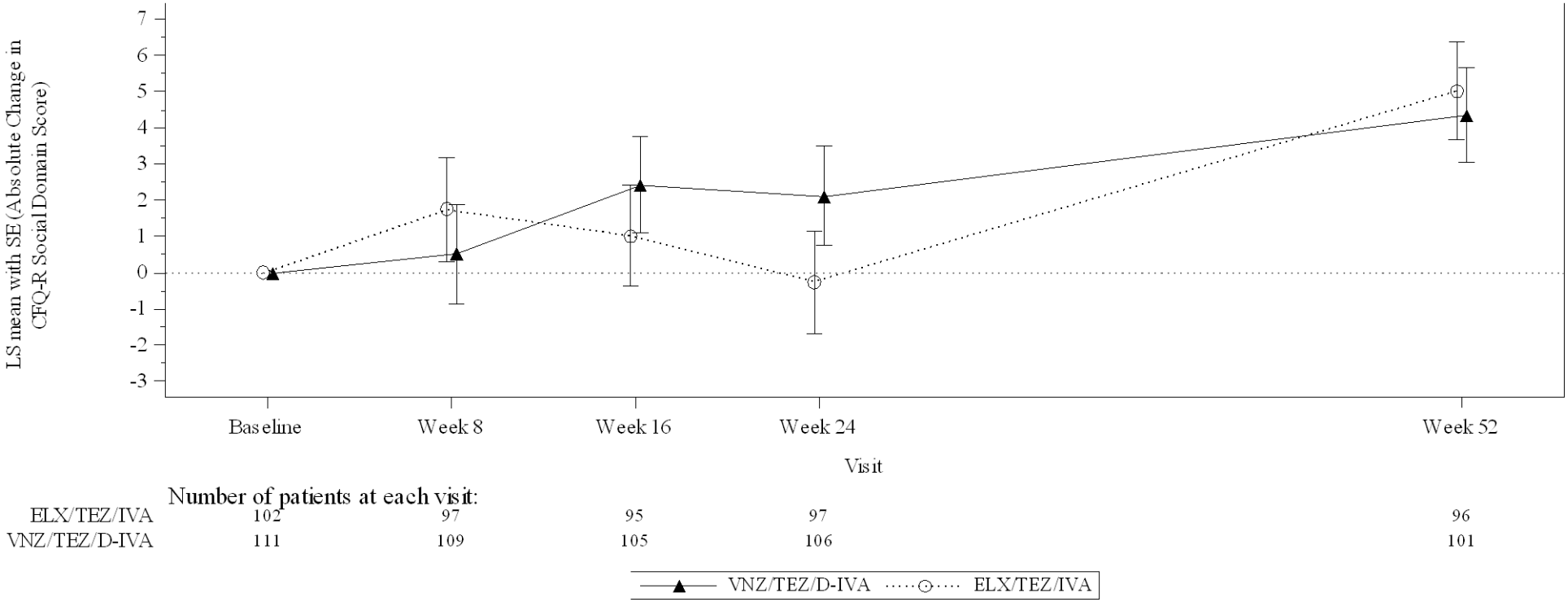
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

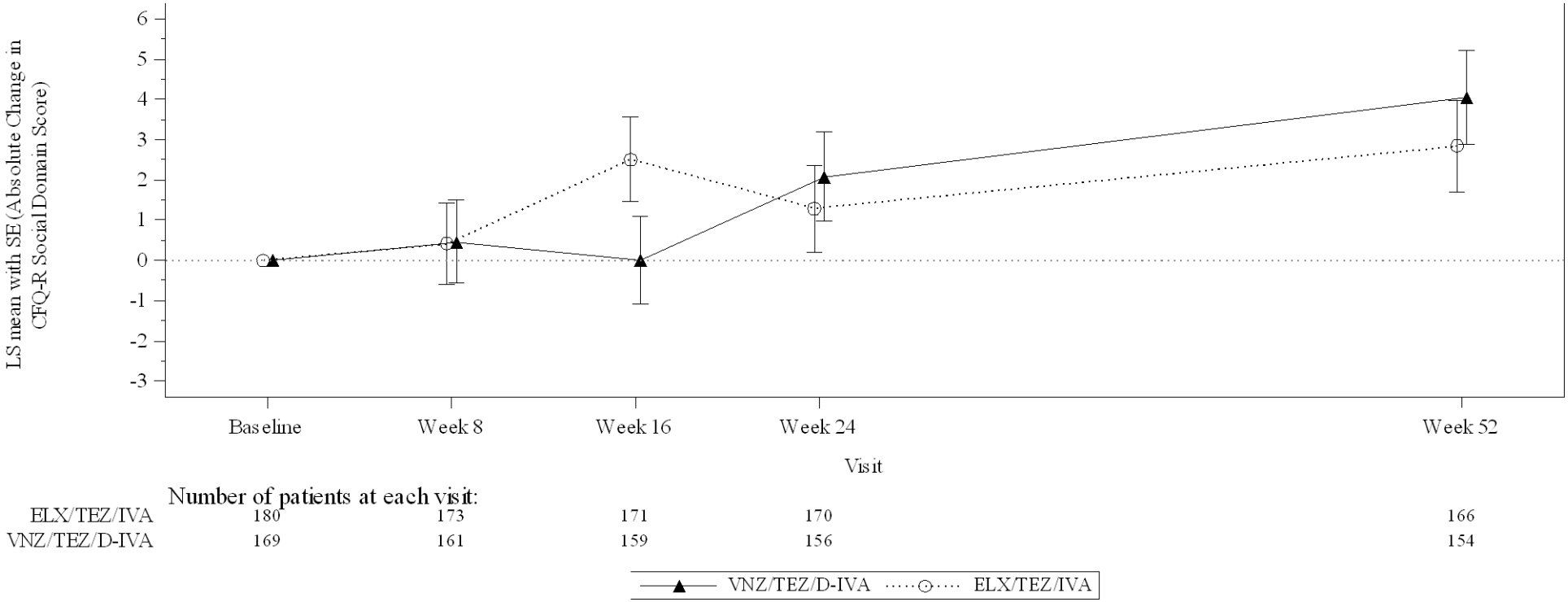
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

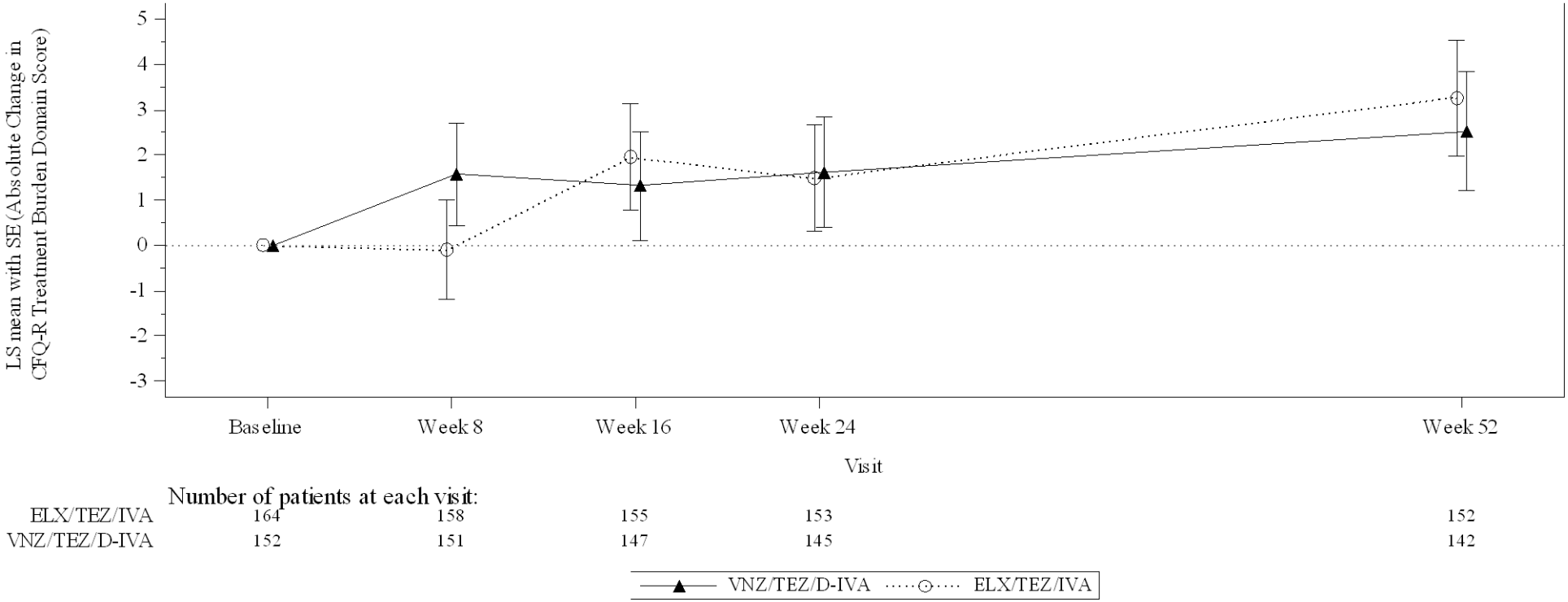
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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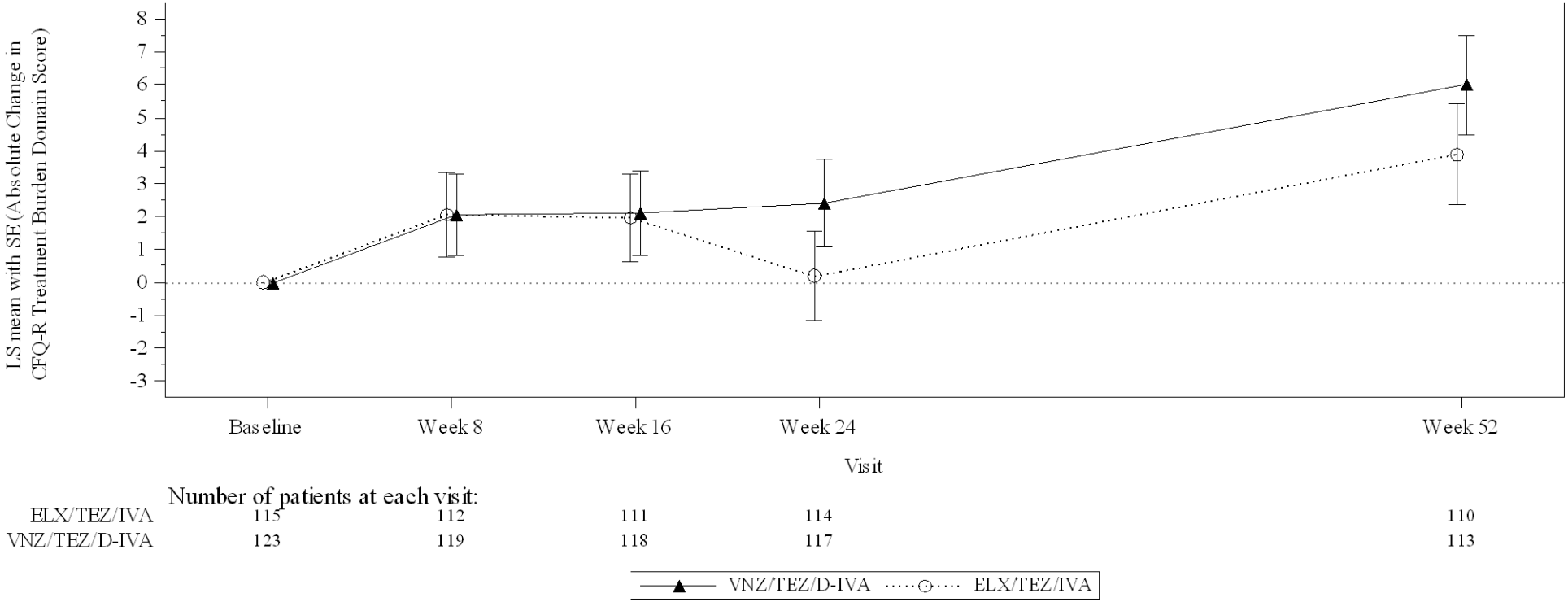
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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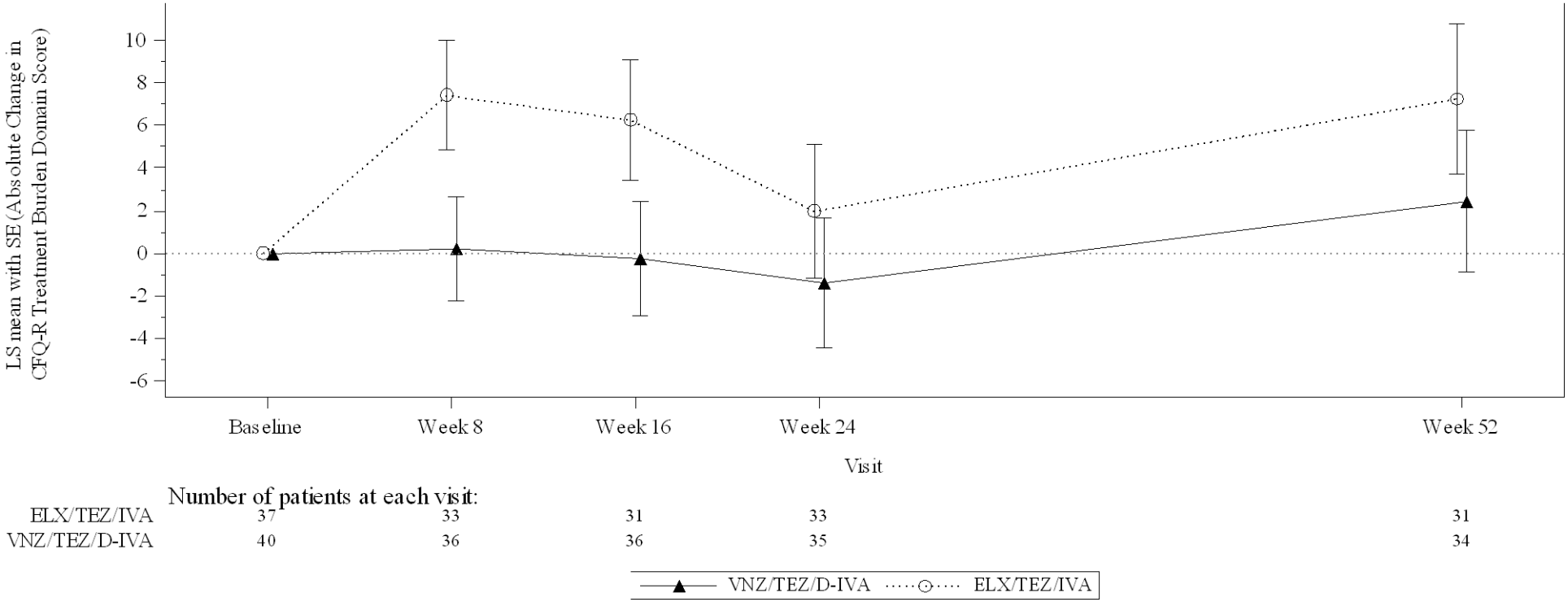
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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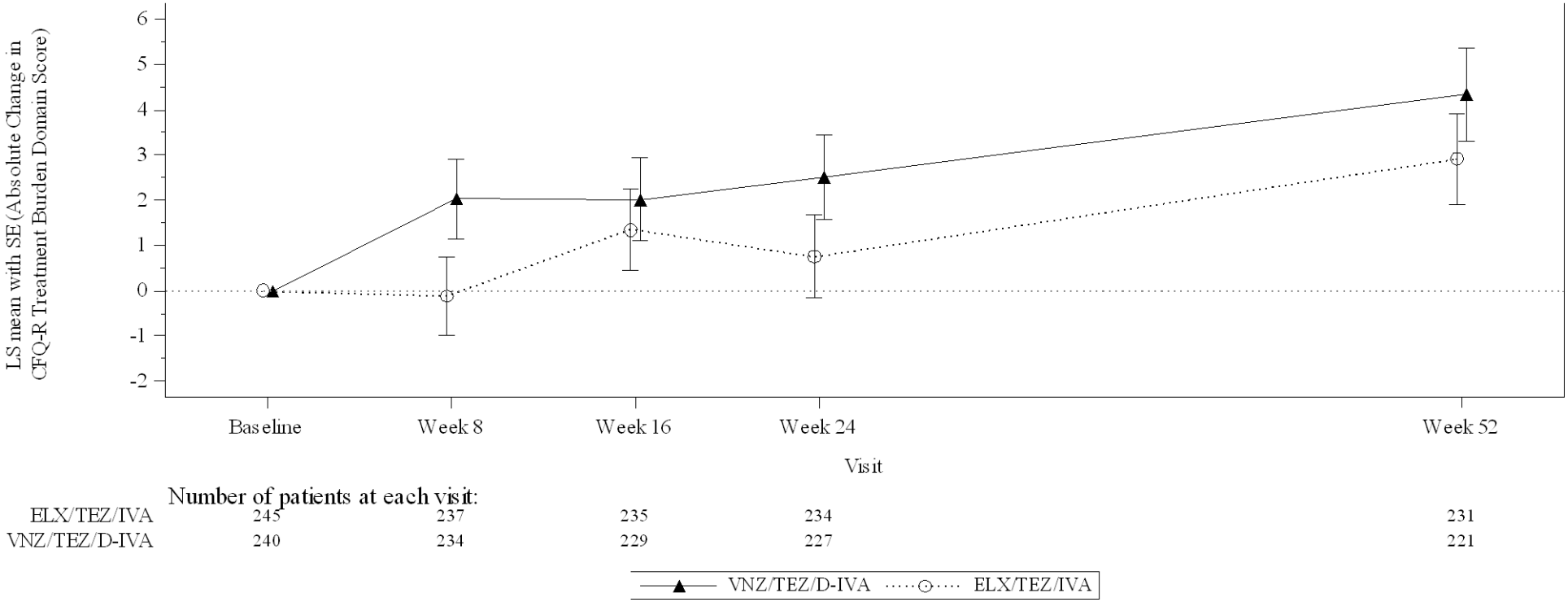
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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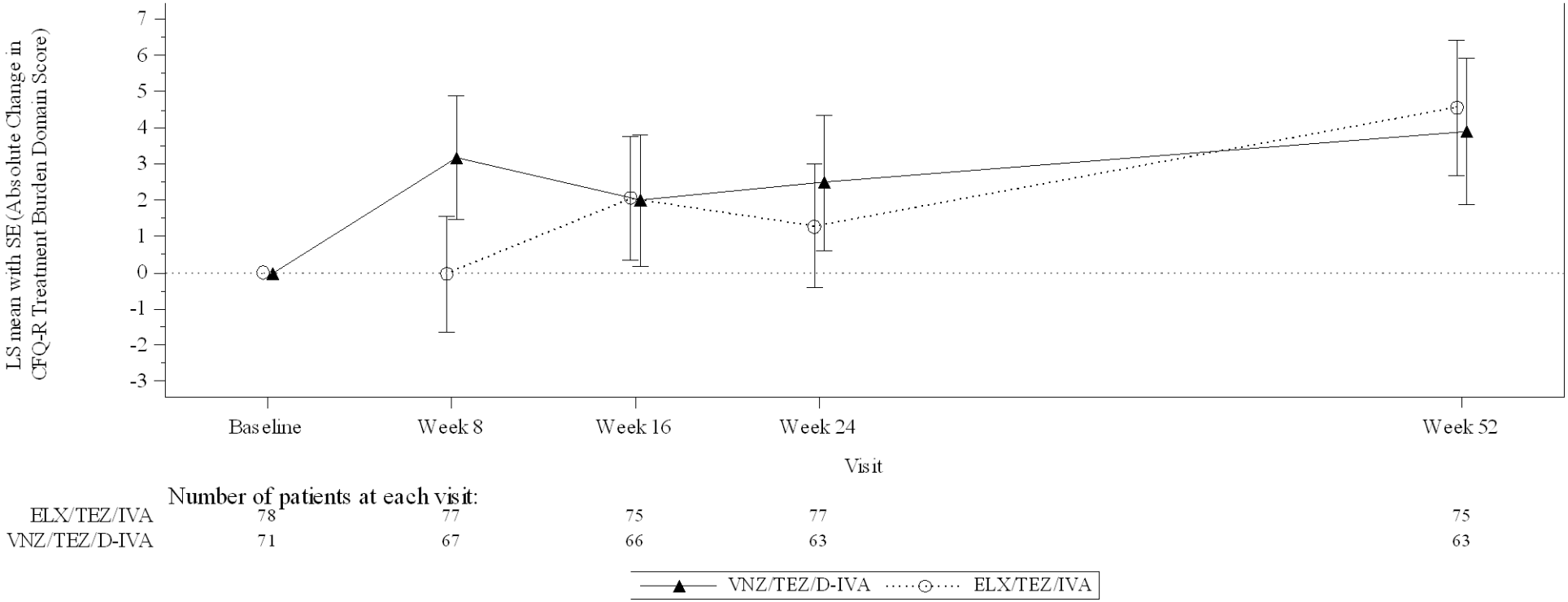
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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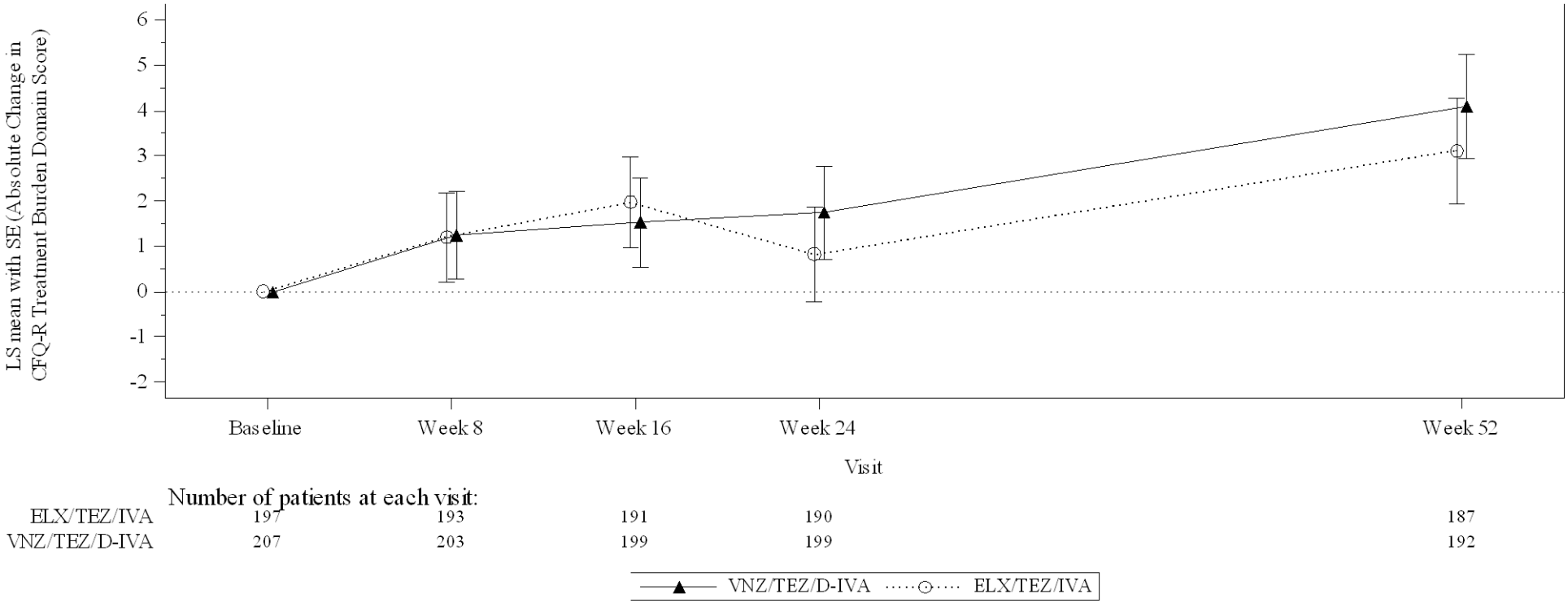
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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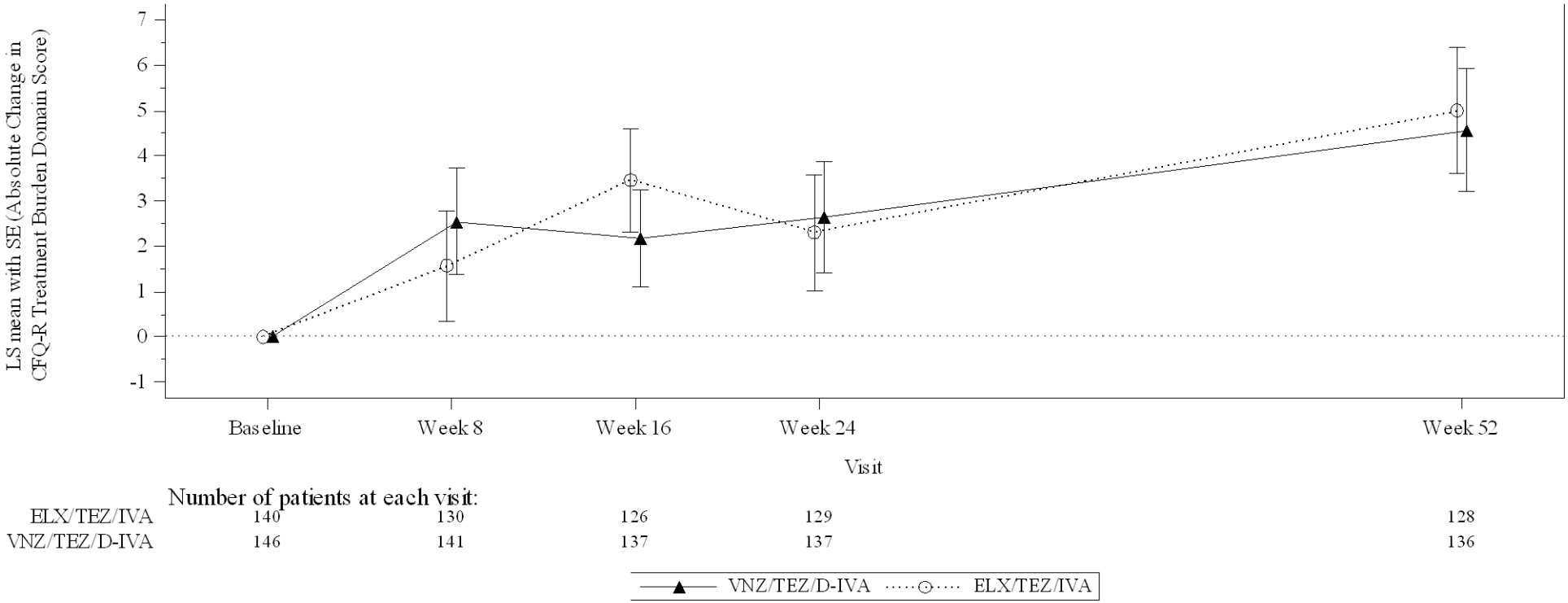
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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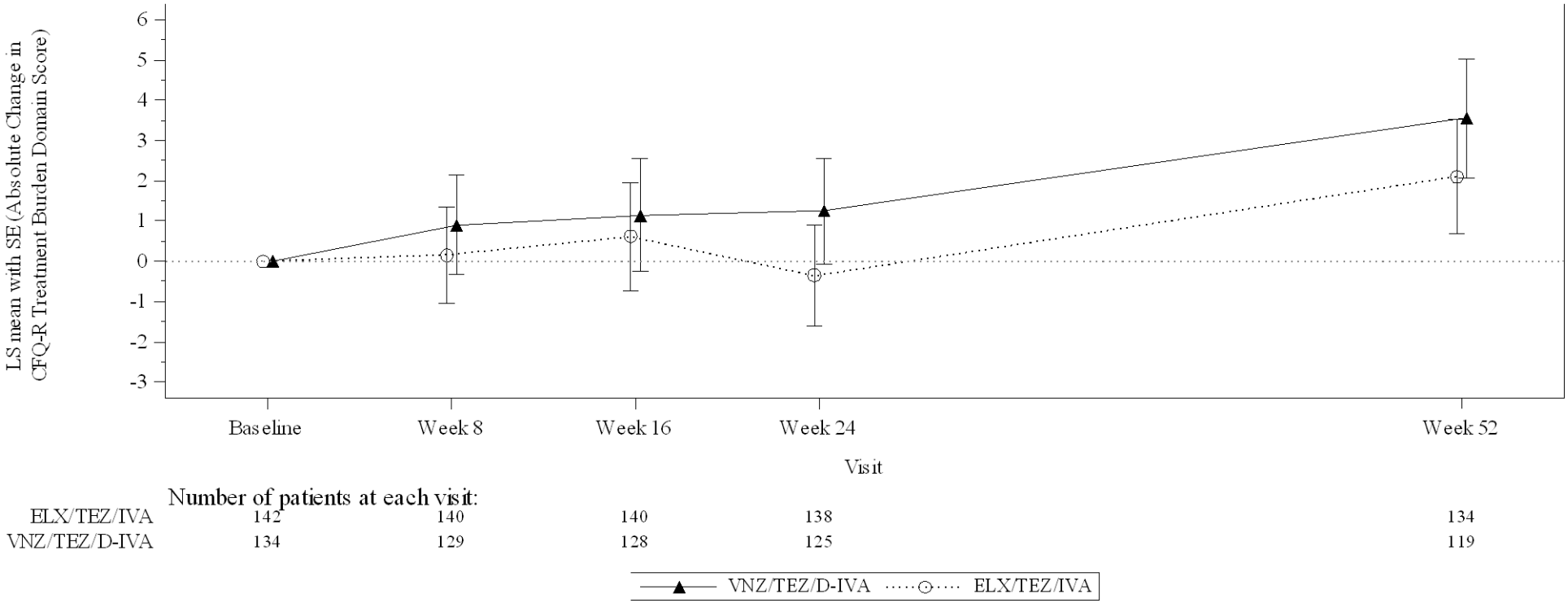
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

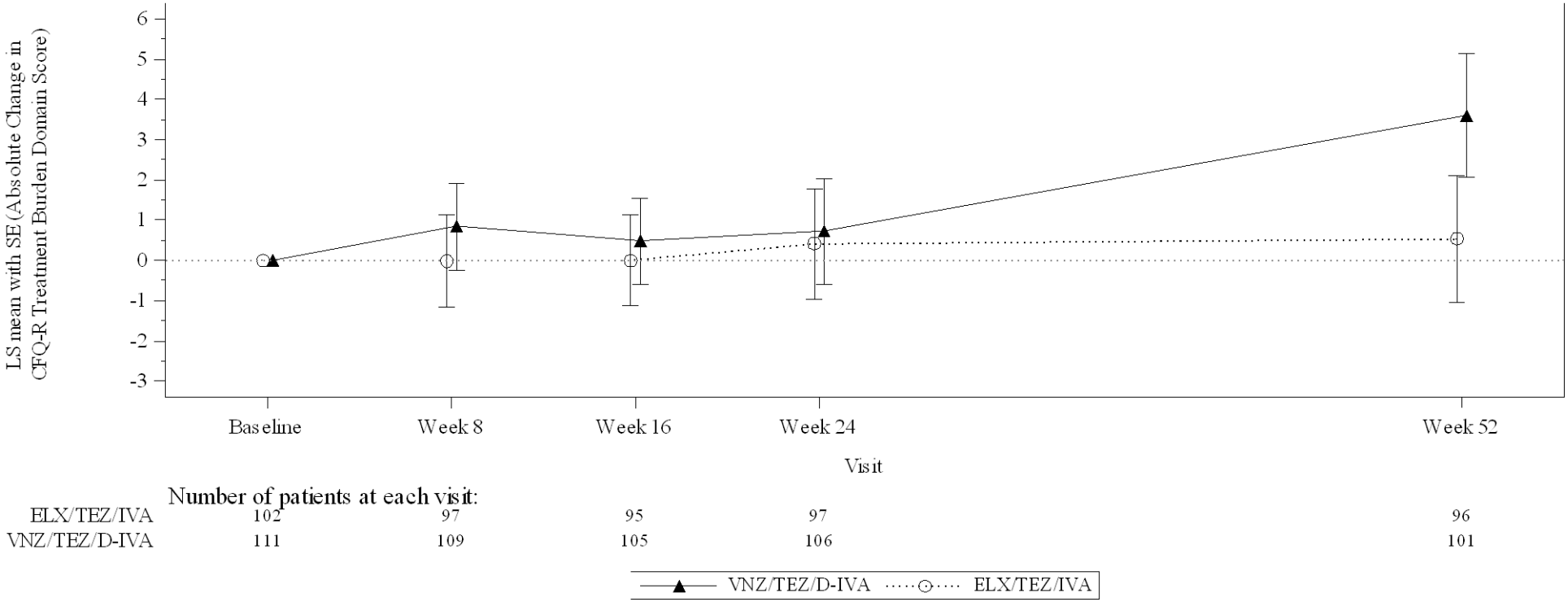
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

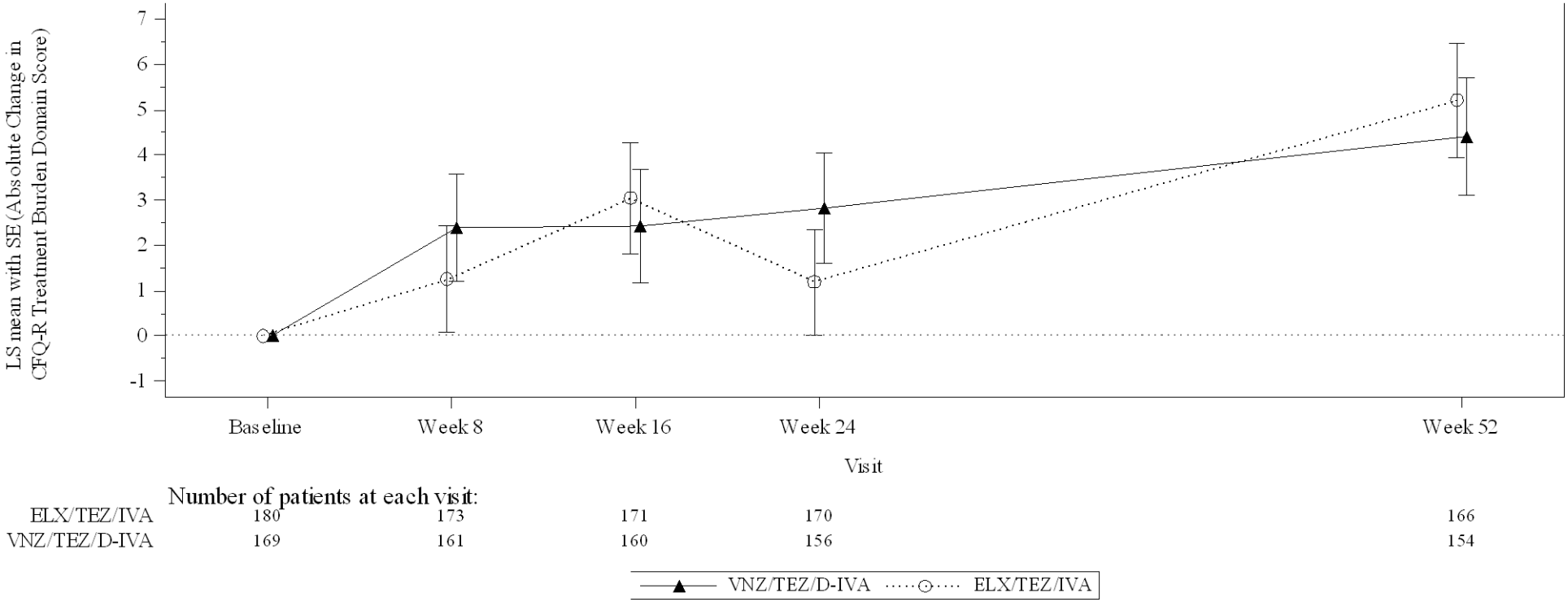
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

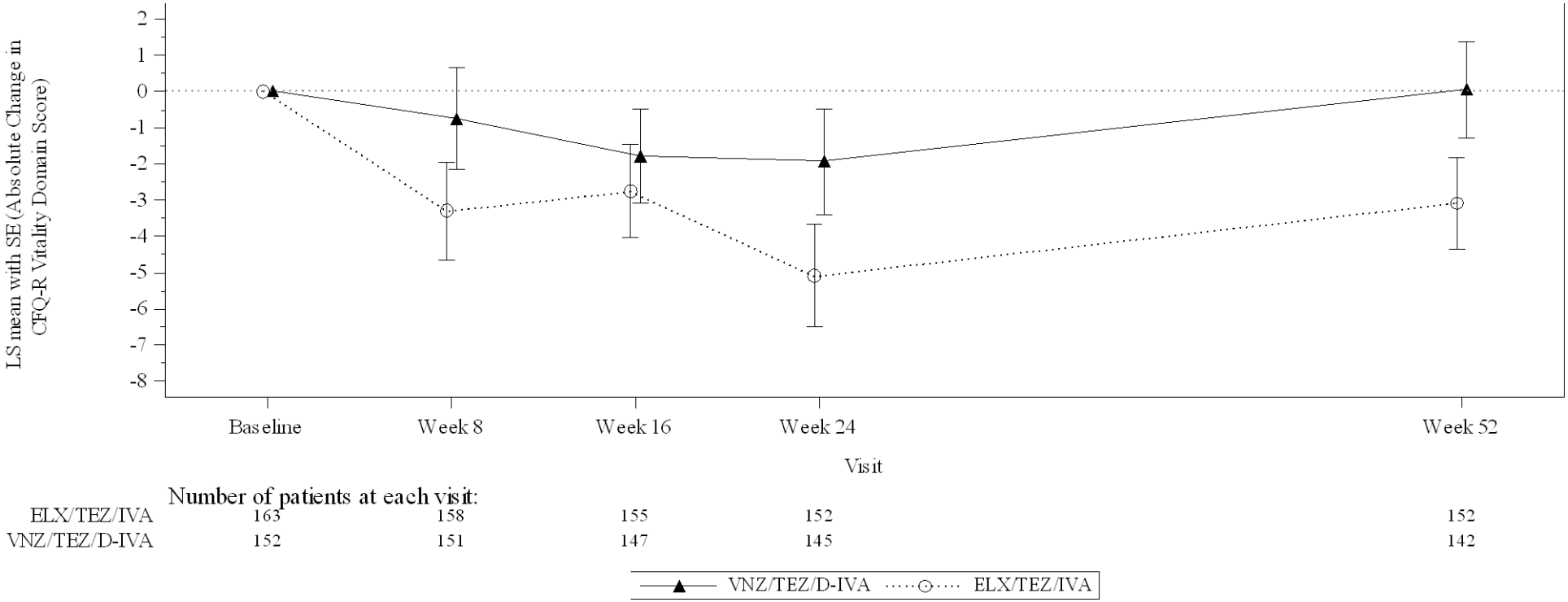
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

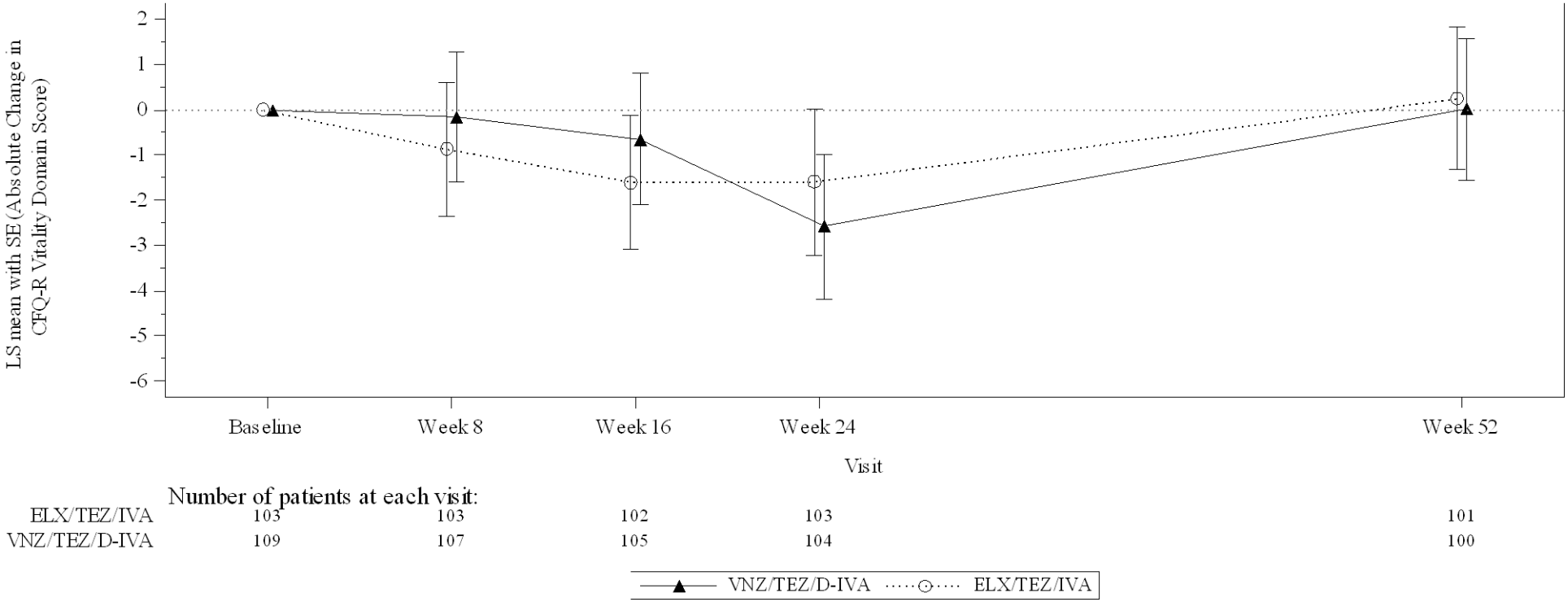
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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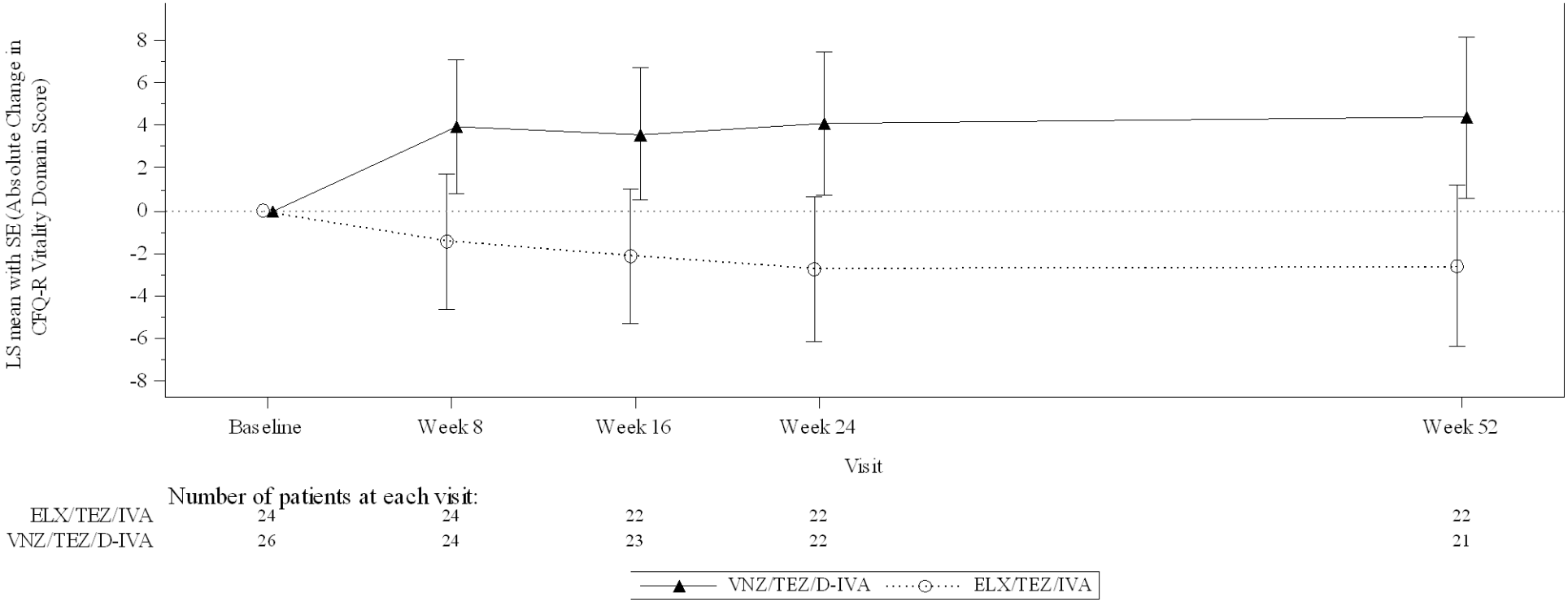
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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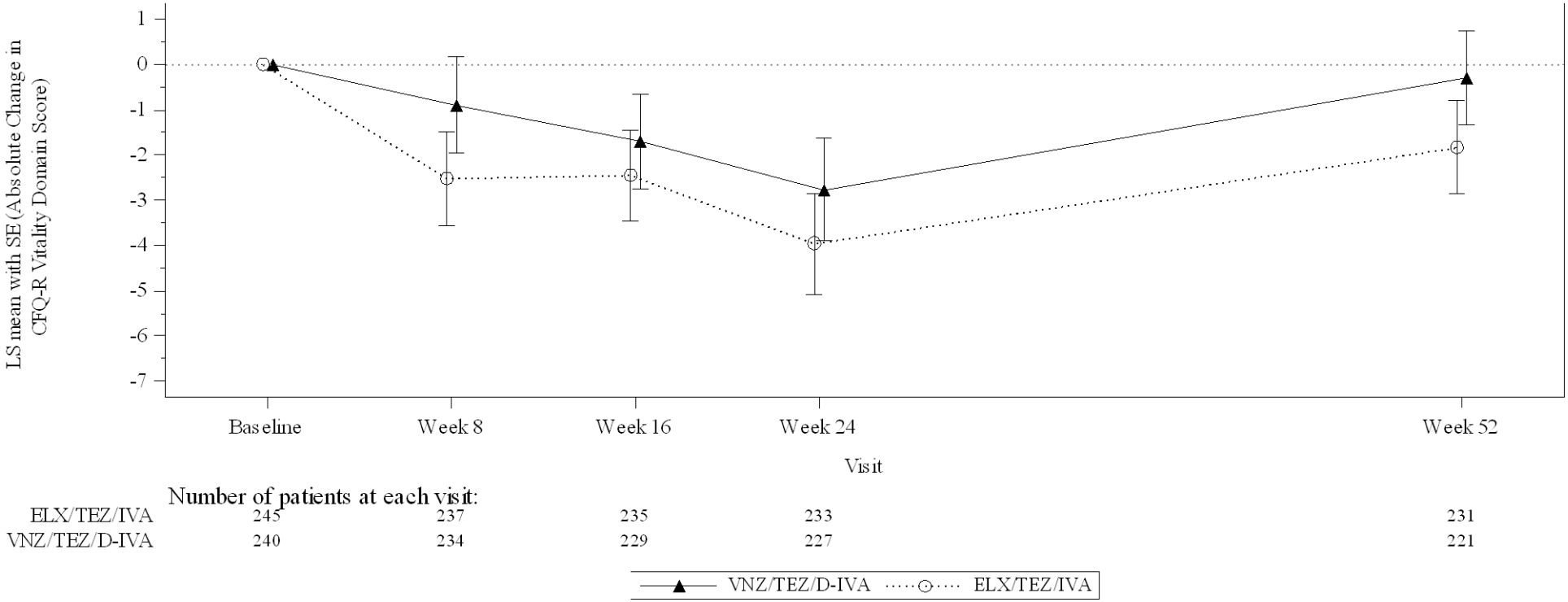
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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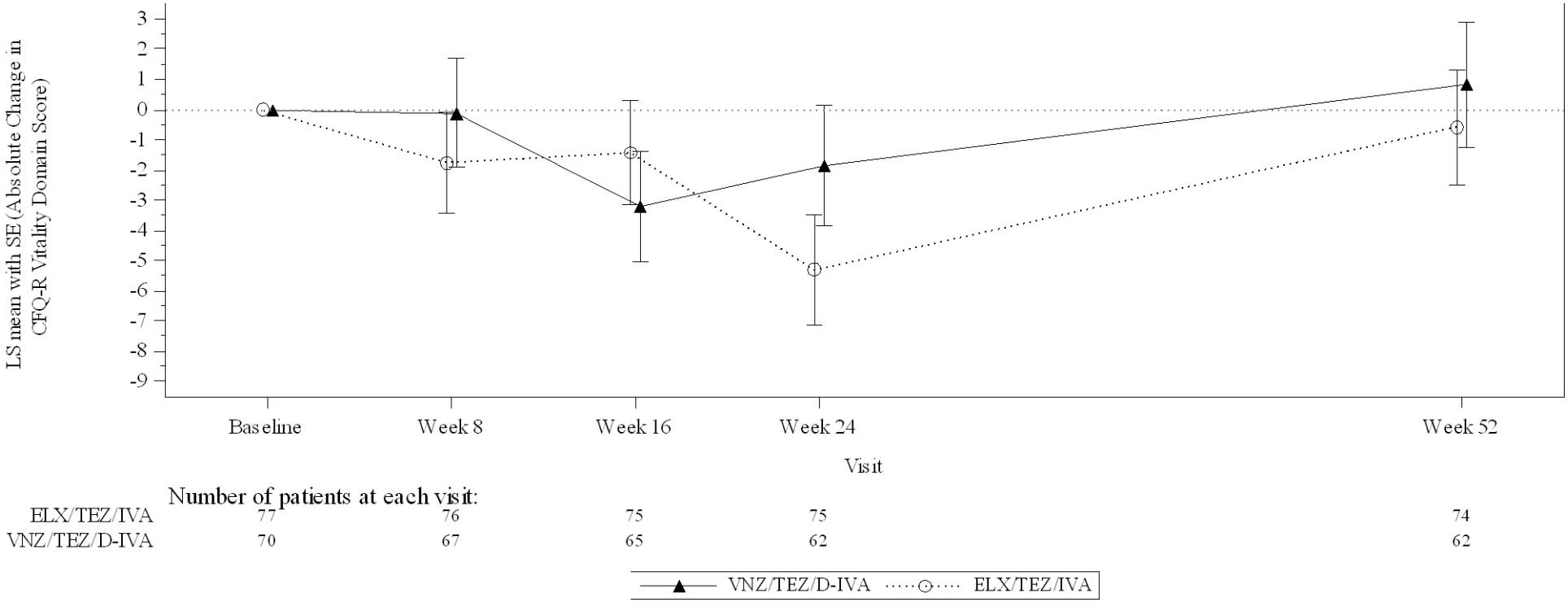
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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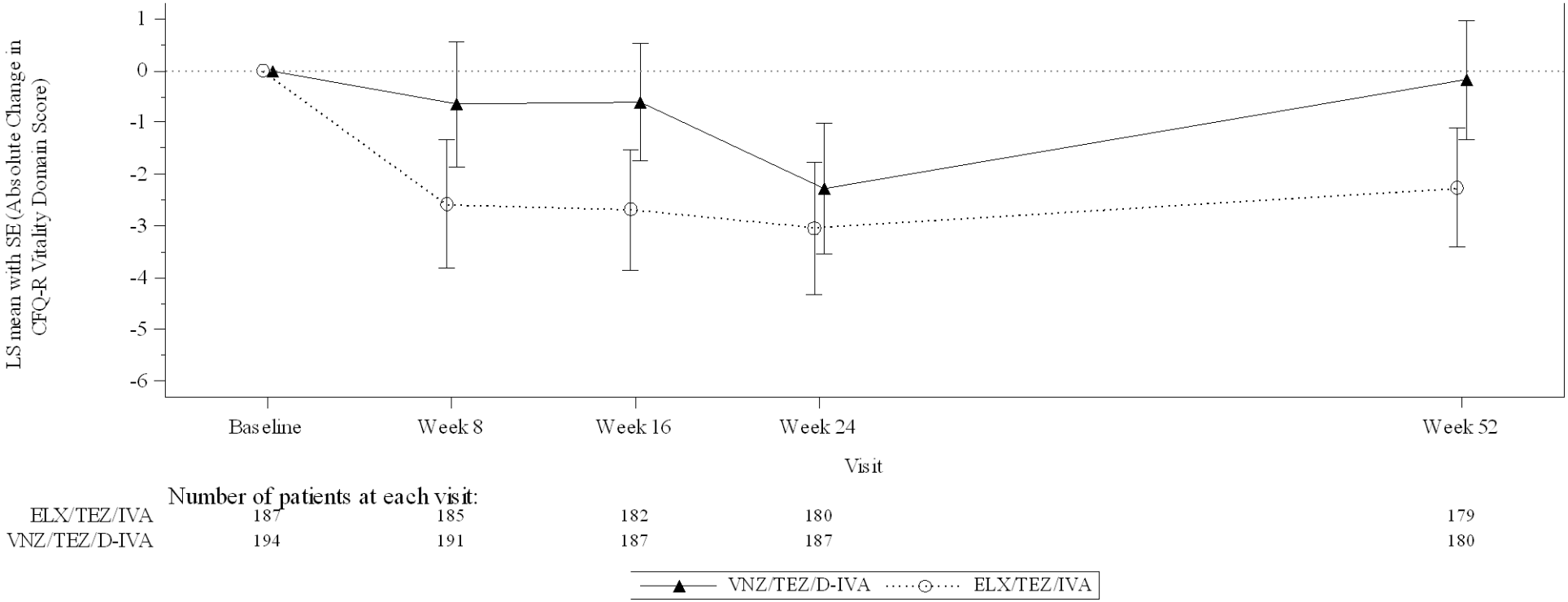
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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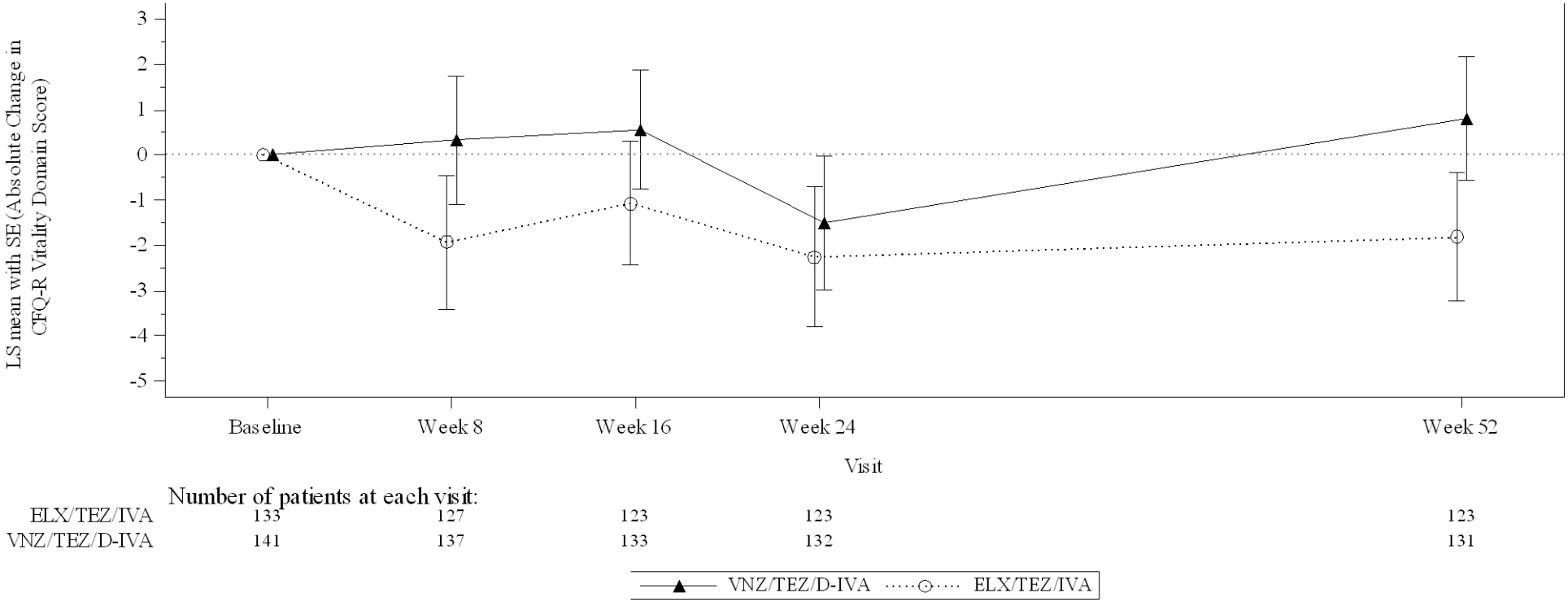
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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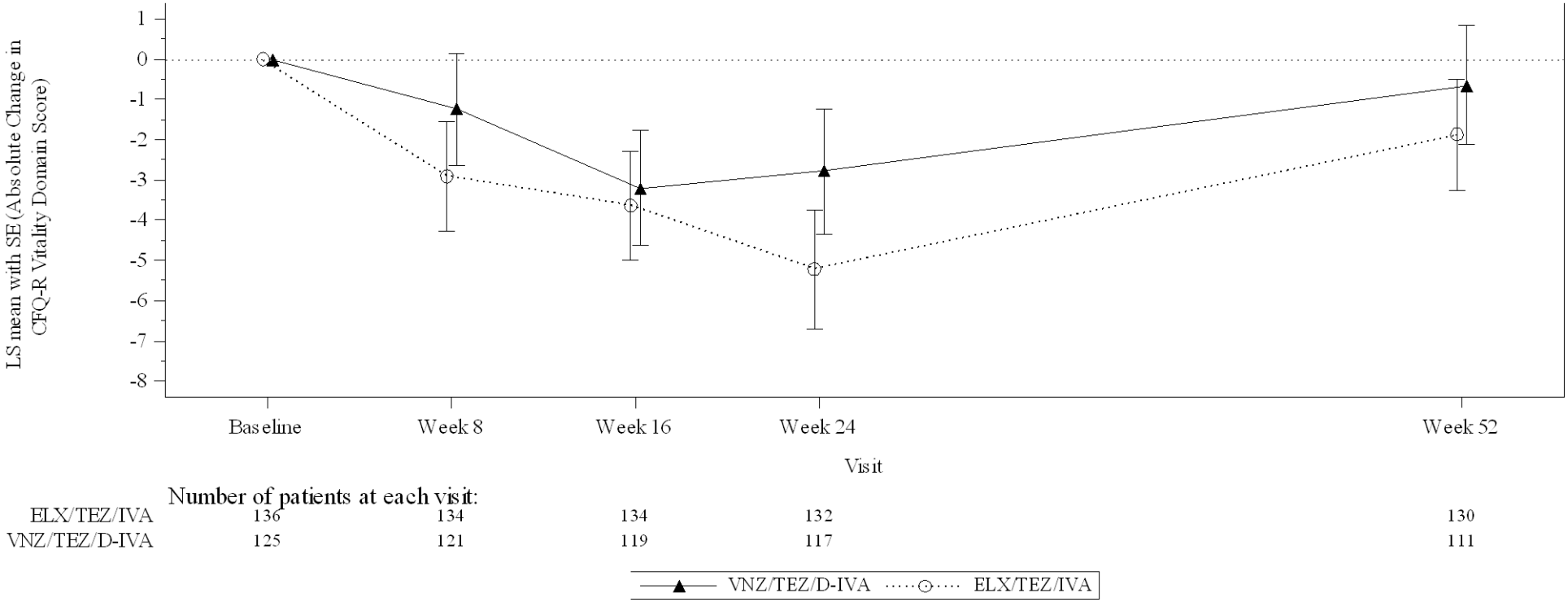
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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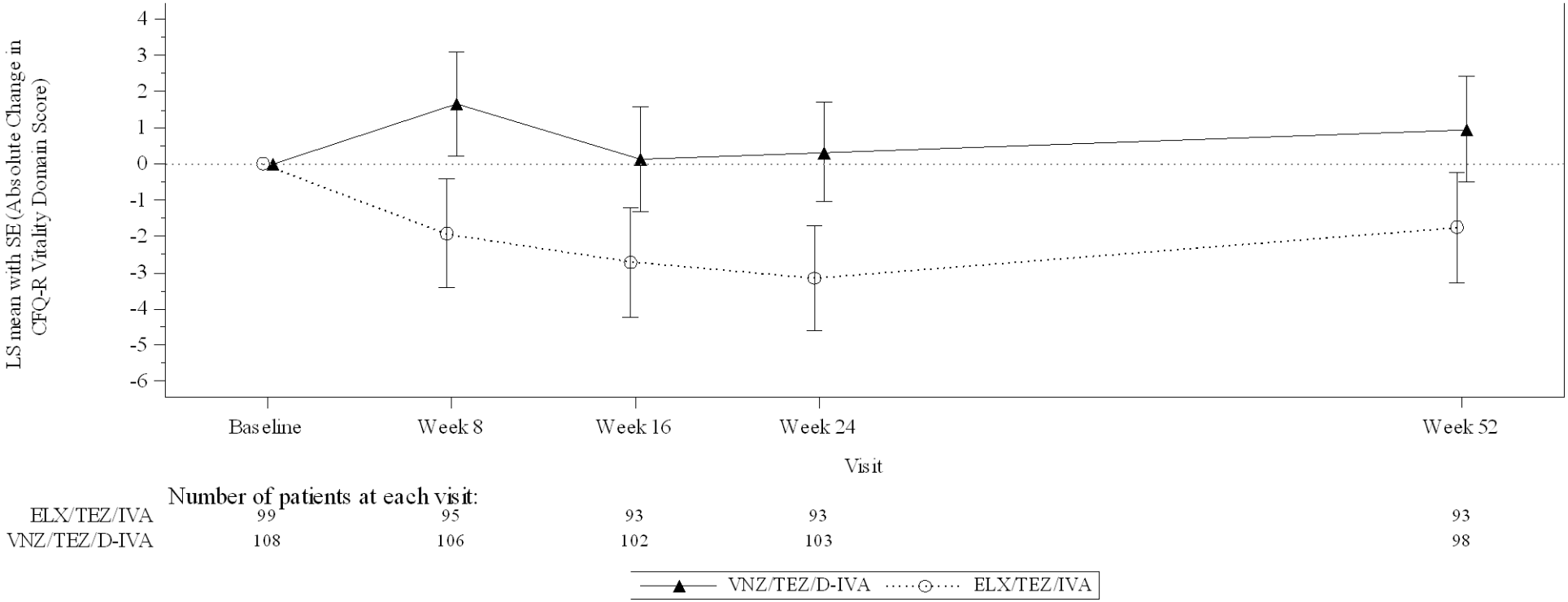
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

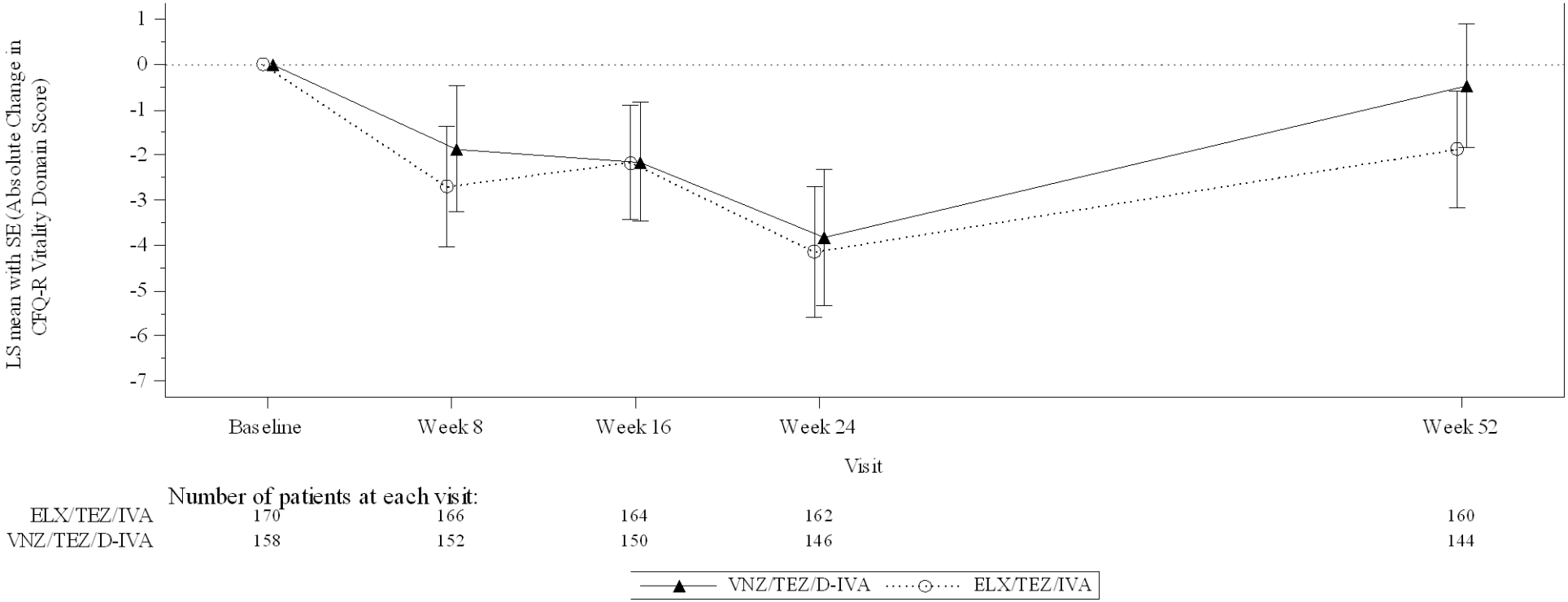
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

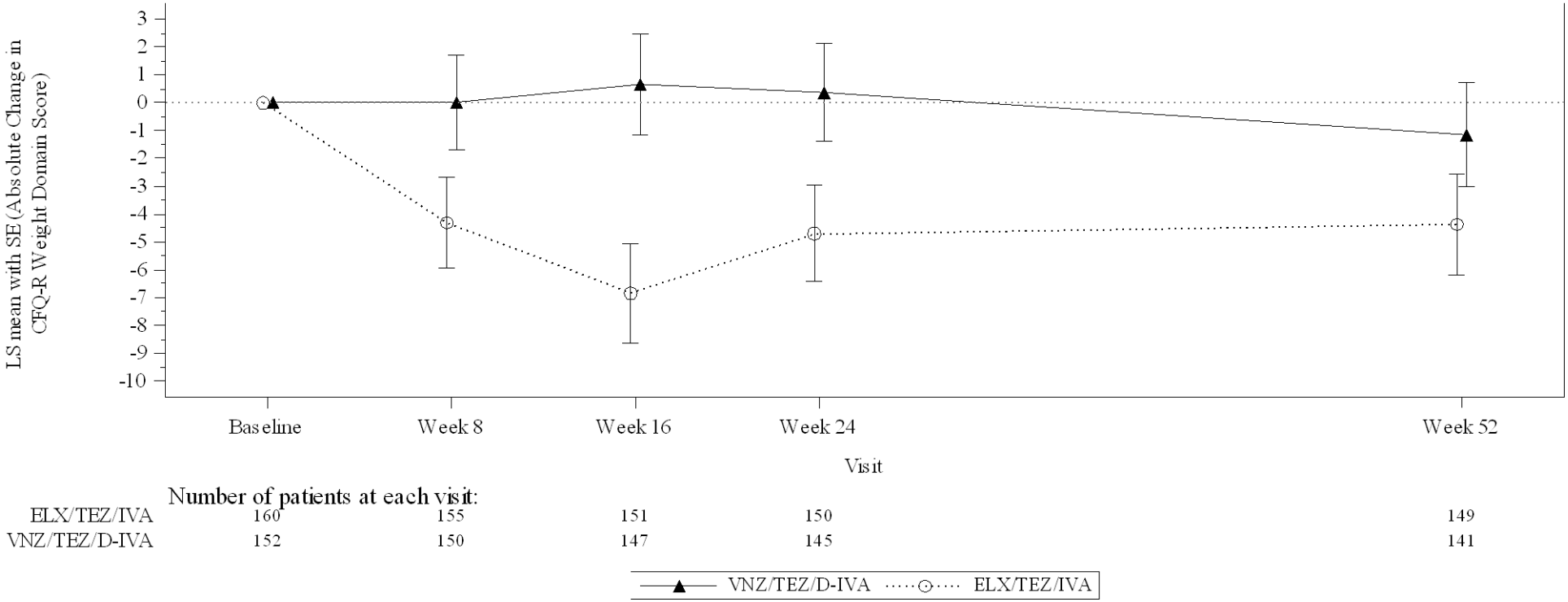
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline <70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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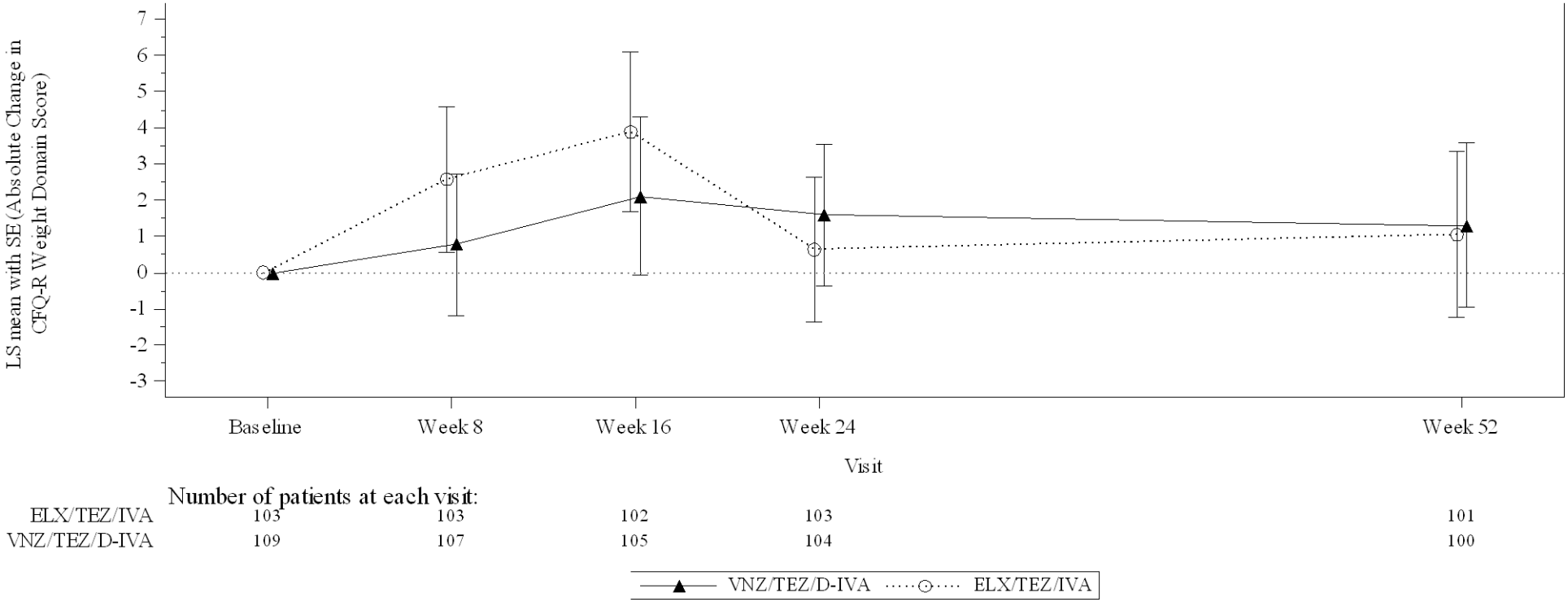
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
$ppFEV_1$ at baseline ≥70 %

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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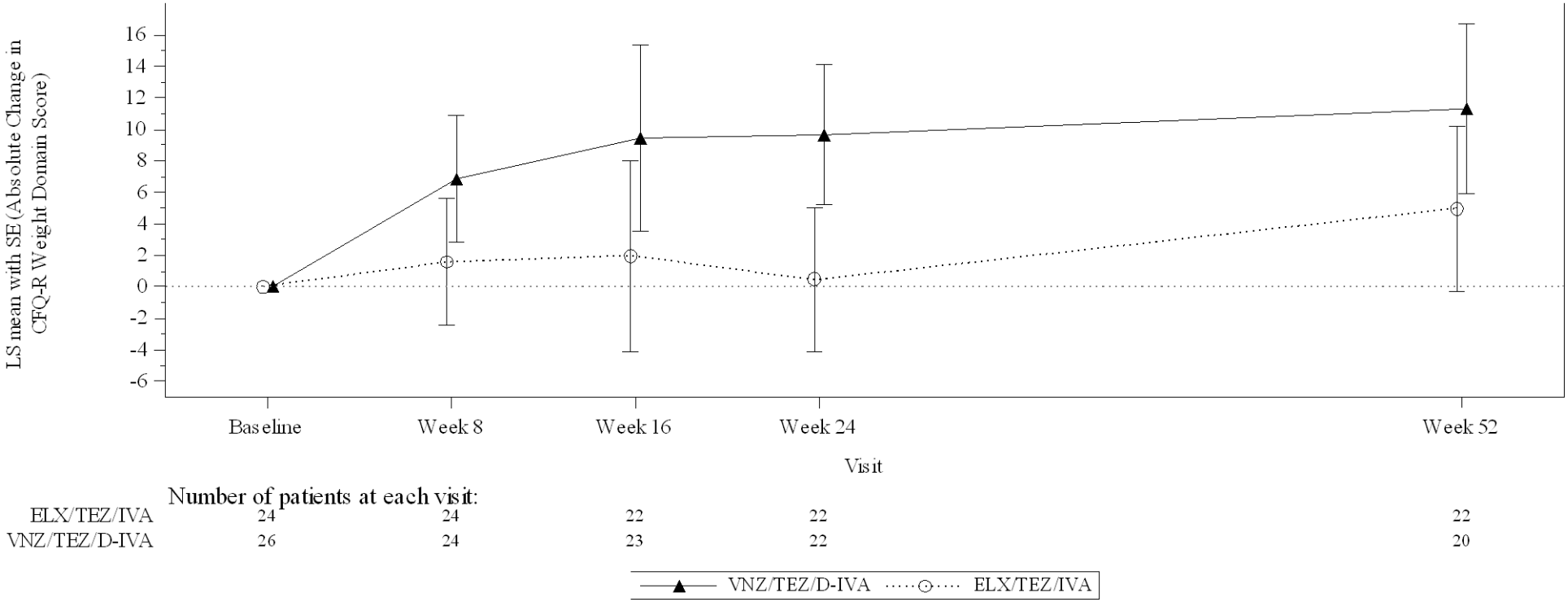
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening <18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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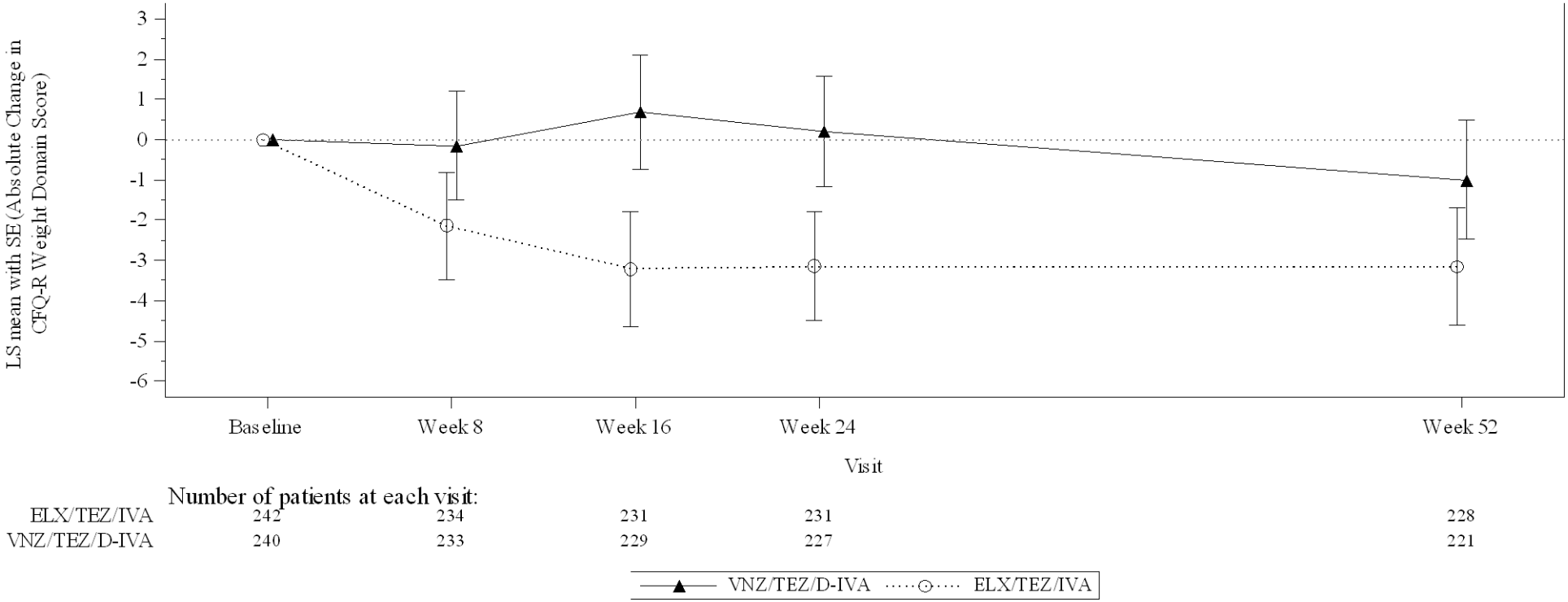
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Age at screening ≥18 years

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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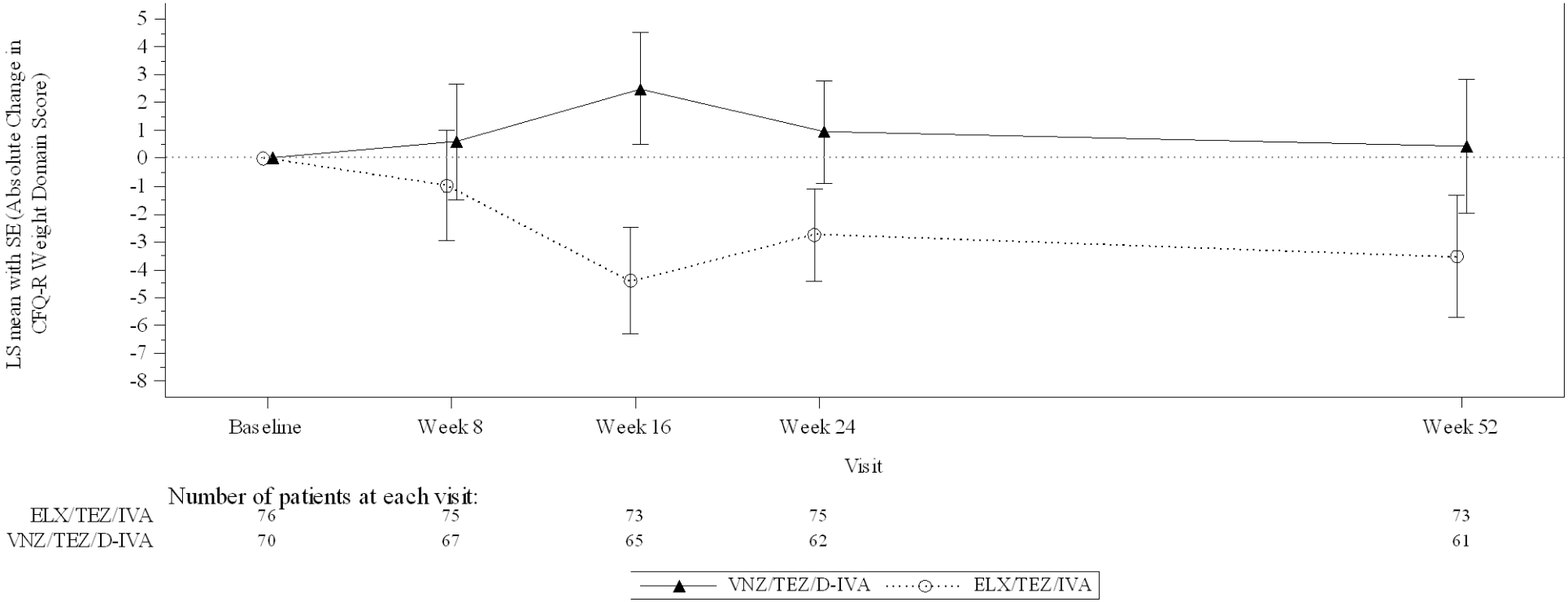
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline <30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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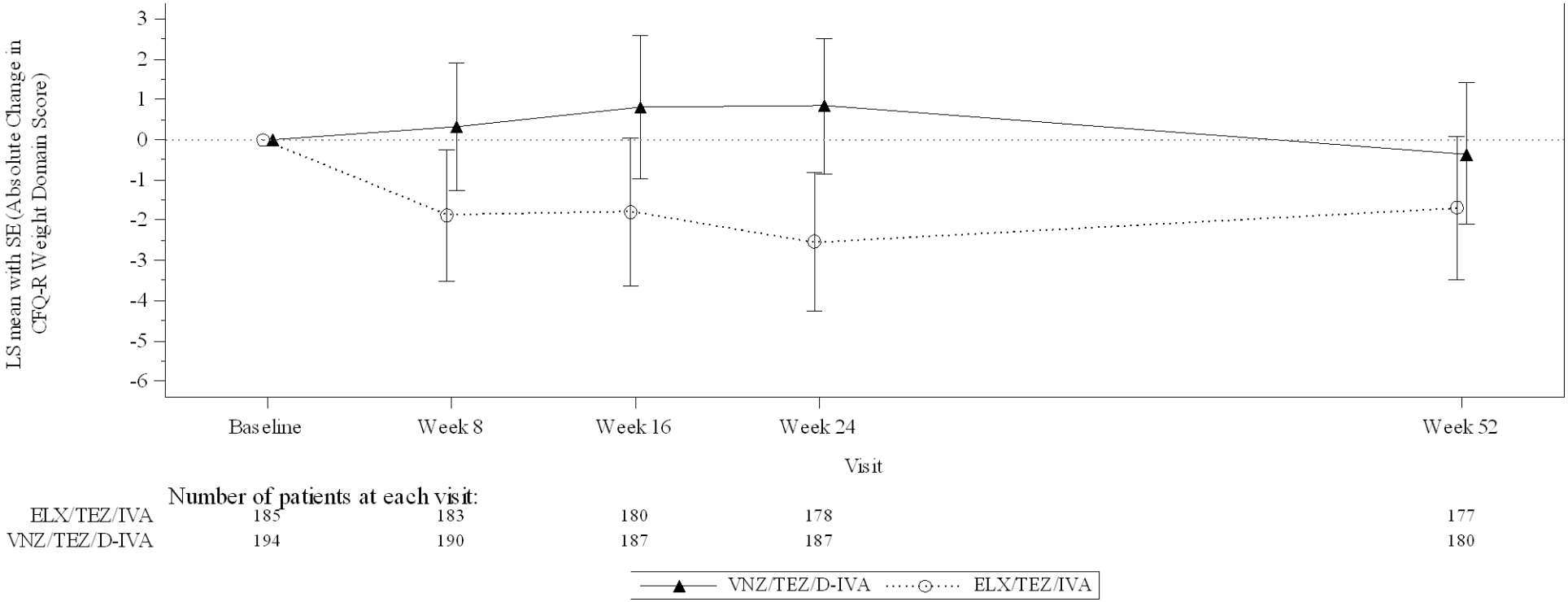
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
SwCl at baseline ≥30 mmol/L

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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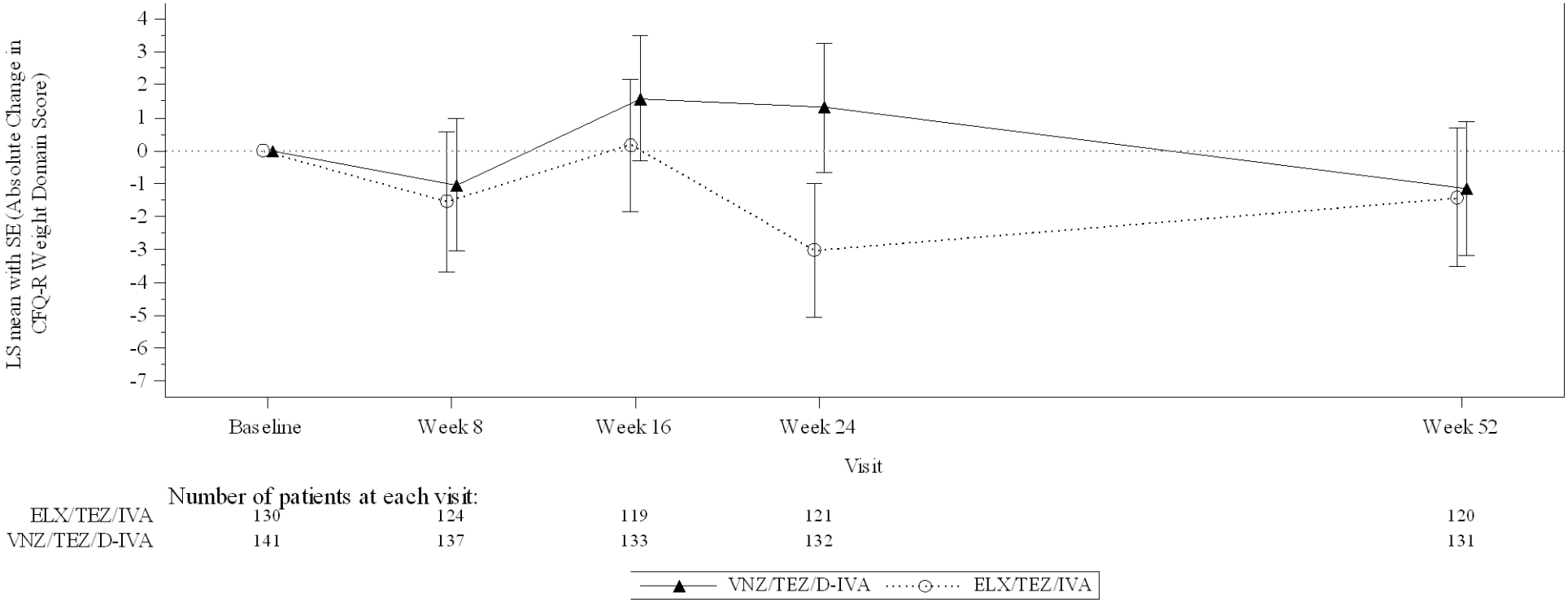
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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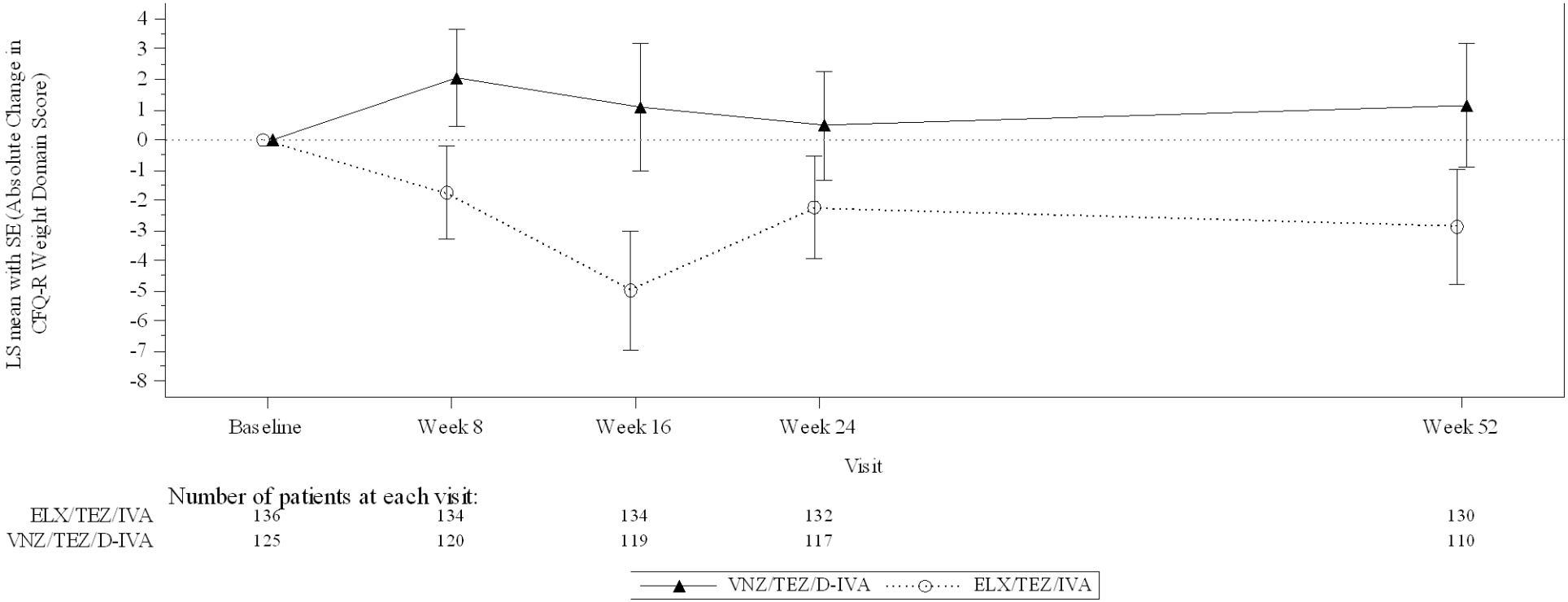
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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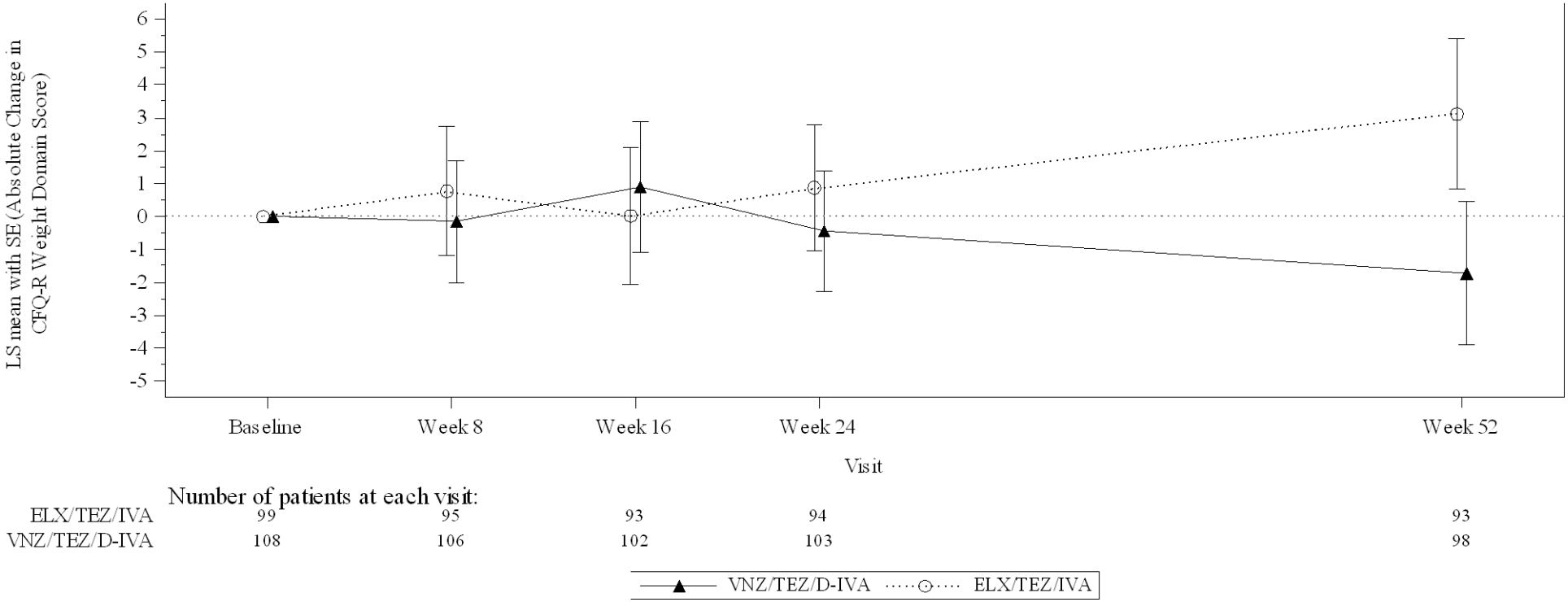
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Zusatzanalysen zur Studie VX20-121-103



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

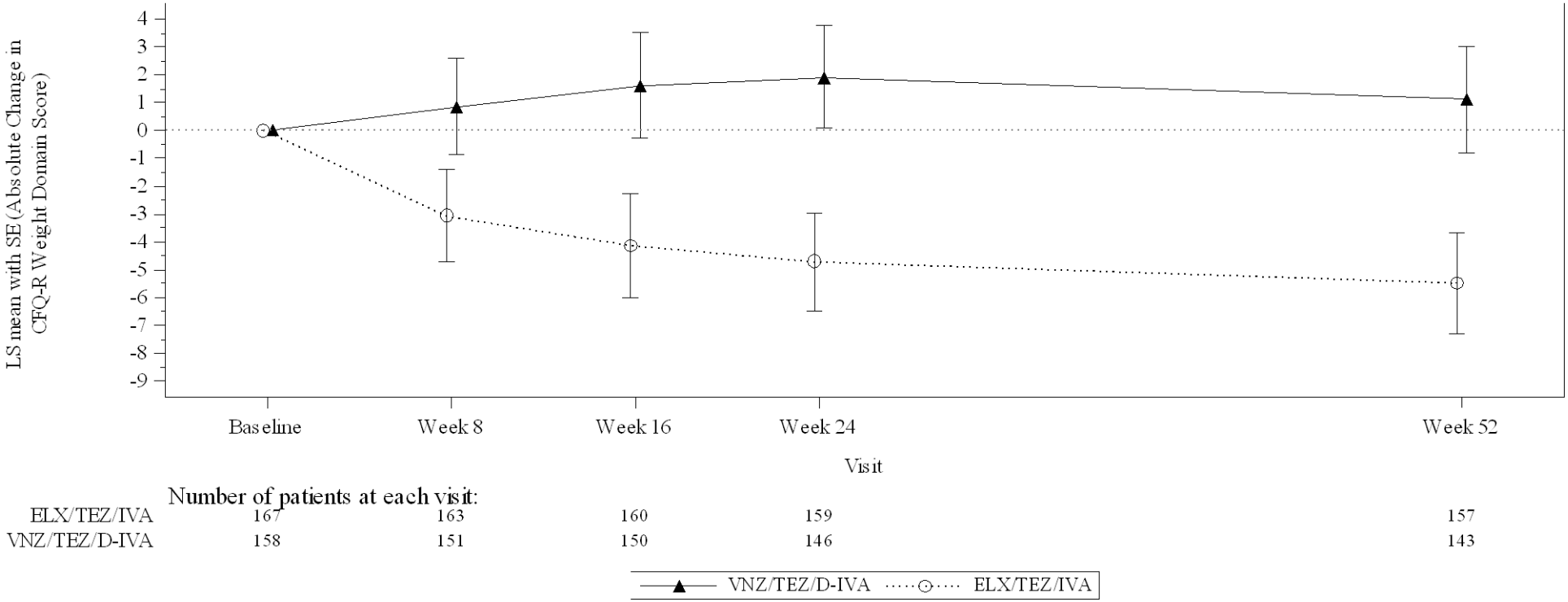
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Figure 2.2.2.9.5
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Zusatzanalysen zur Studie VX20-121-103

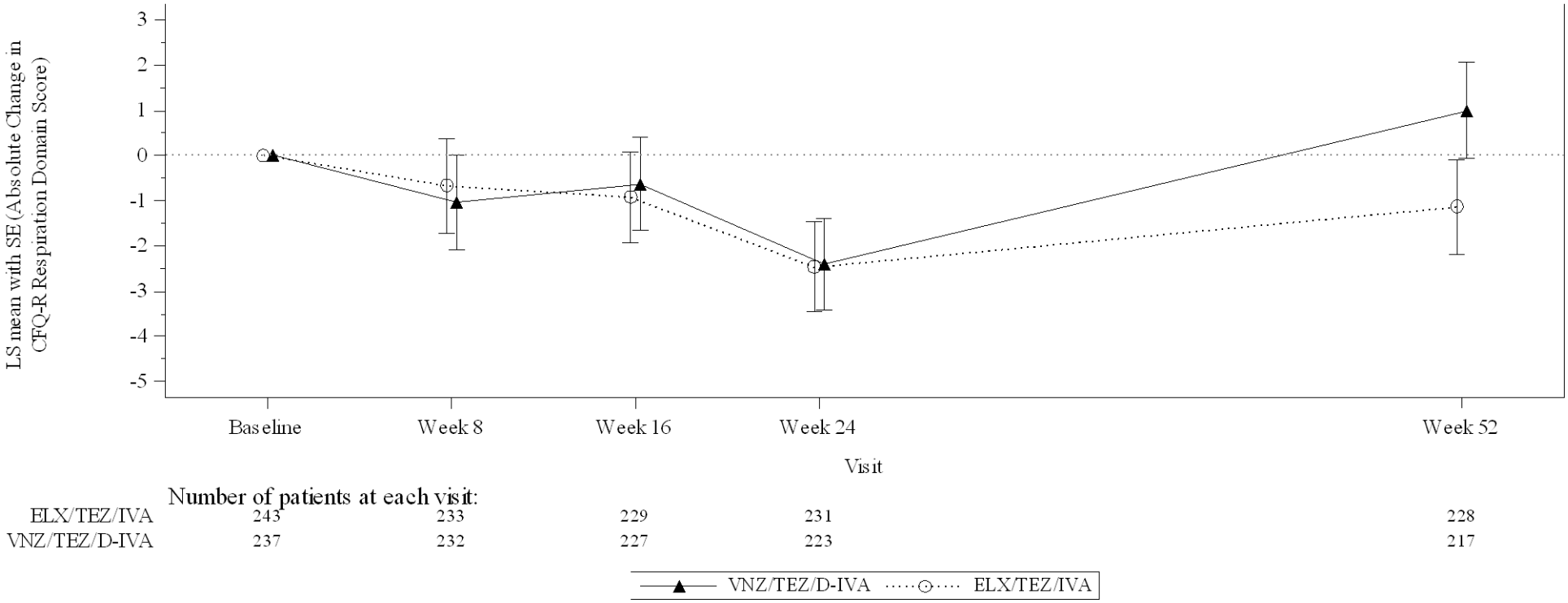


- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group (F/F, F/G, F/RF, TCR/non-F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. For "Age at screening" subgroup factor, Age at screening (<18 years vs ≥18 years) covariate is removed from MMRM.

Program: GMA\VX121\germandossier\clinstat_prod\121-103\f-qs-abs-cfqr-ag12-52wks-sub-103.sas Creation: 07JAN2025 11:40

Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

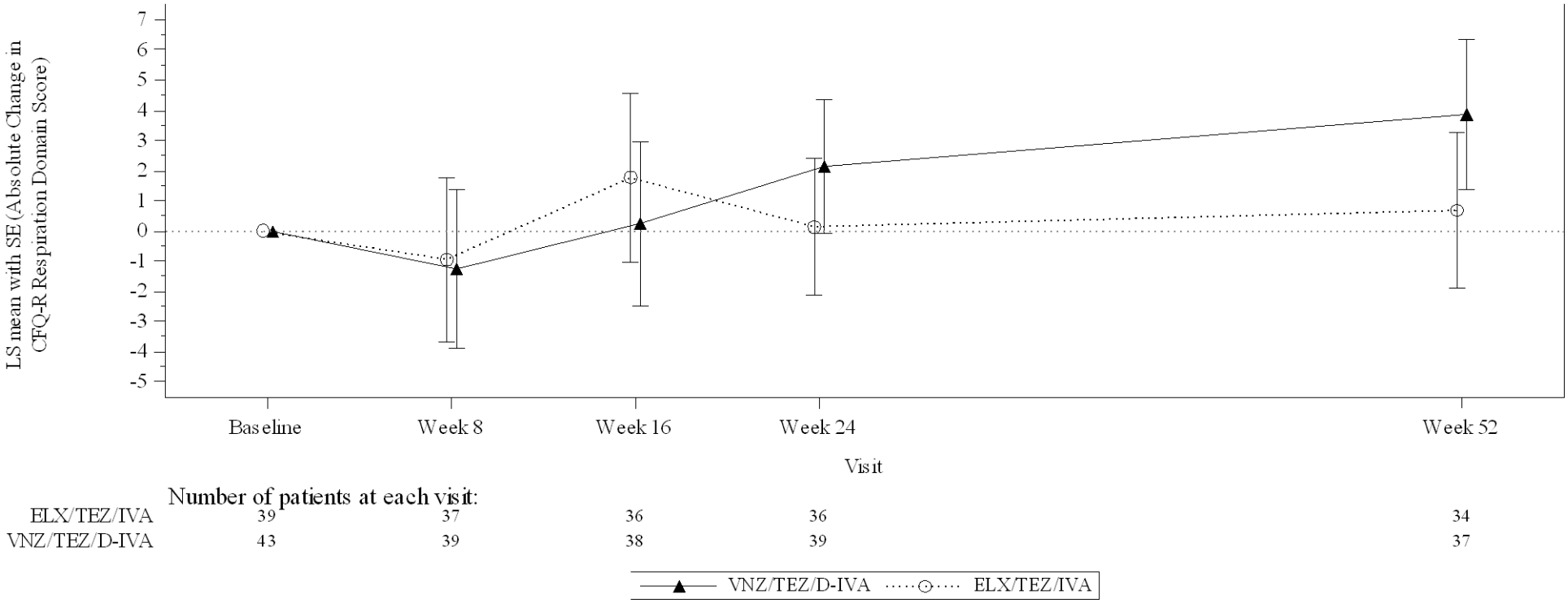
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

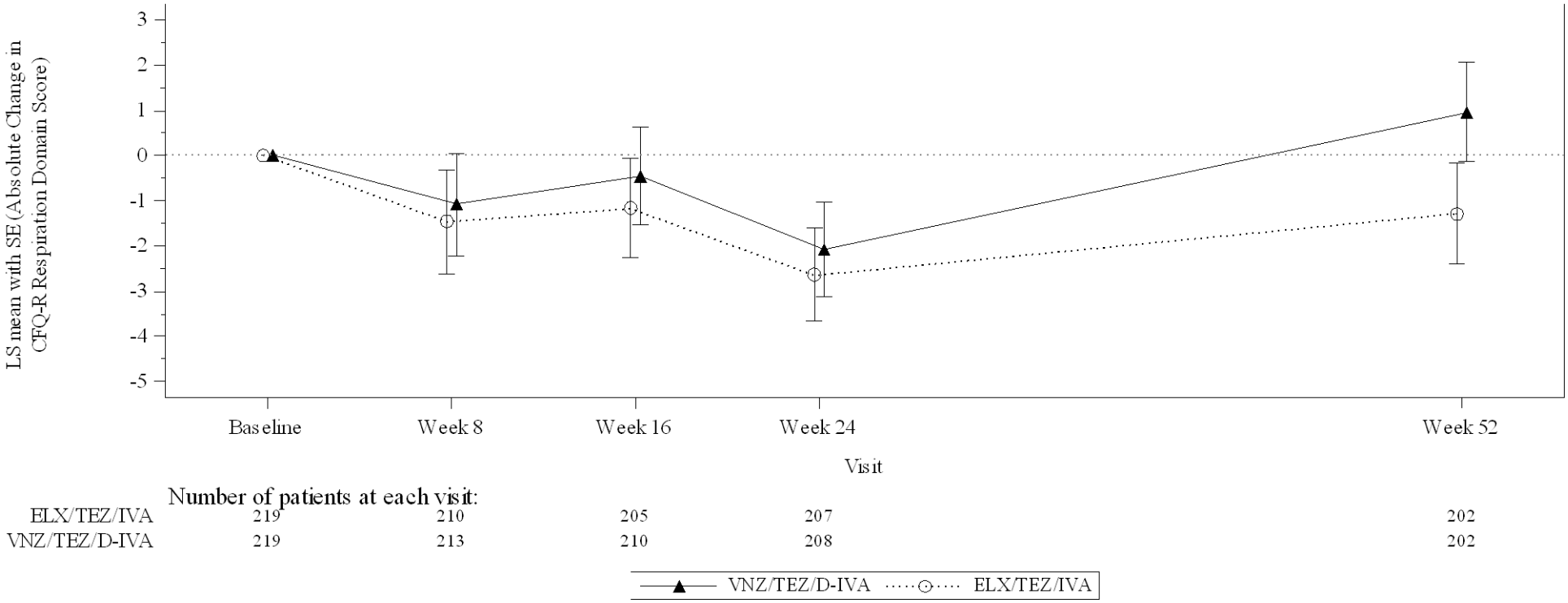
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Domain: Respiration
Prior CFTR modulator use: No



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

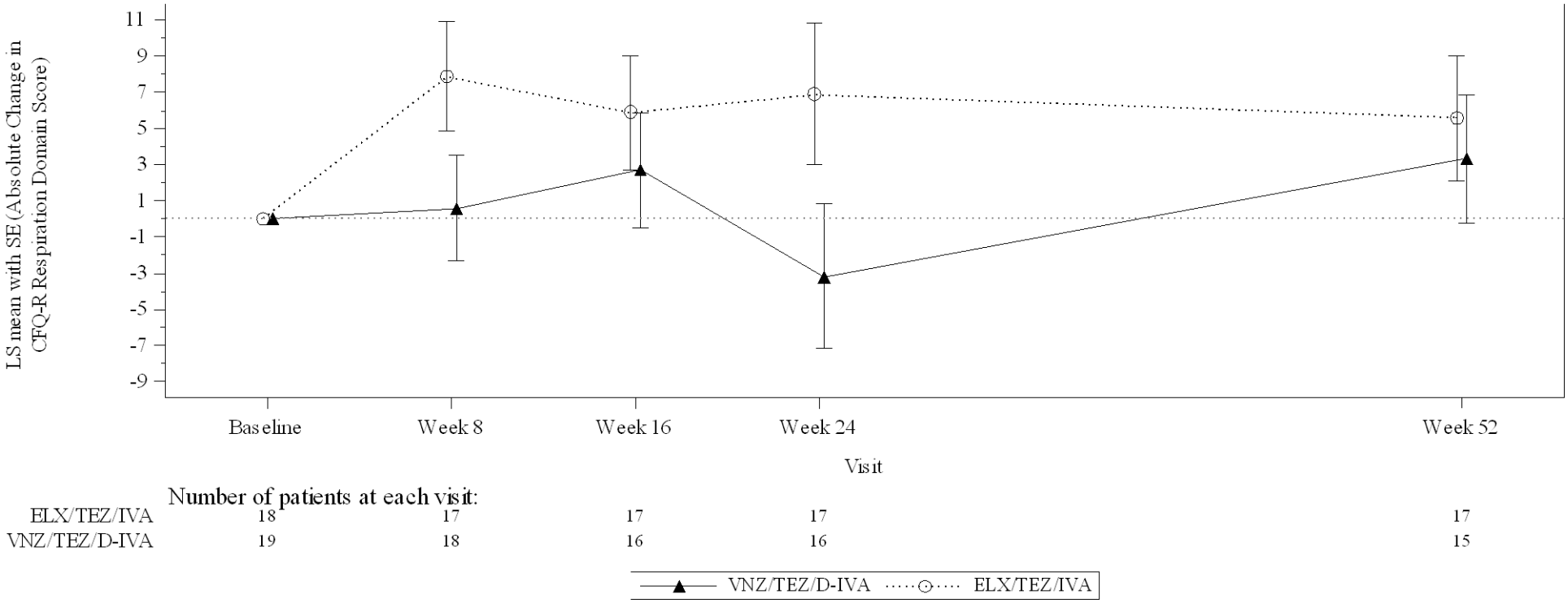
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Genotype group: F/F



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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

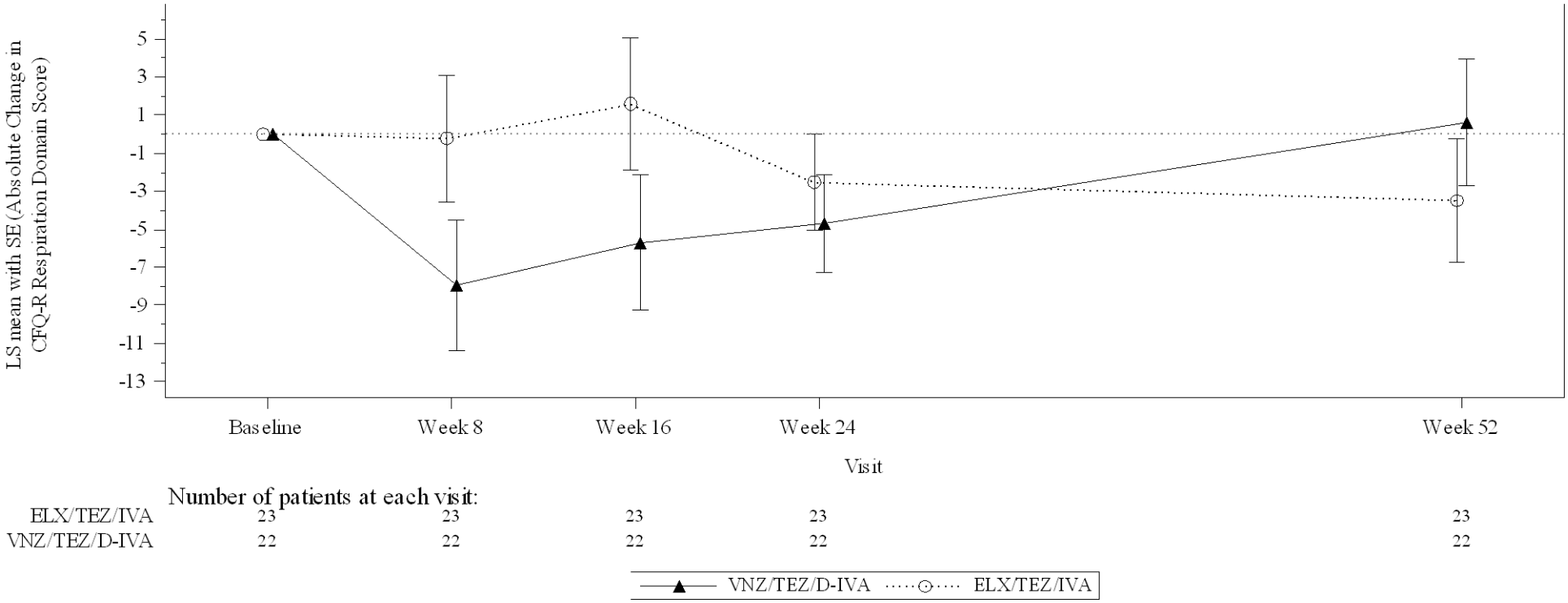
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Genotype group: F/G



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

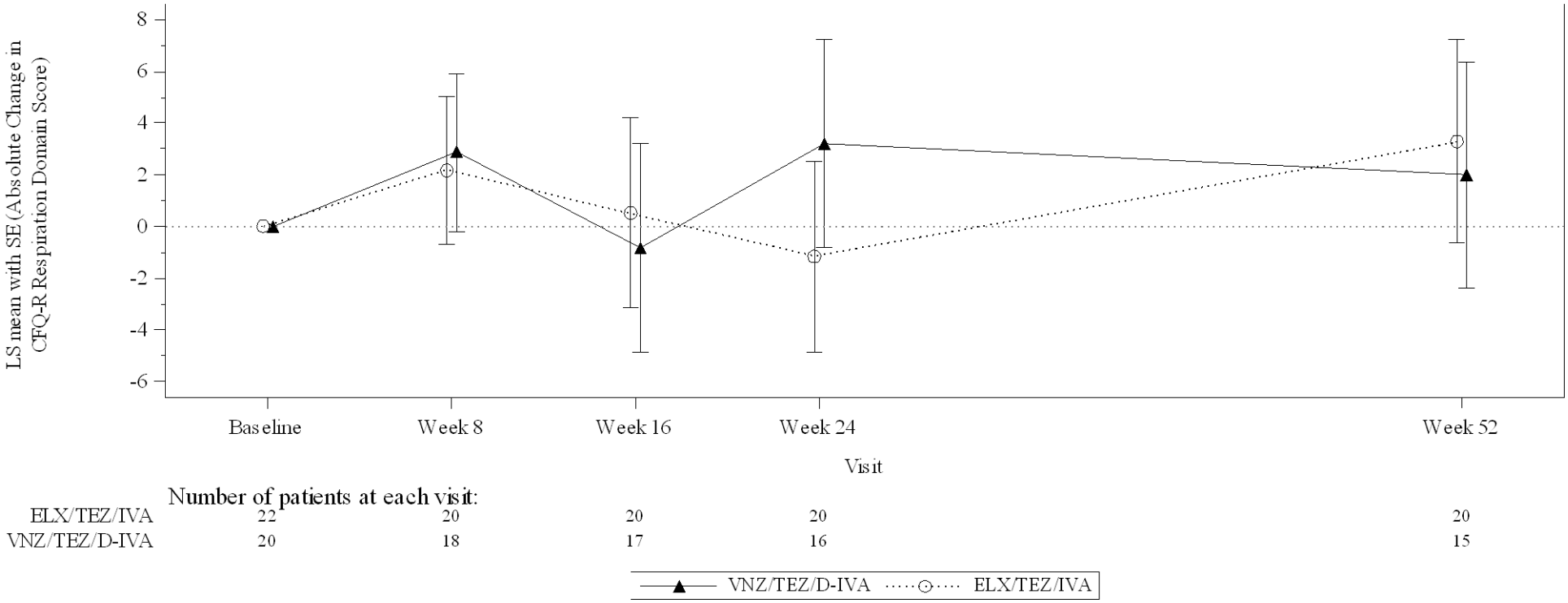
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Genotype group: F/RF



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

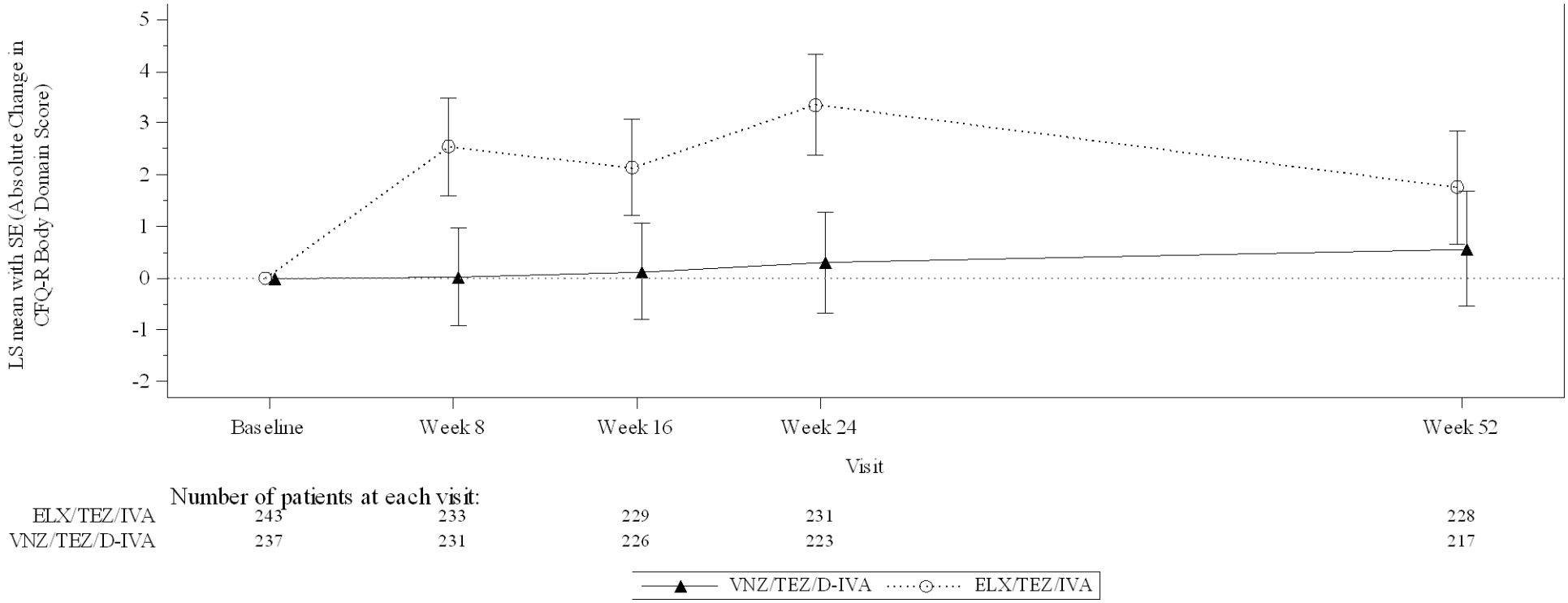
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration
Genotype group: TCR/non-F



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

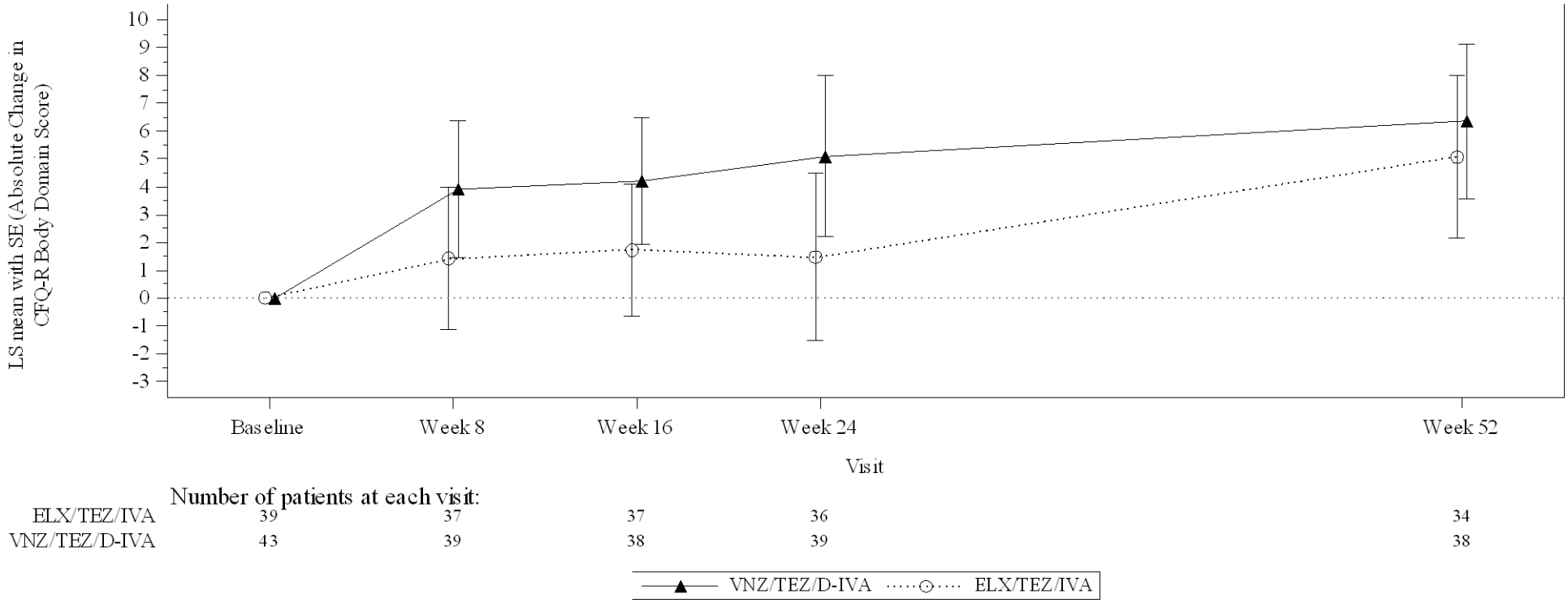
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Domain: Body
Prior CFTR modulator use: Yes



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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

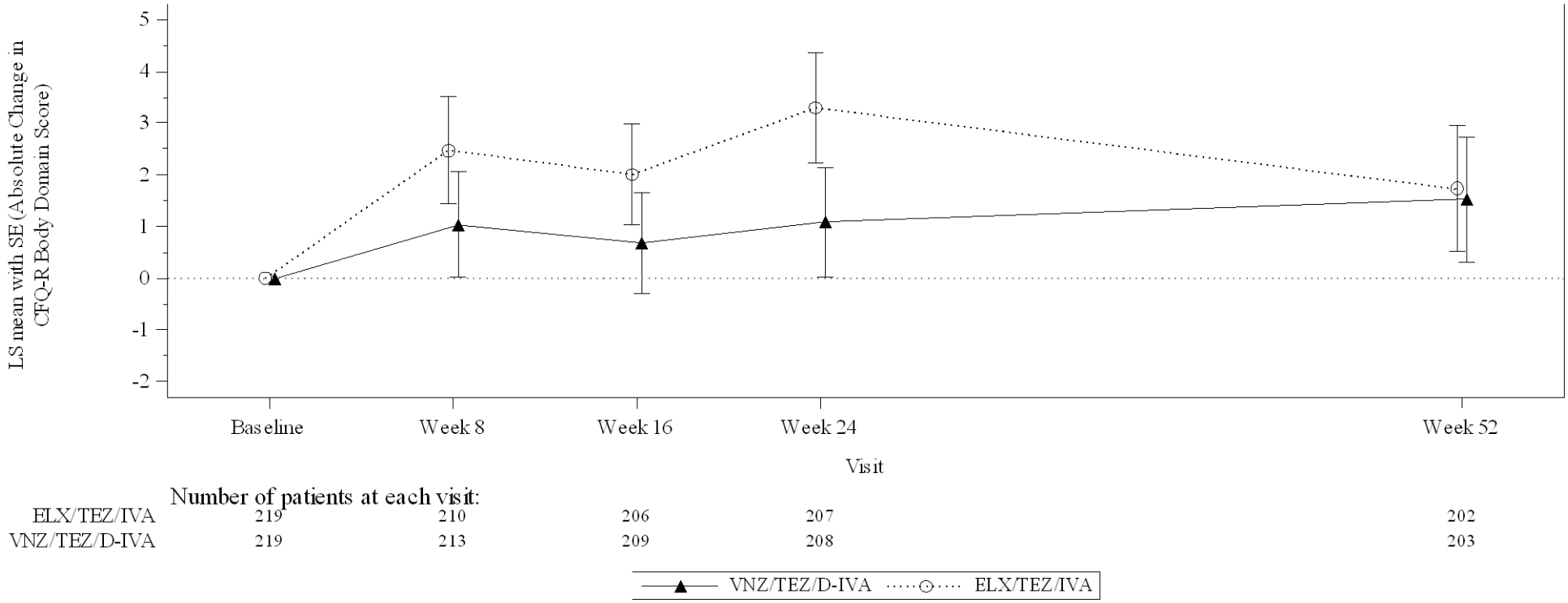
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Domain: Body
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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

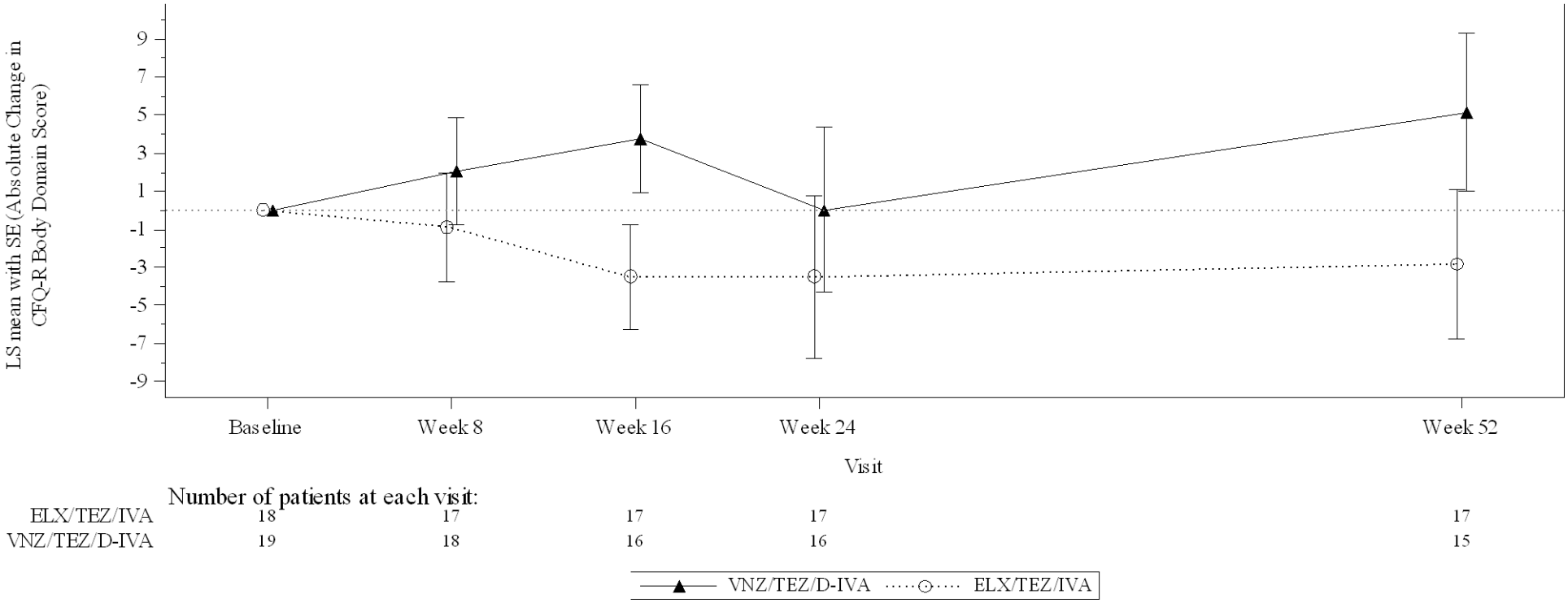
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Genotype group: F/F



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

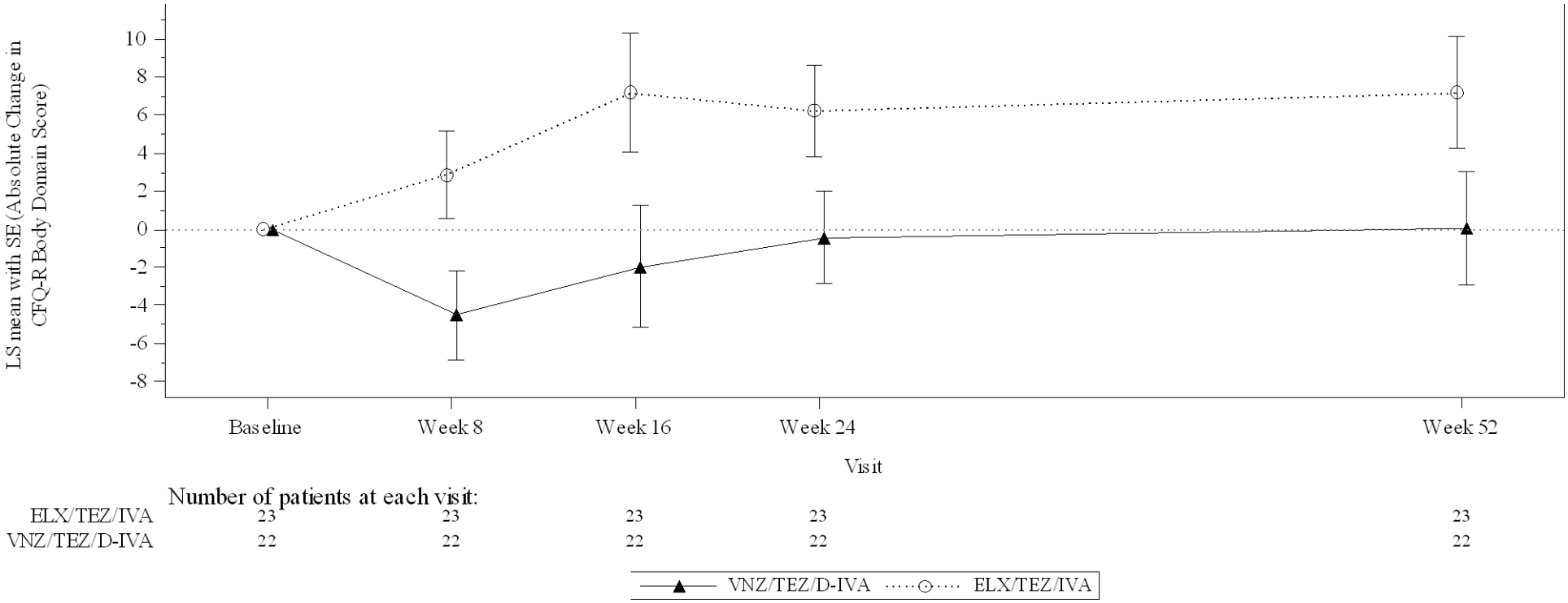
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Genotype group: F/G



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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

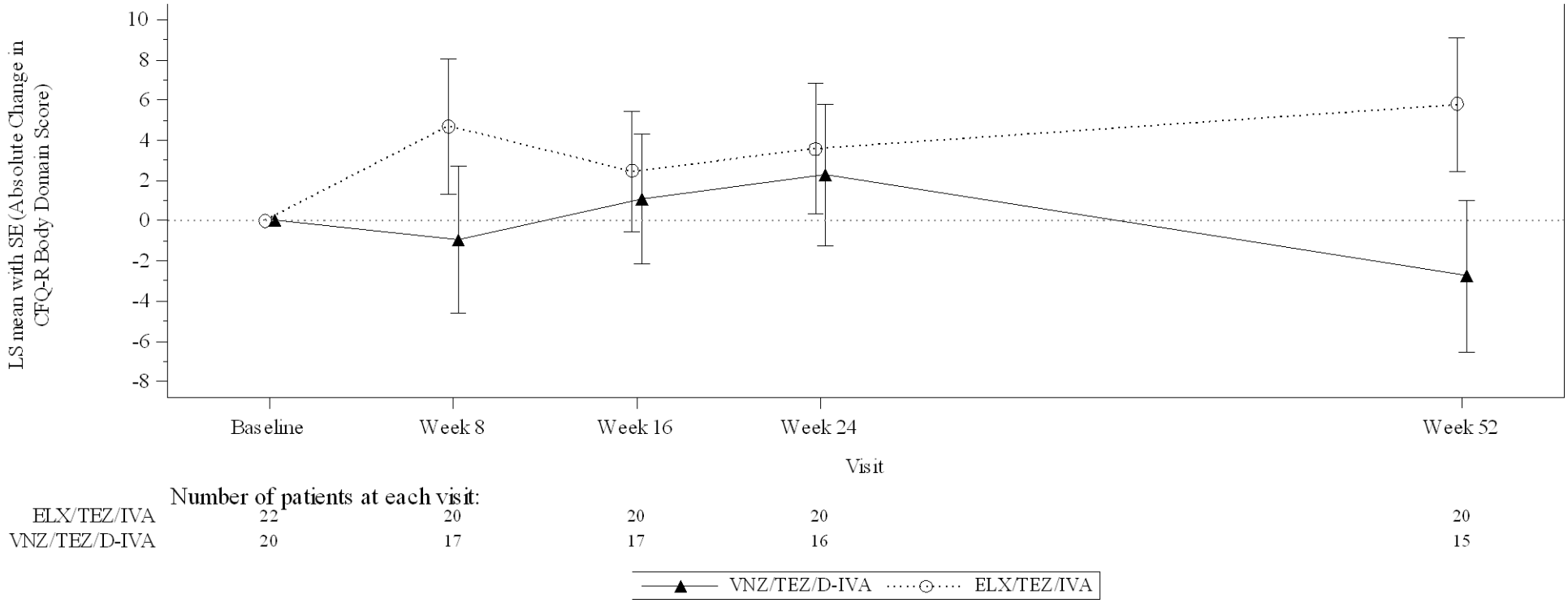
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Genotype group: F/RF



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

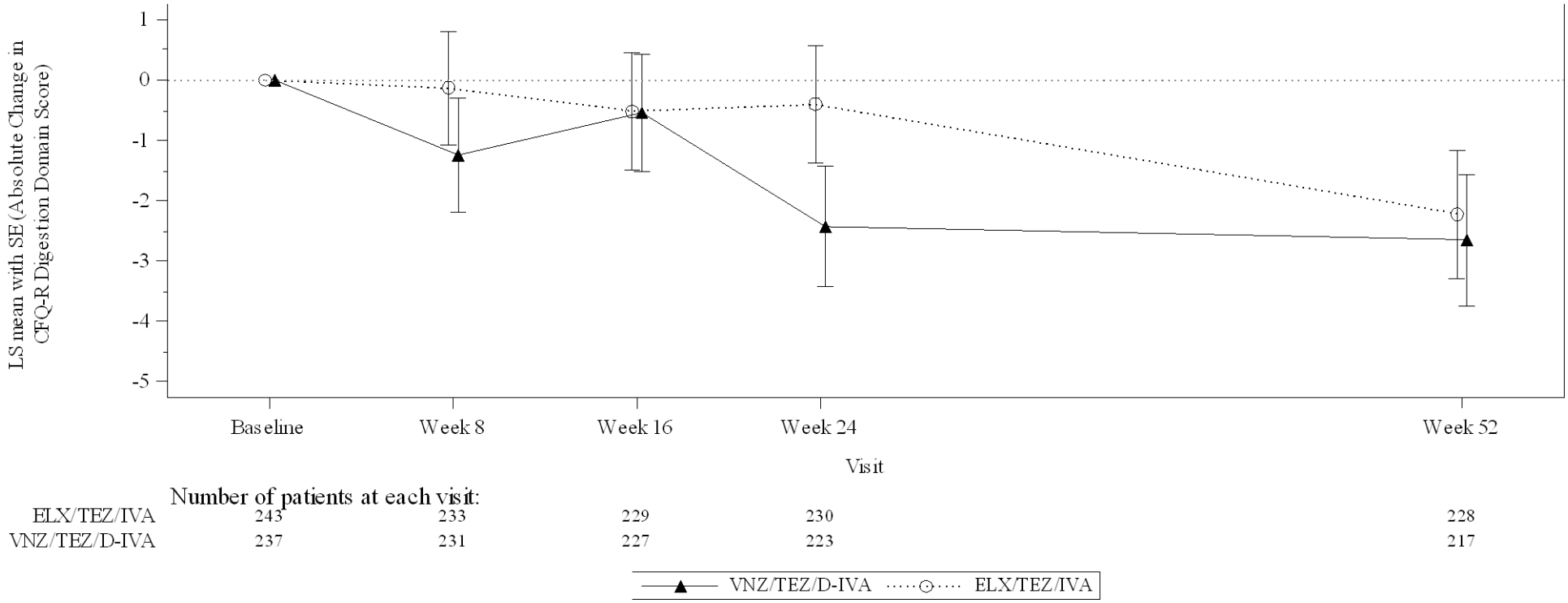
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body
Genotype group: TCR/non-F



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

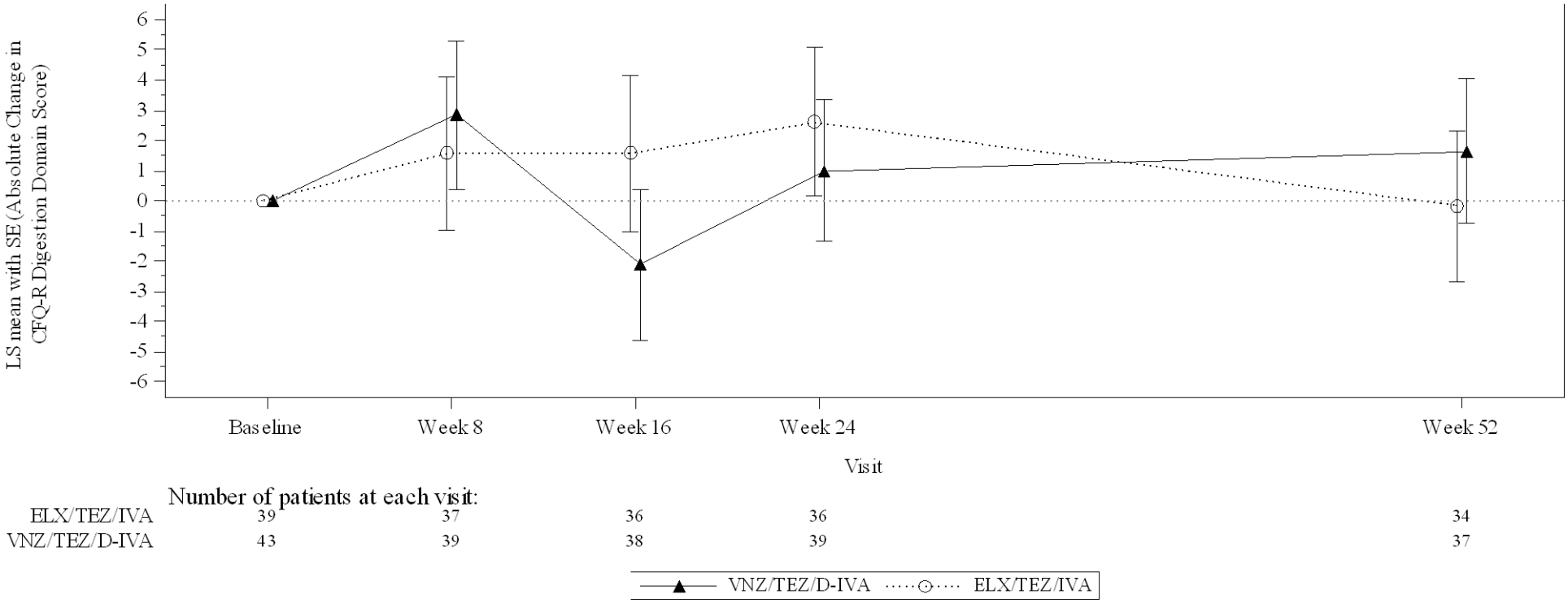
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Domain: Digestion
Prior CFTR modulator use: Yes



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1) at least 10 subjects in each subgroup (per factor), and 2) for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

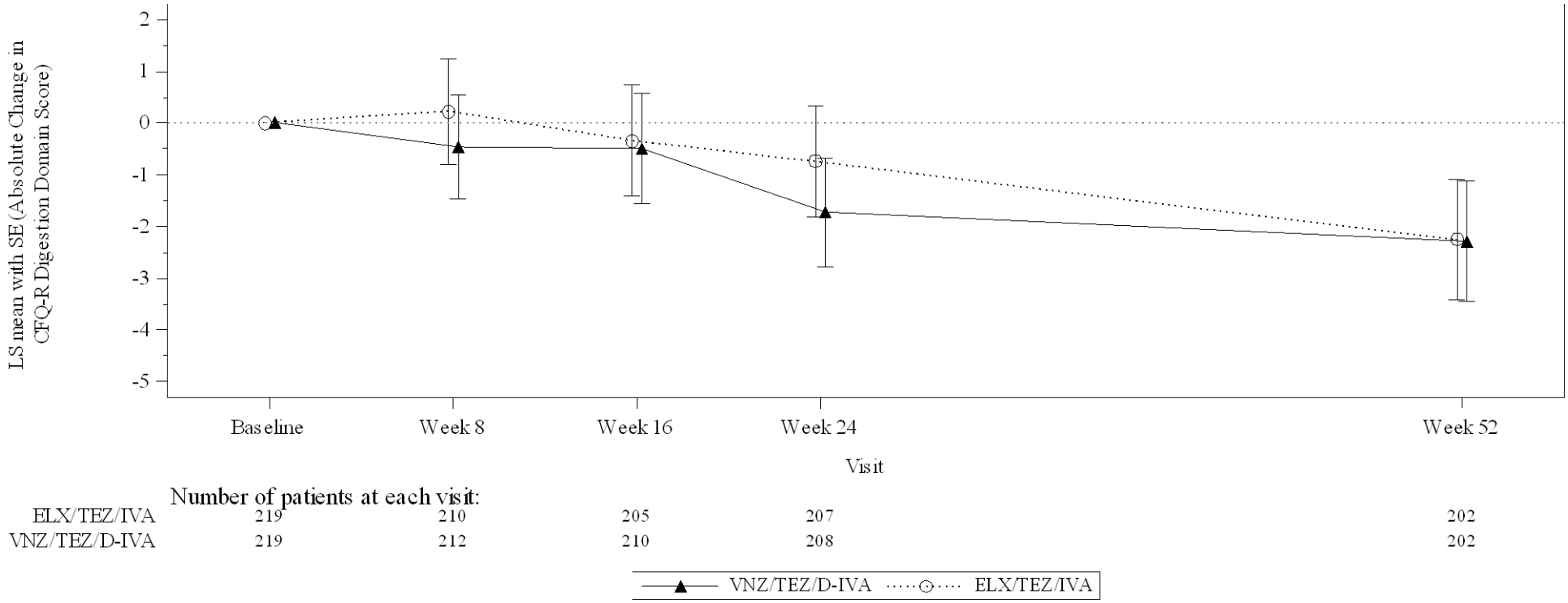
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Prior CFTR modulator use: No



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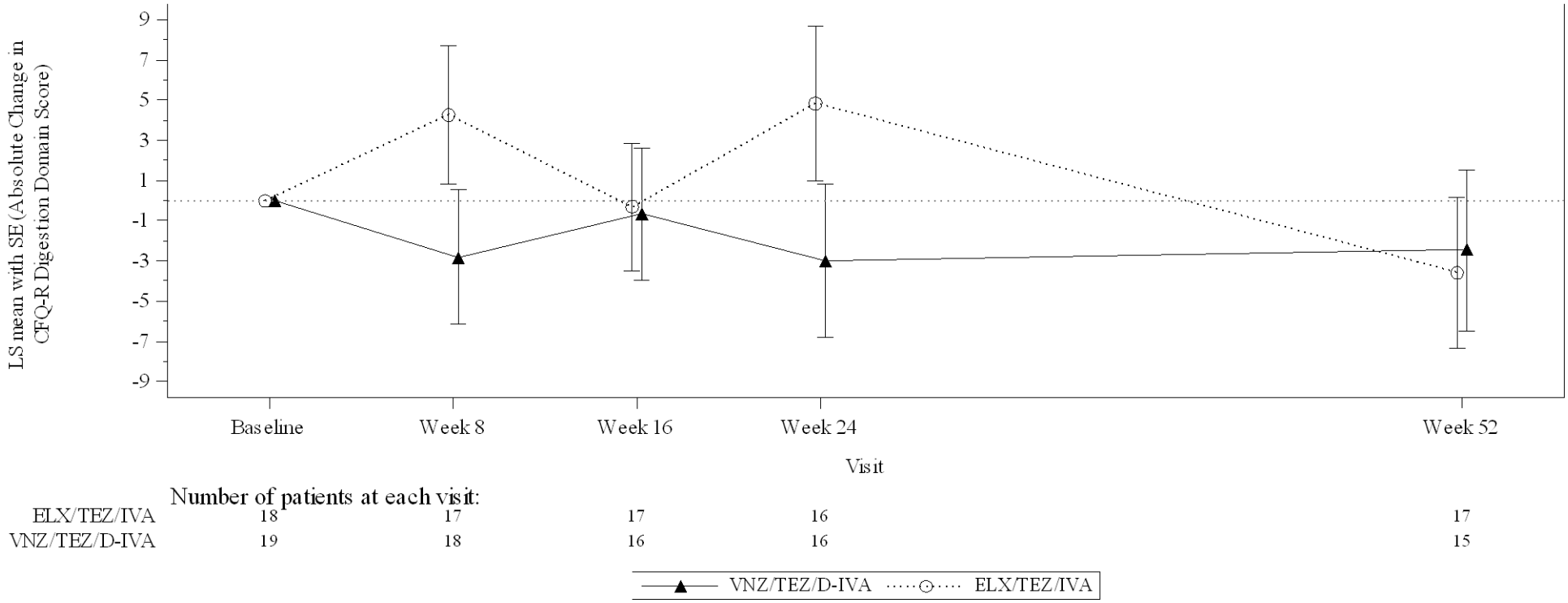
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Genotype group: F/F



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Full Analysis Set

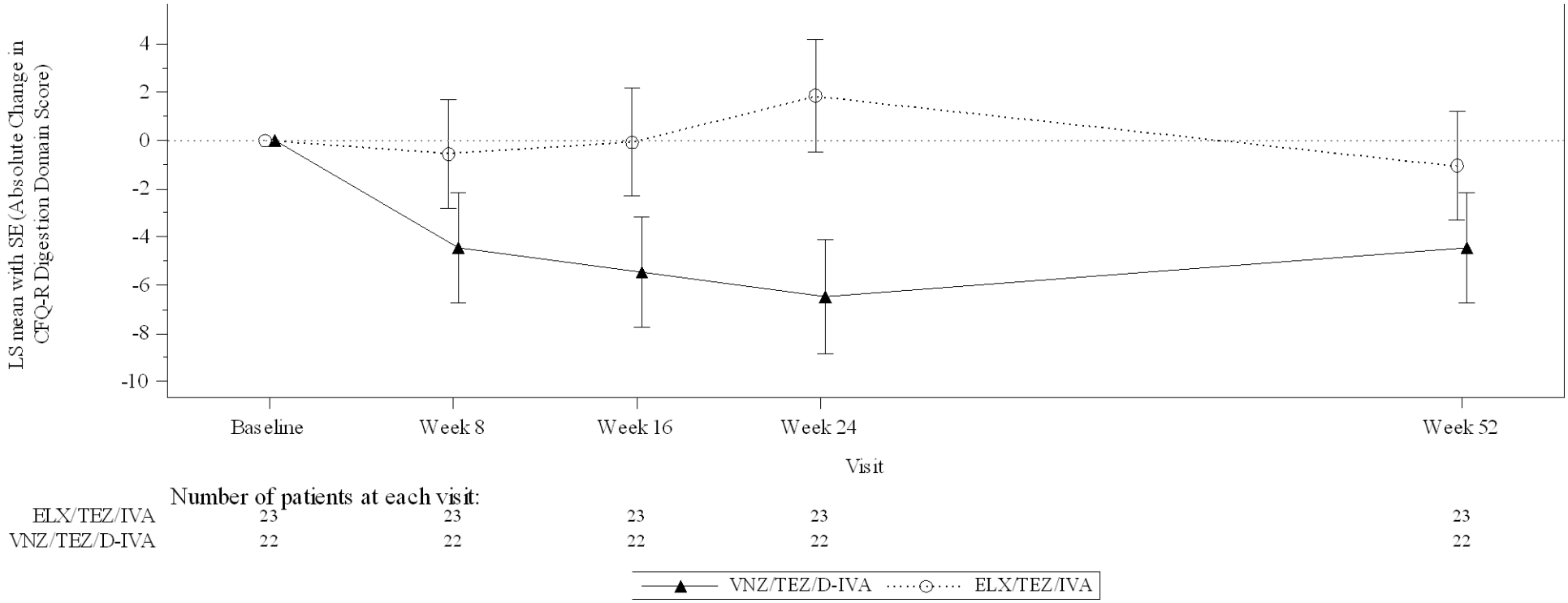
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion
Genotype group: F/G



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Full Analysis Set

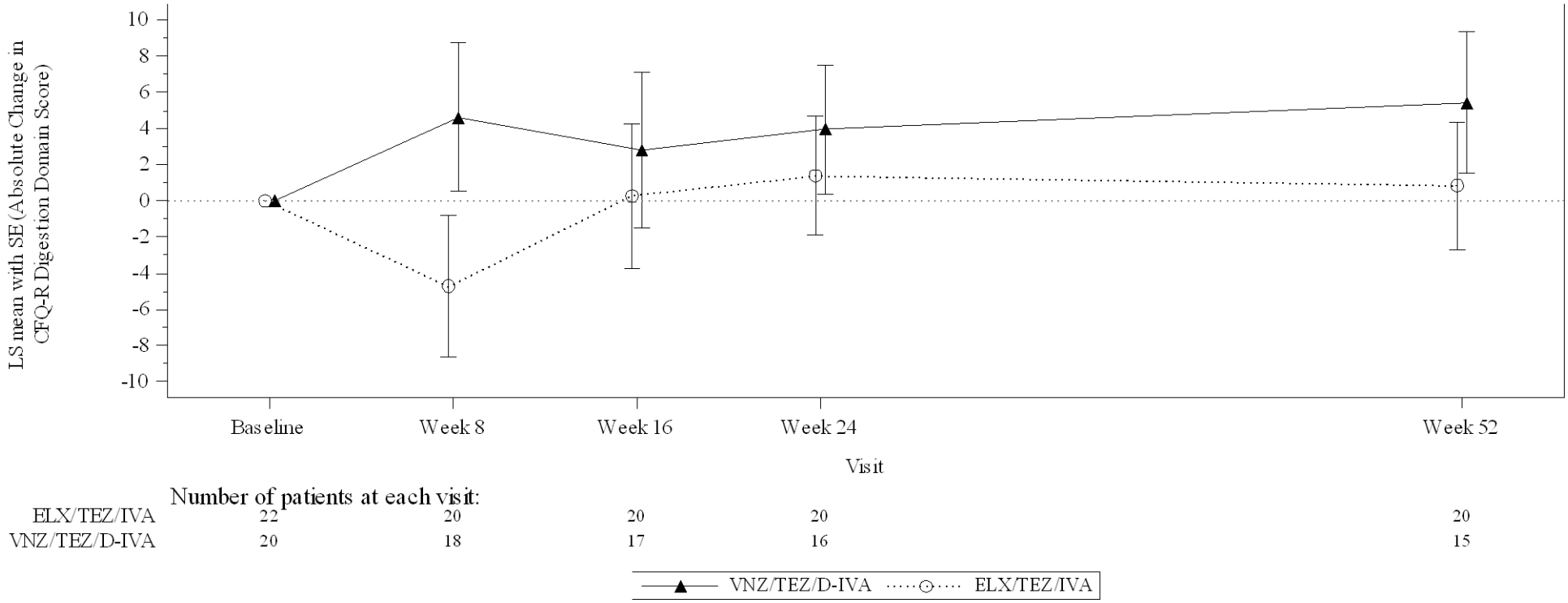
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Domain: Digestion
Genotype group: F/RF



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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

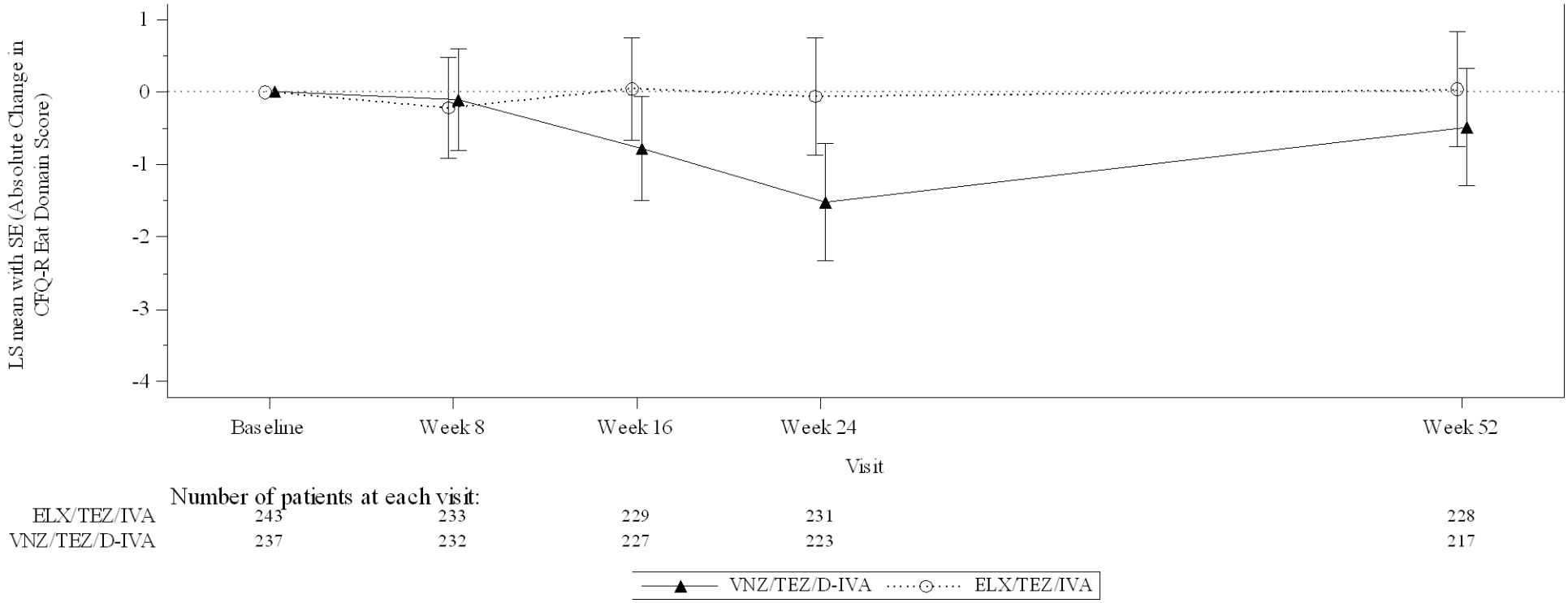
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
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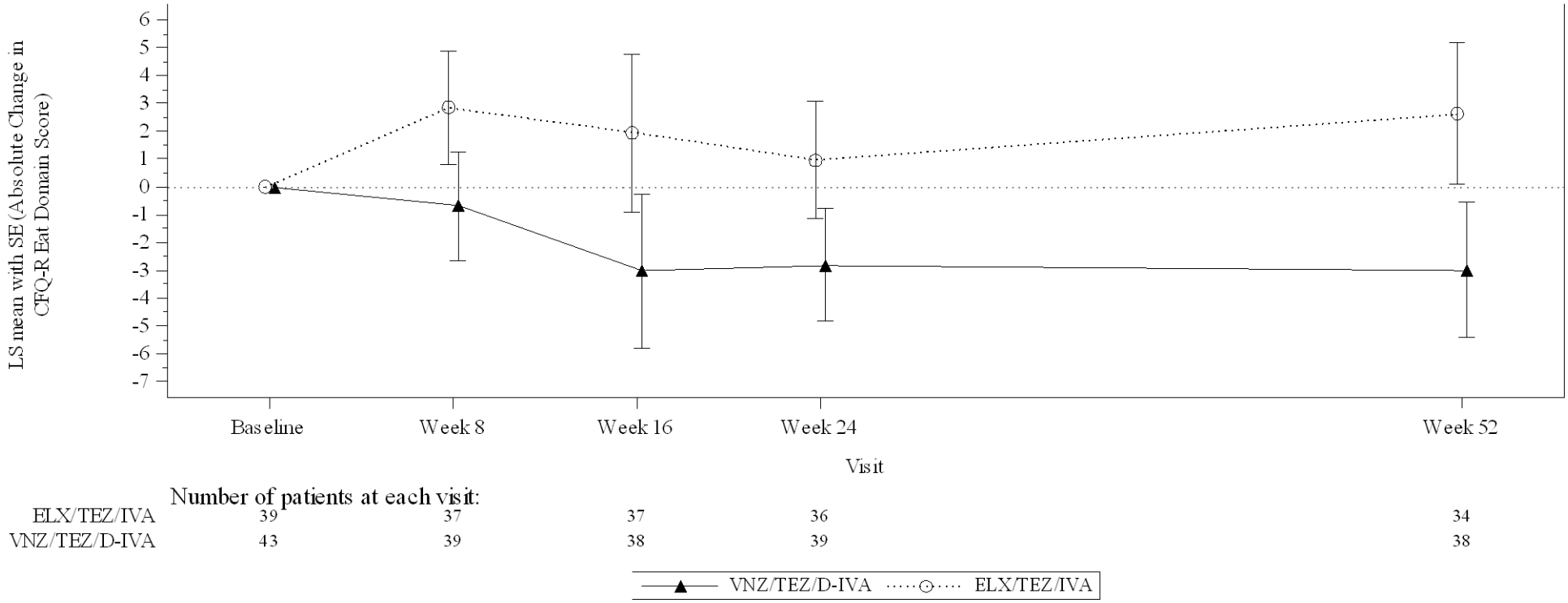
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat
Prior CFTR modulator use: Yes



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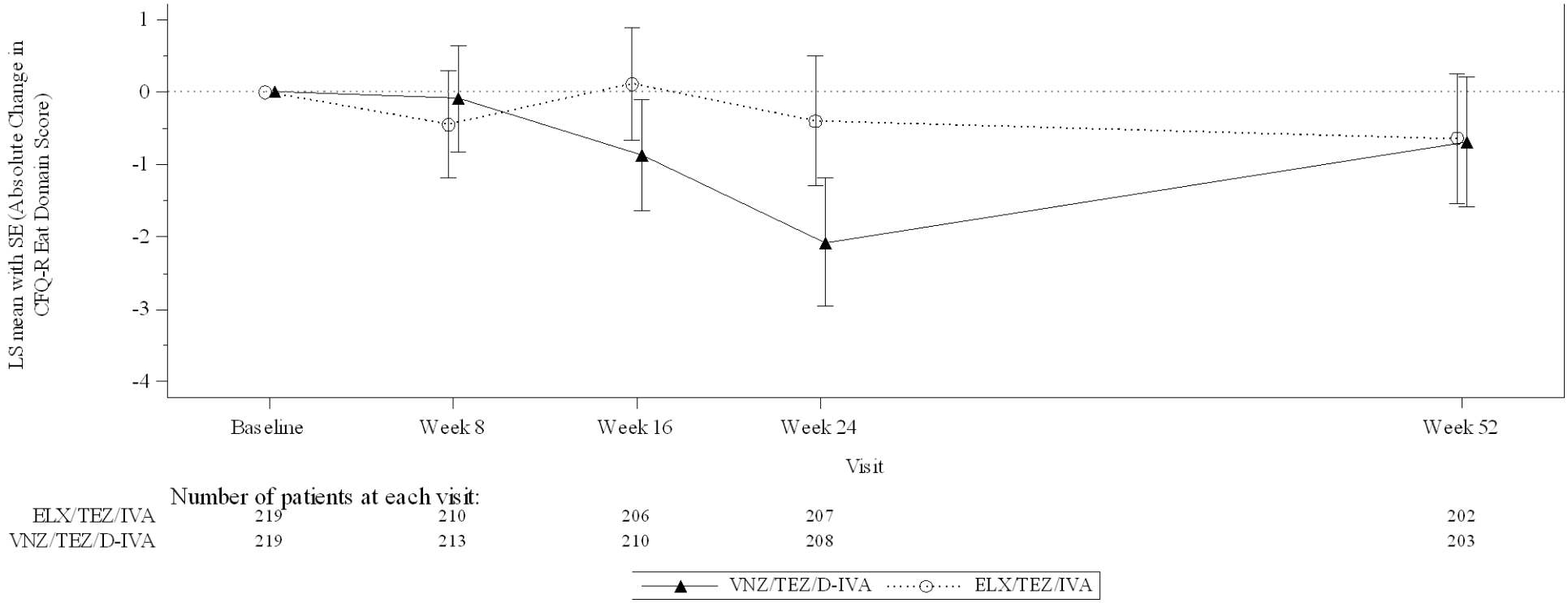
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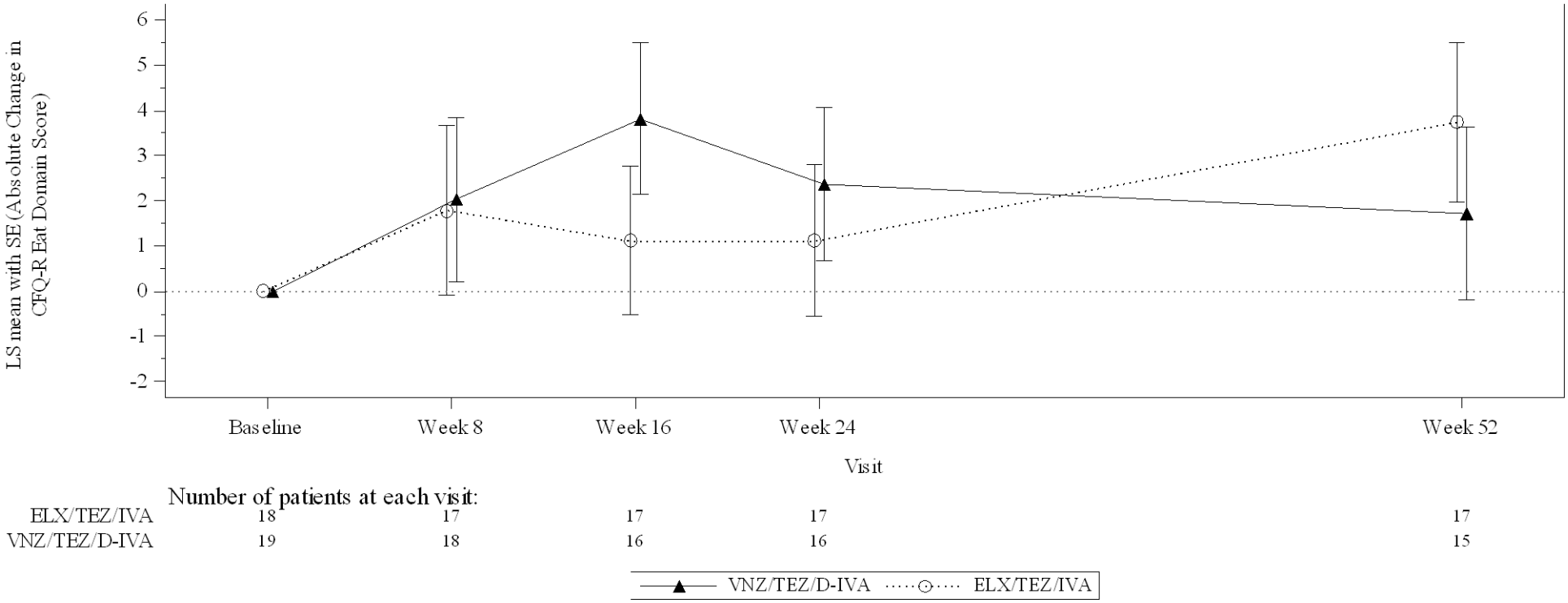
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Genotype group: F/F



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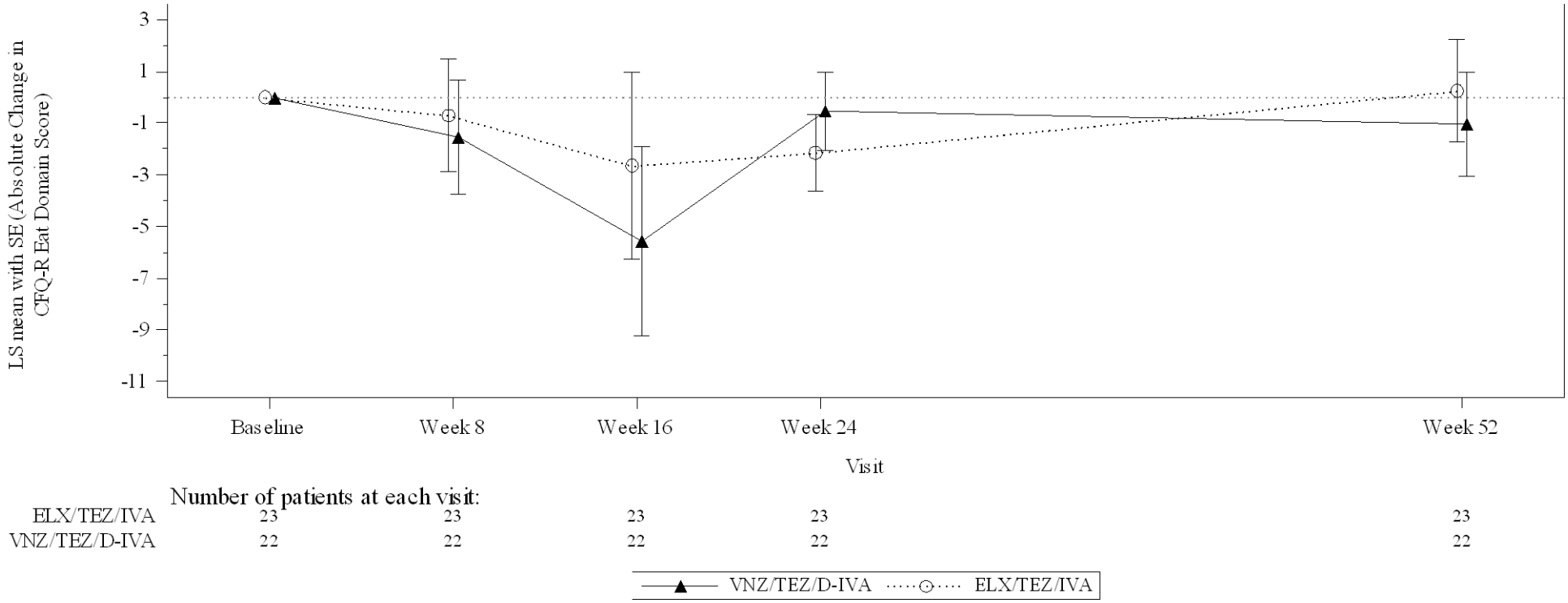
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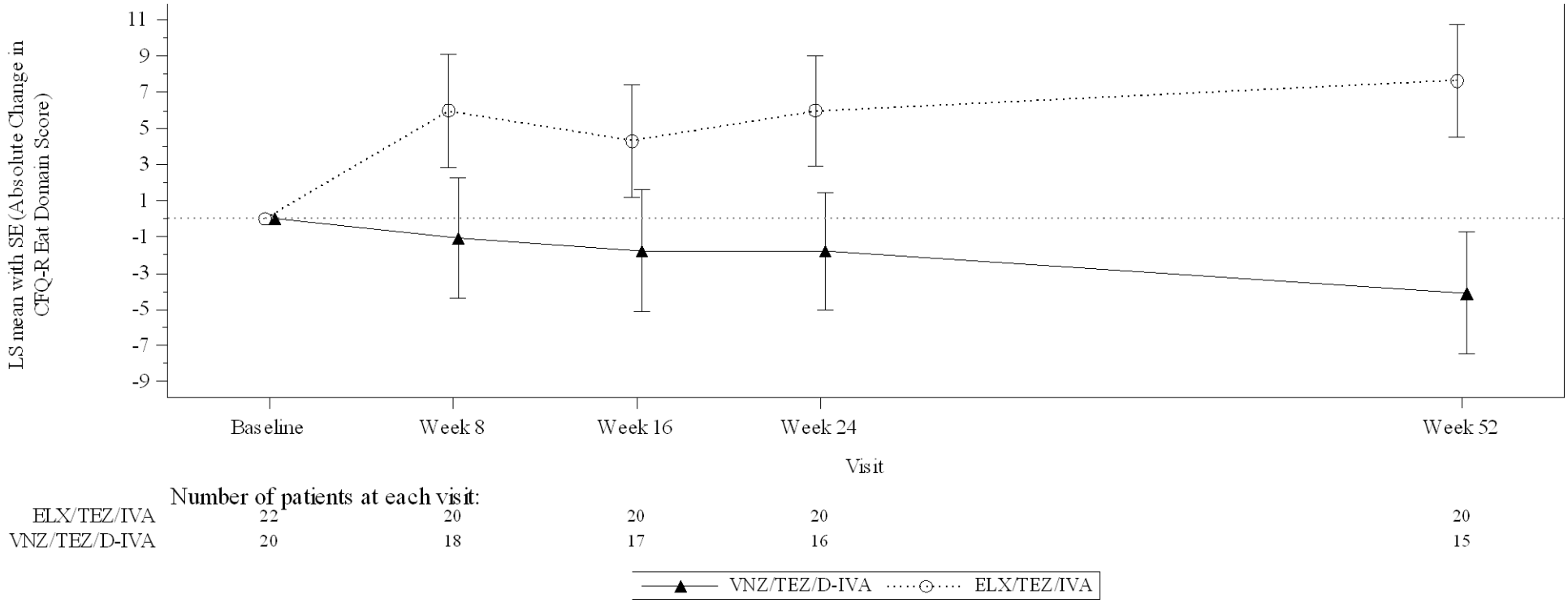
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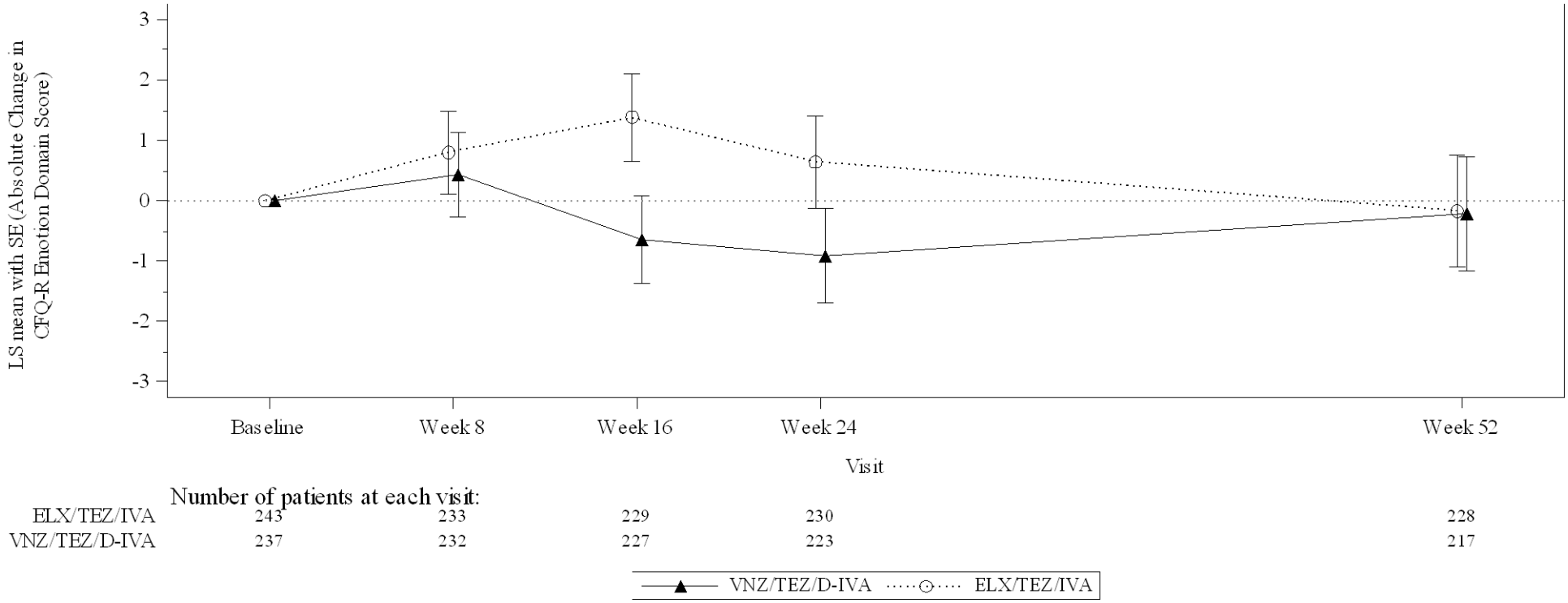
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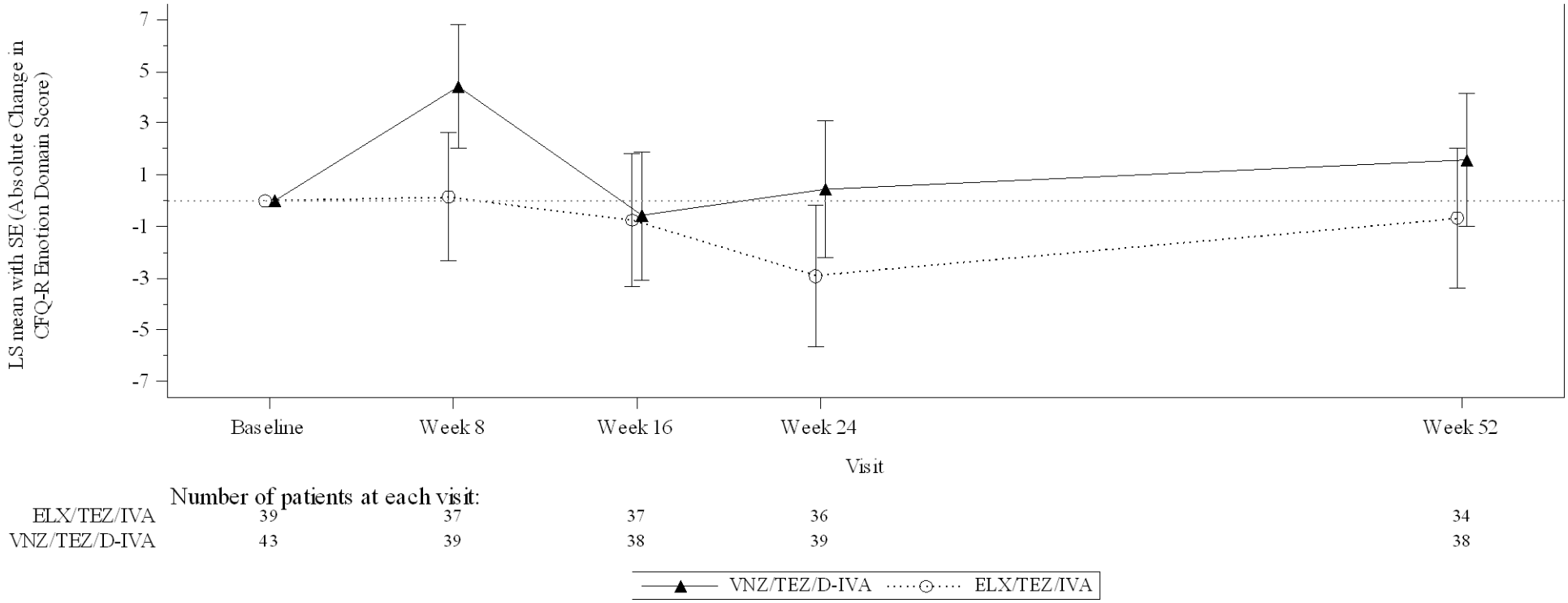
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Prior CFTR modulator use: Yes



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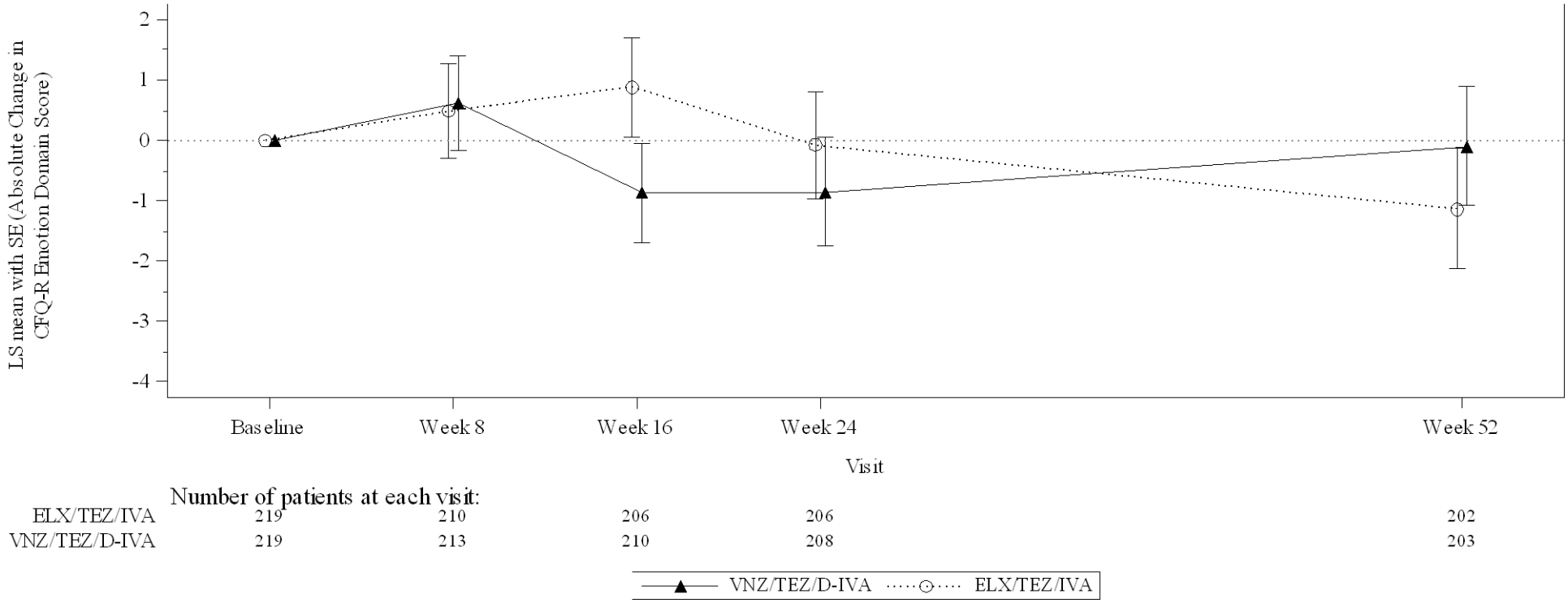
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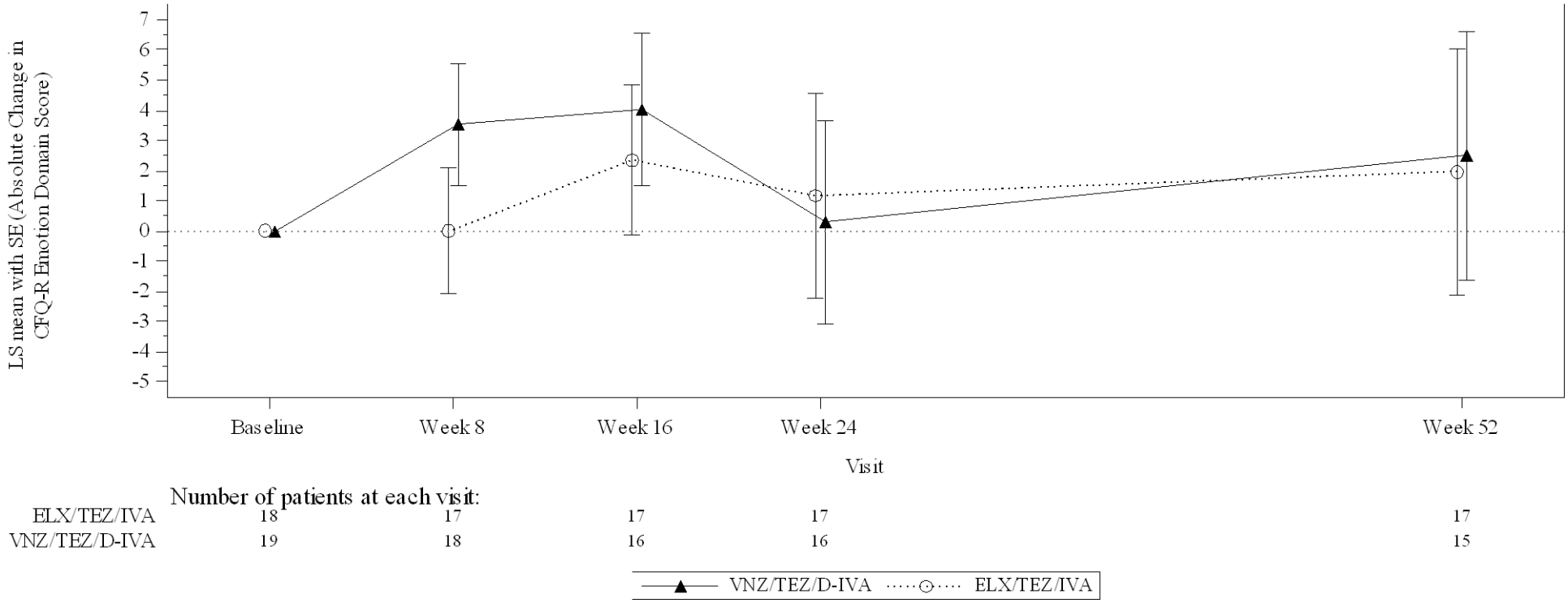
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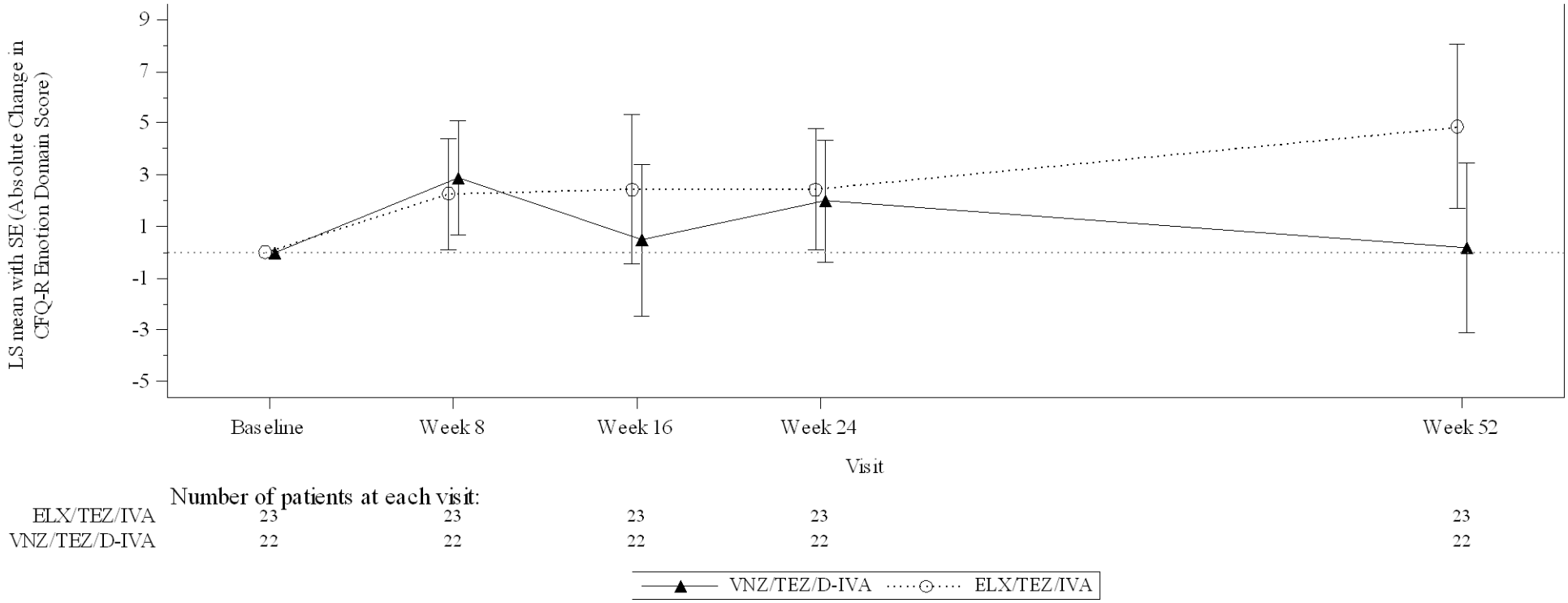
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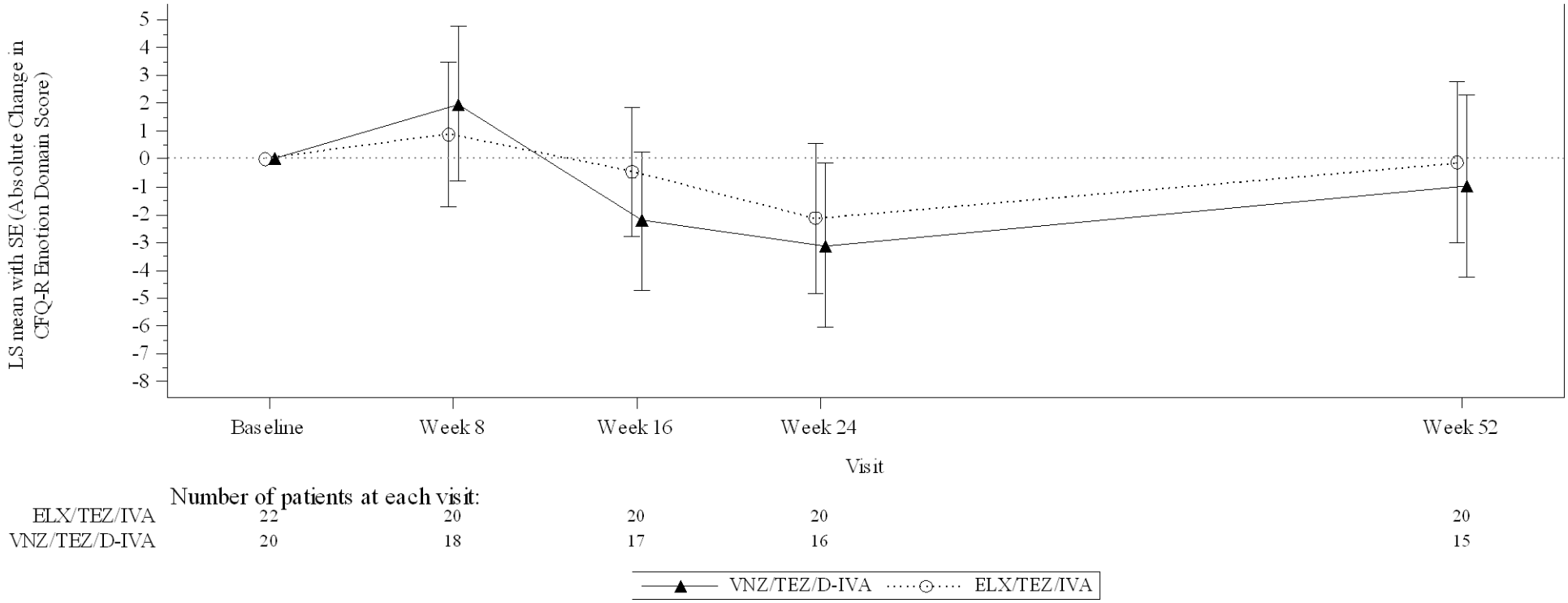
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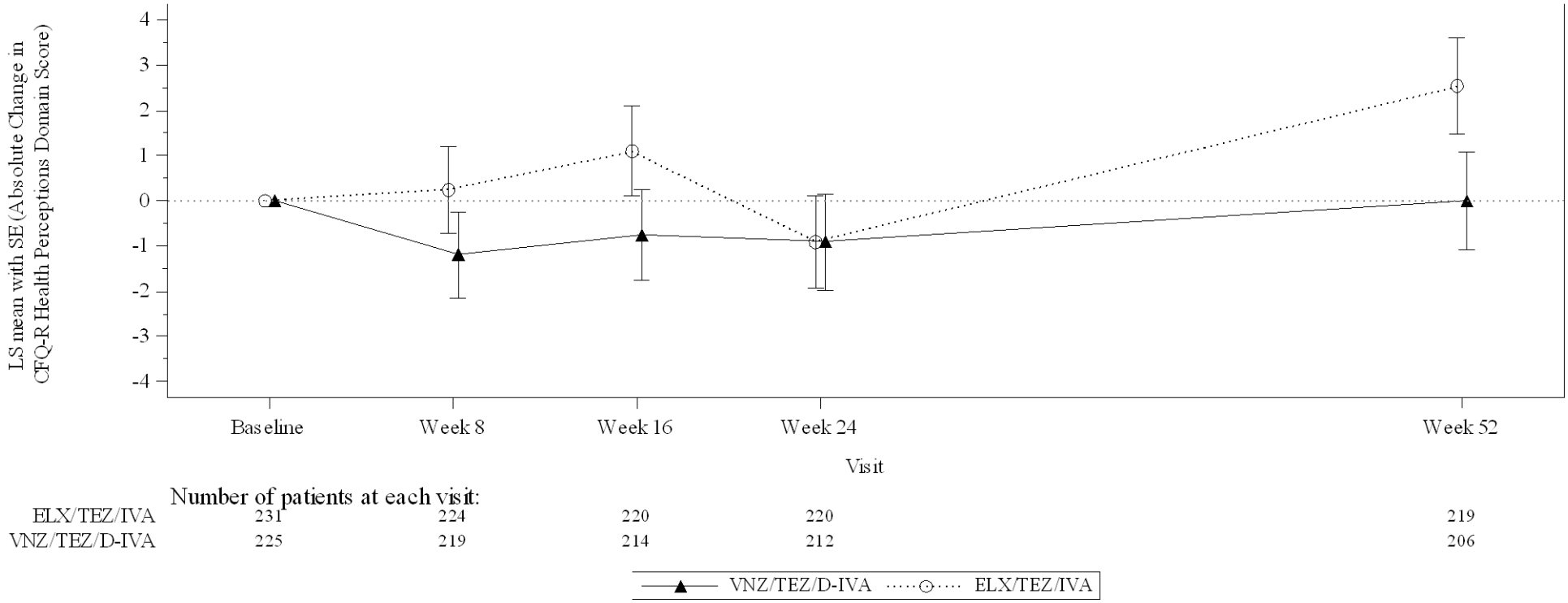
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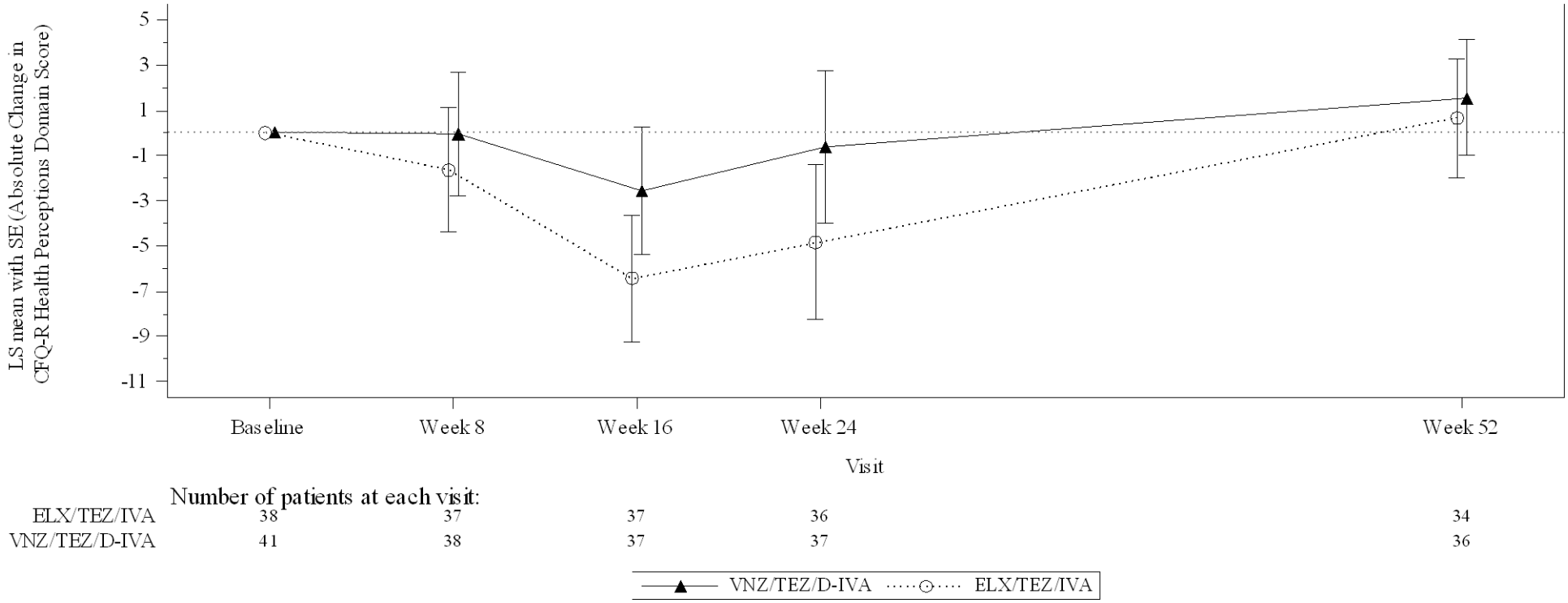
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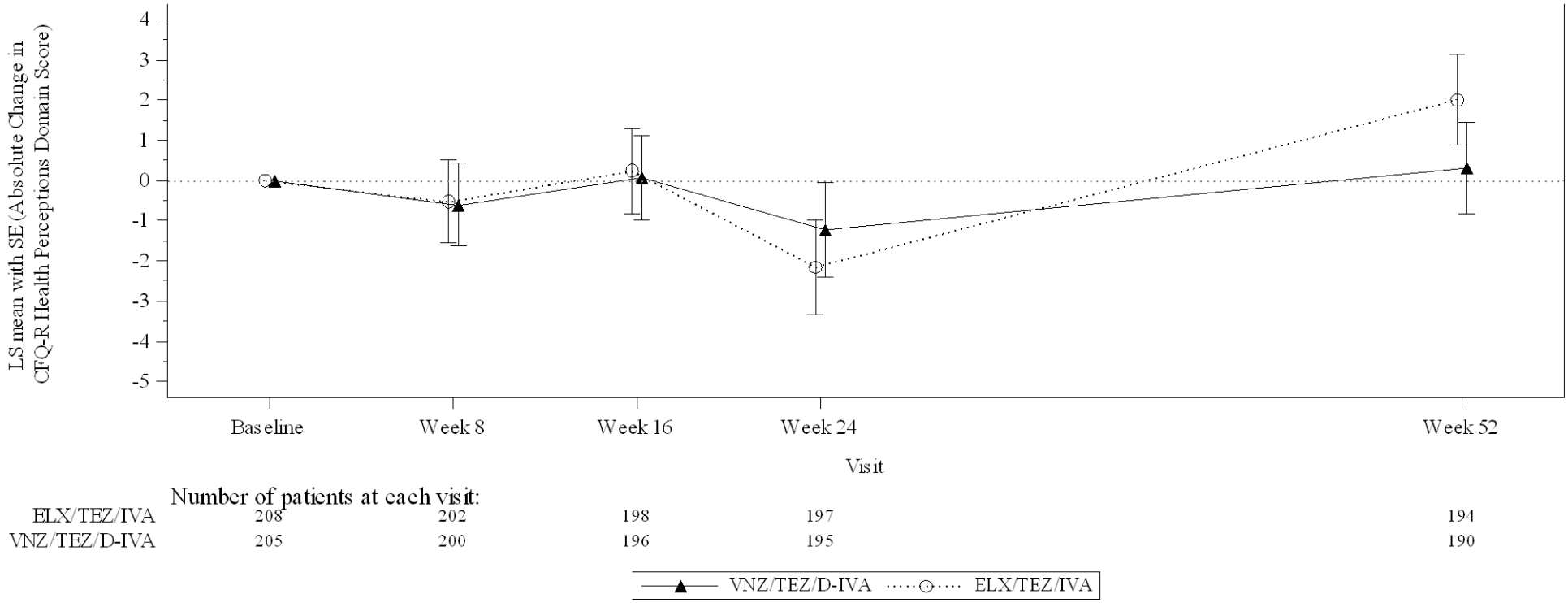
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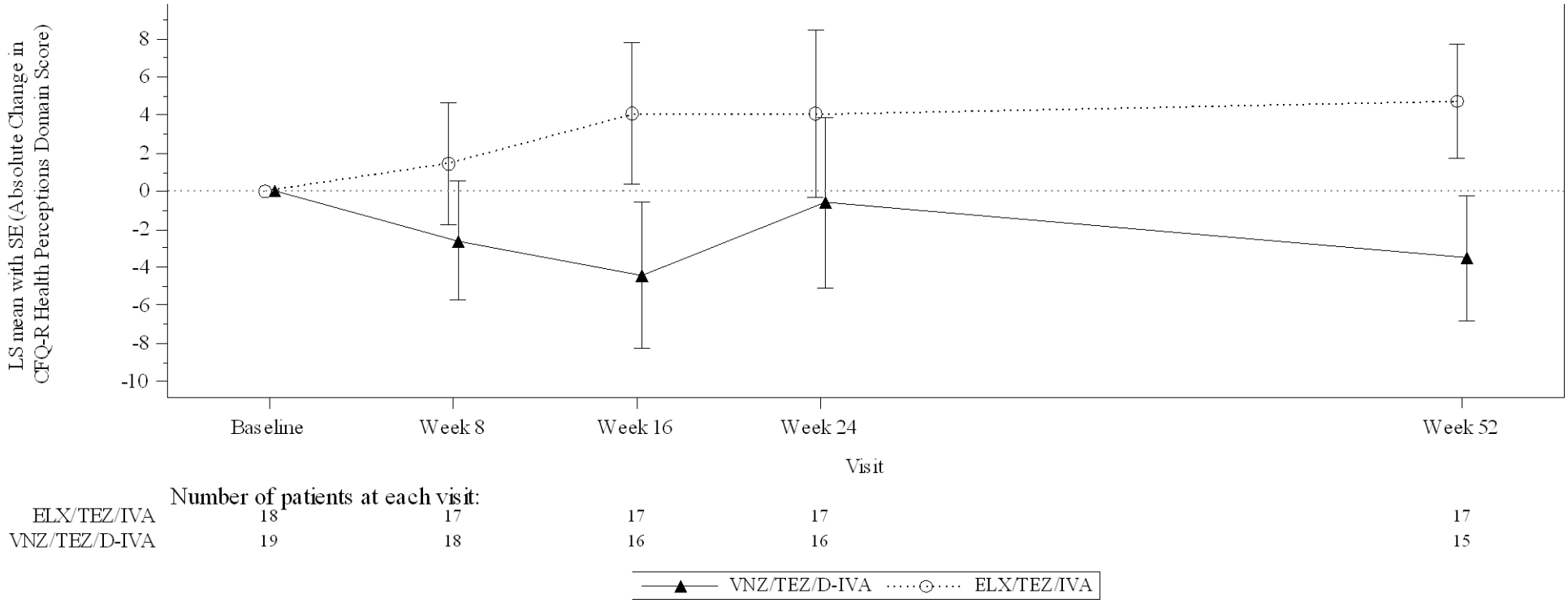
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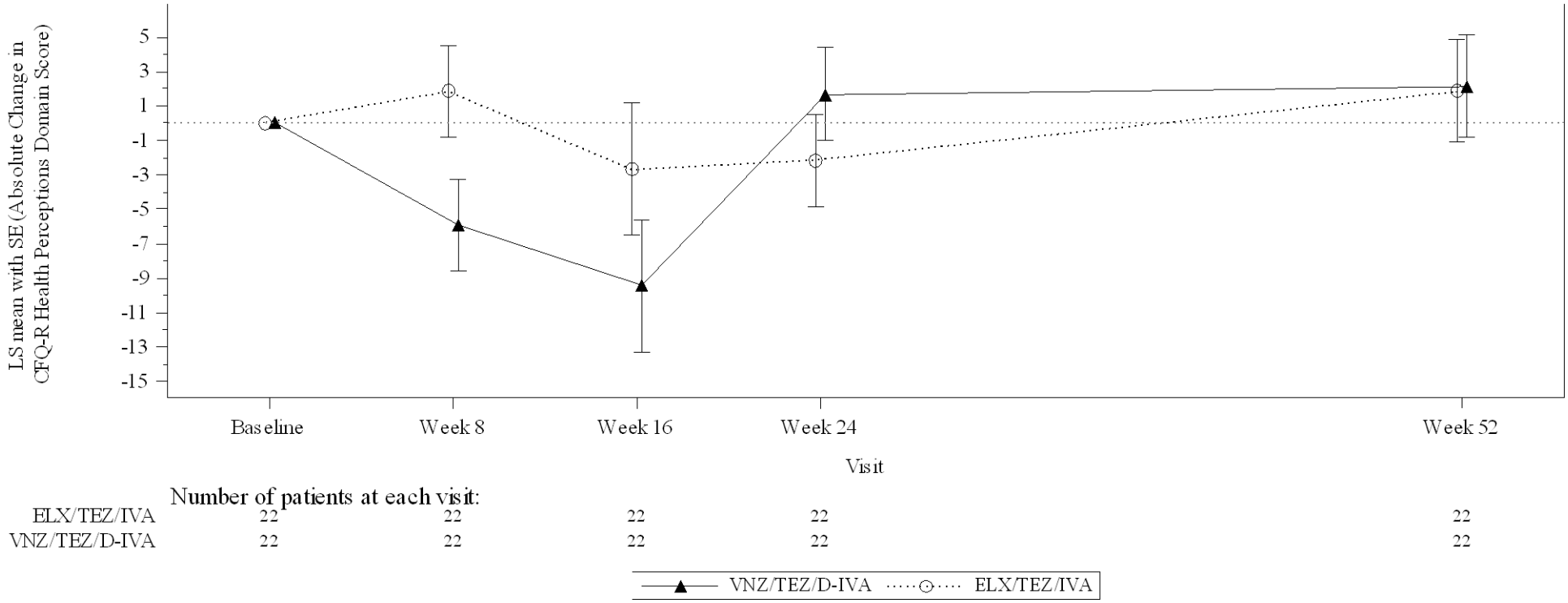
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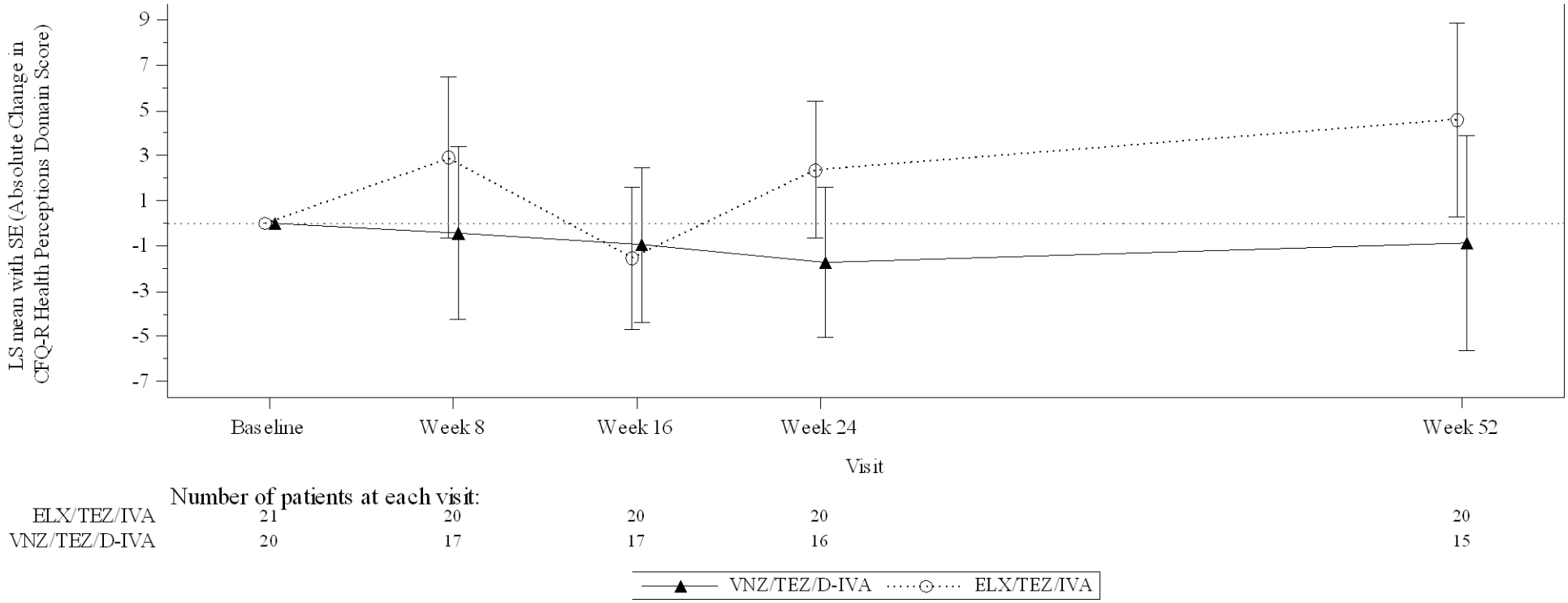
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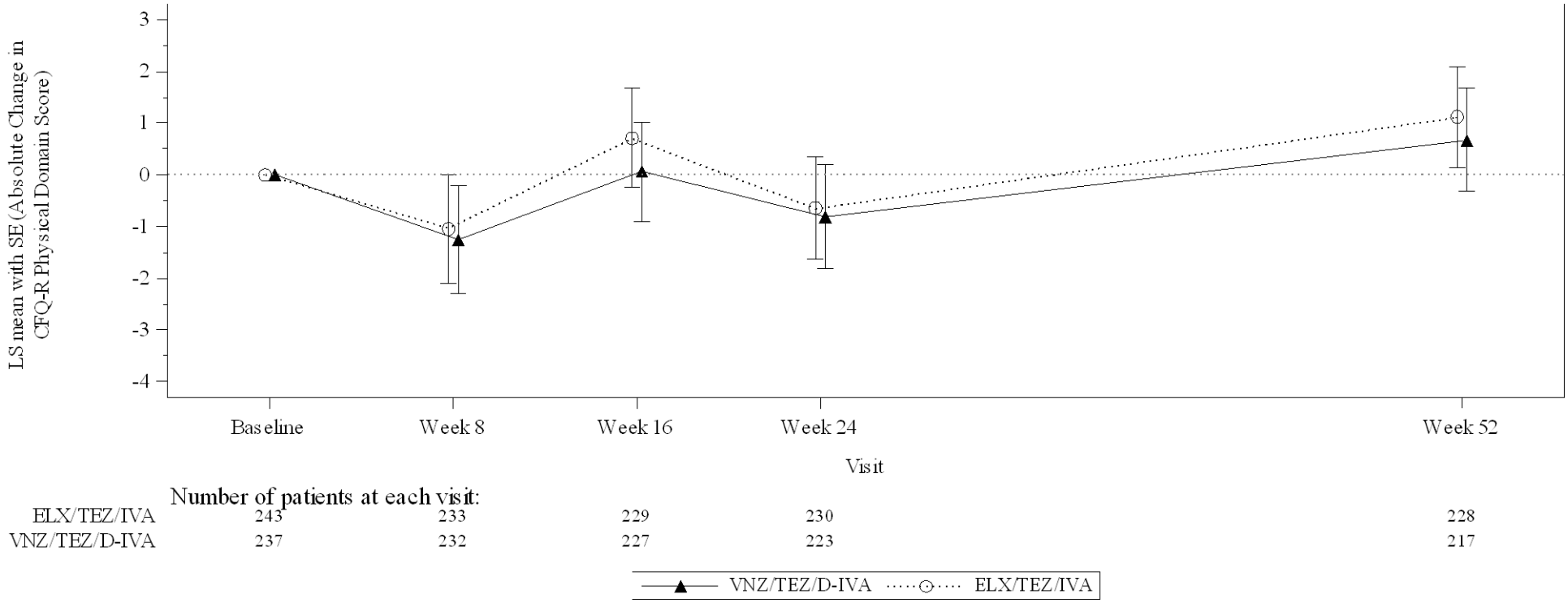
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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

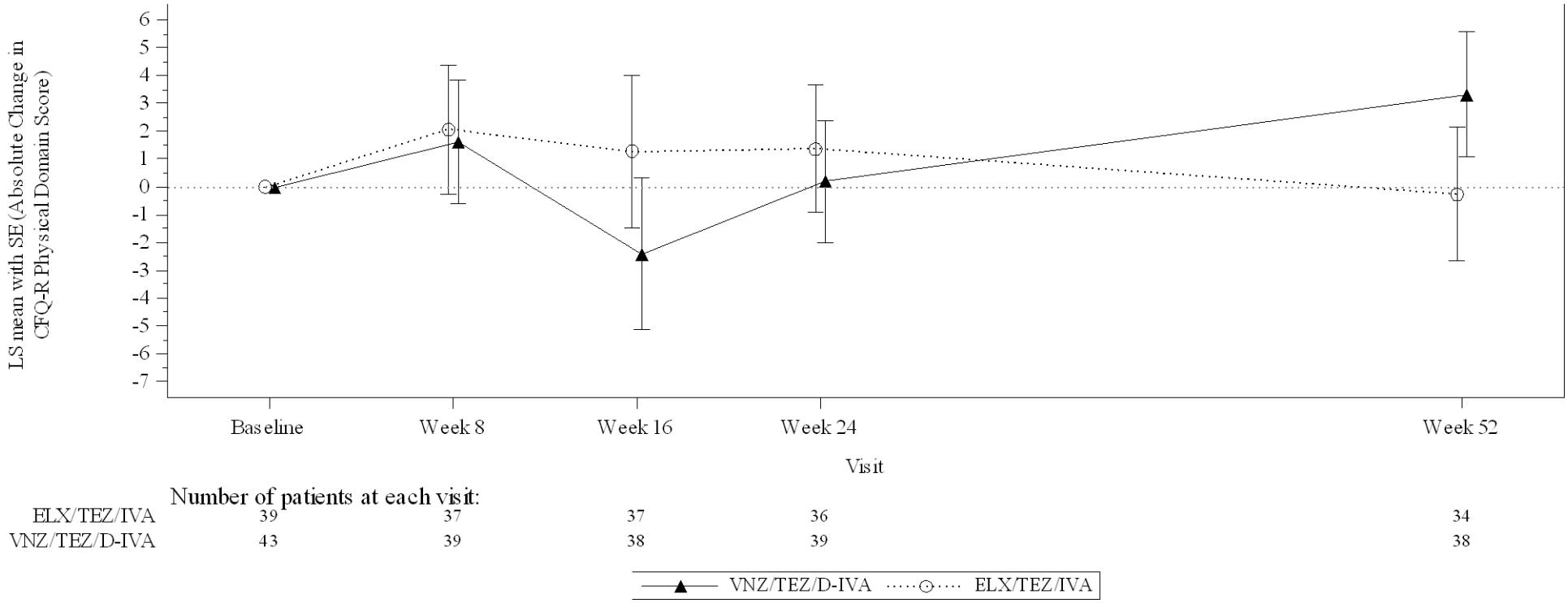
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical
Prior CFTR modulator use: Yes



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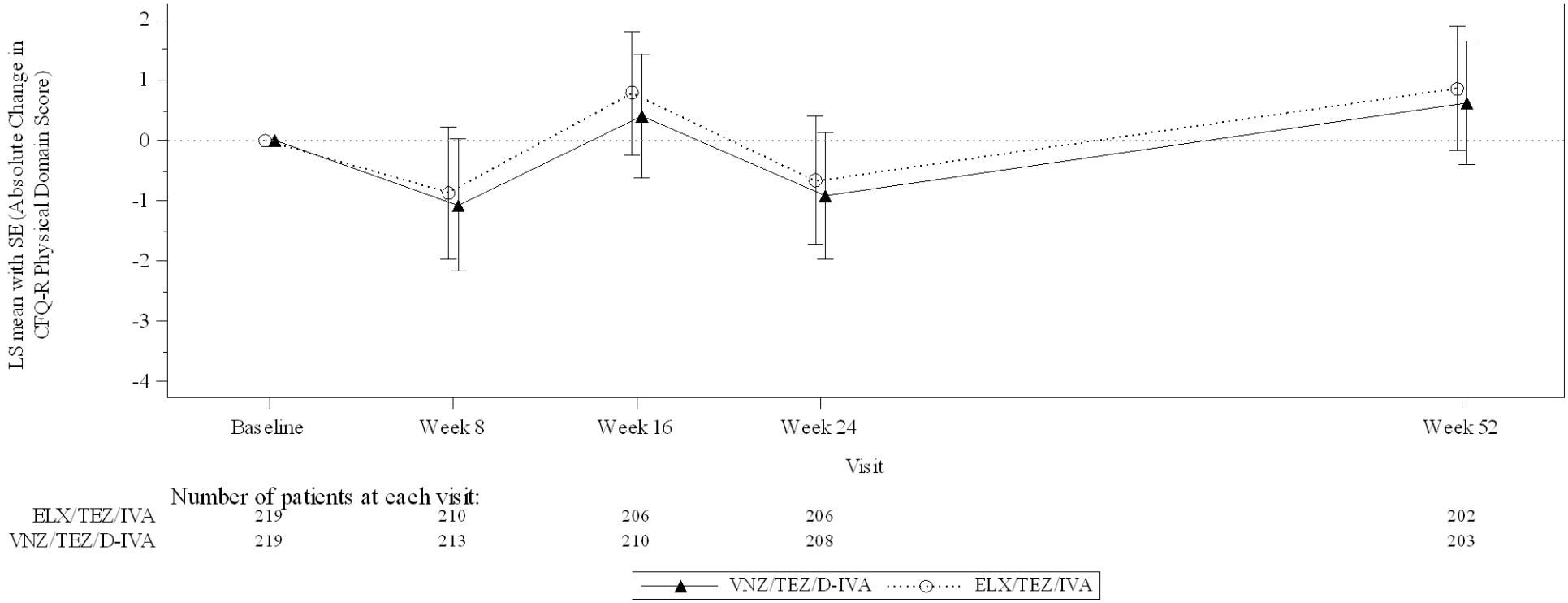
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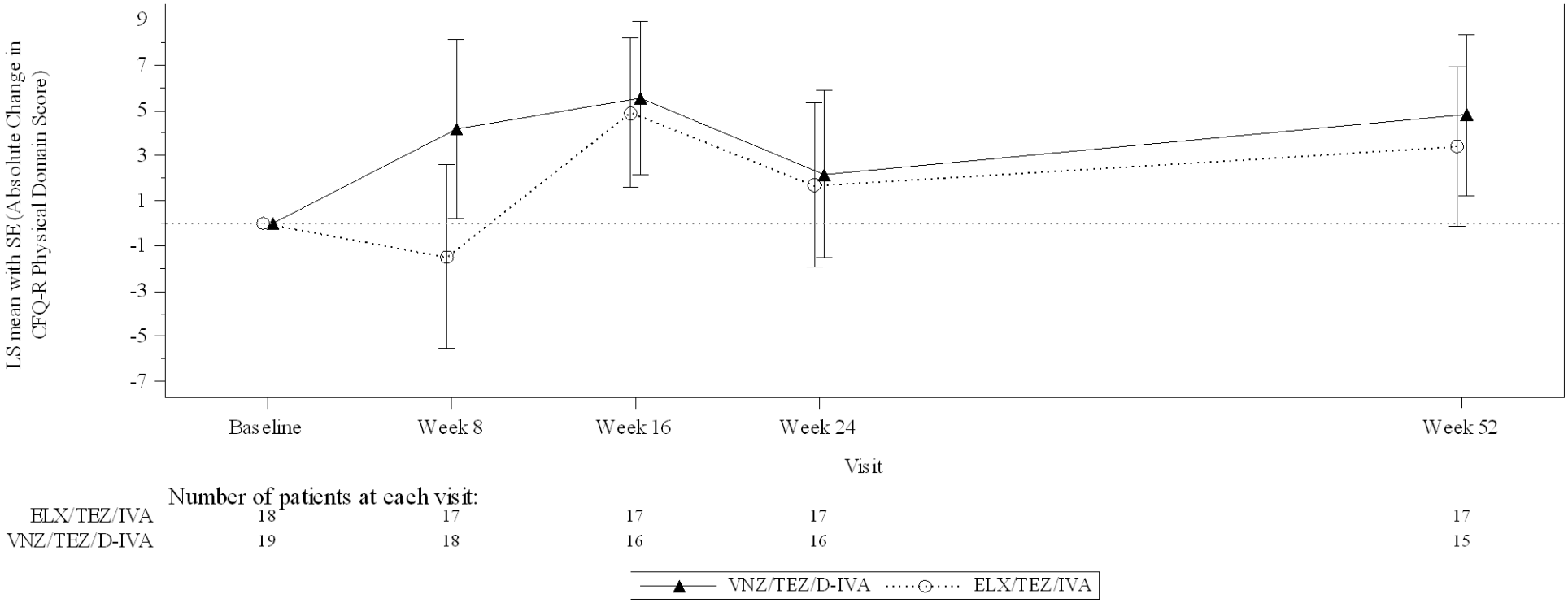
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
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Genotype group: F/F



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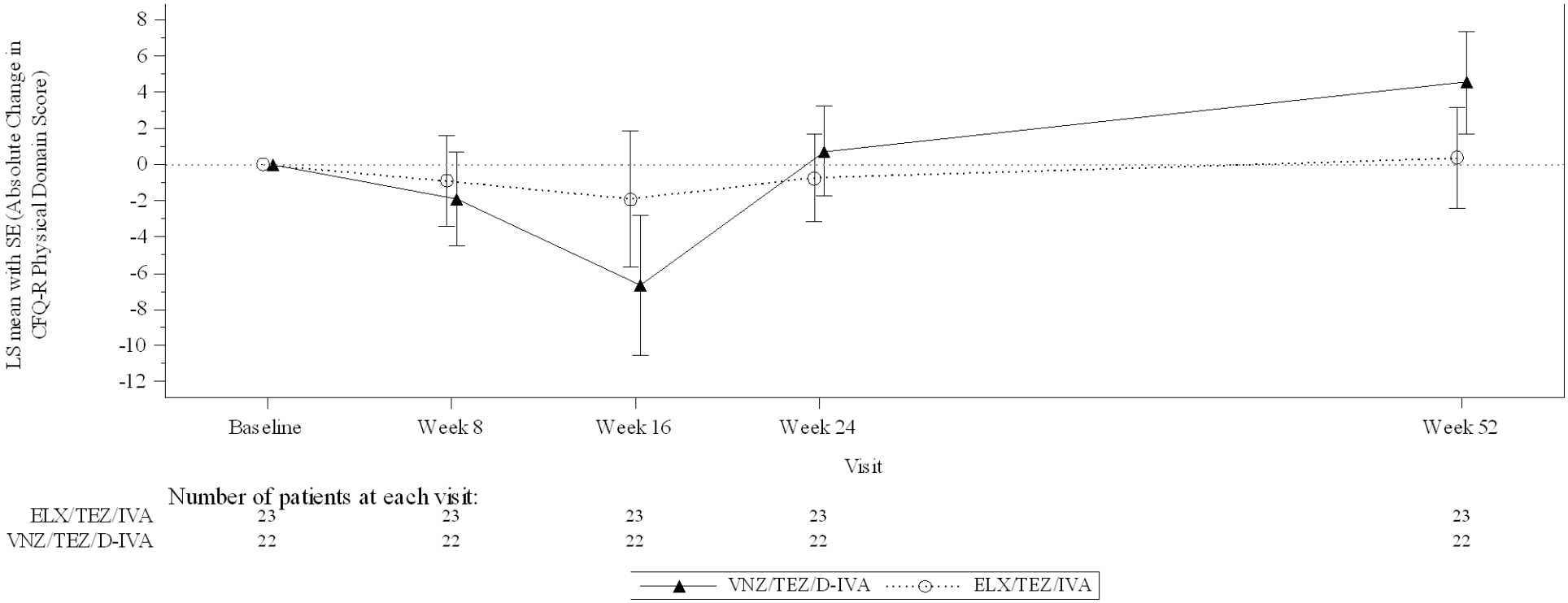
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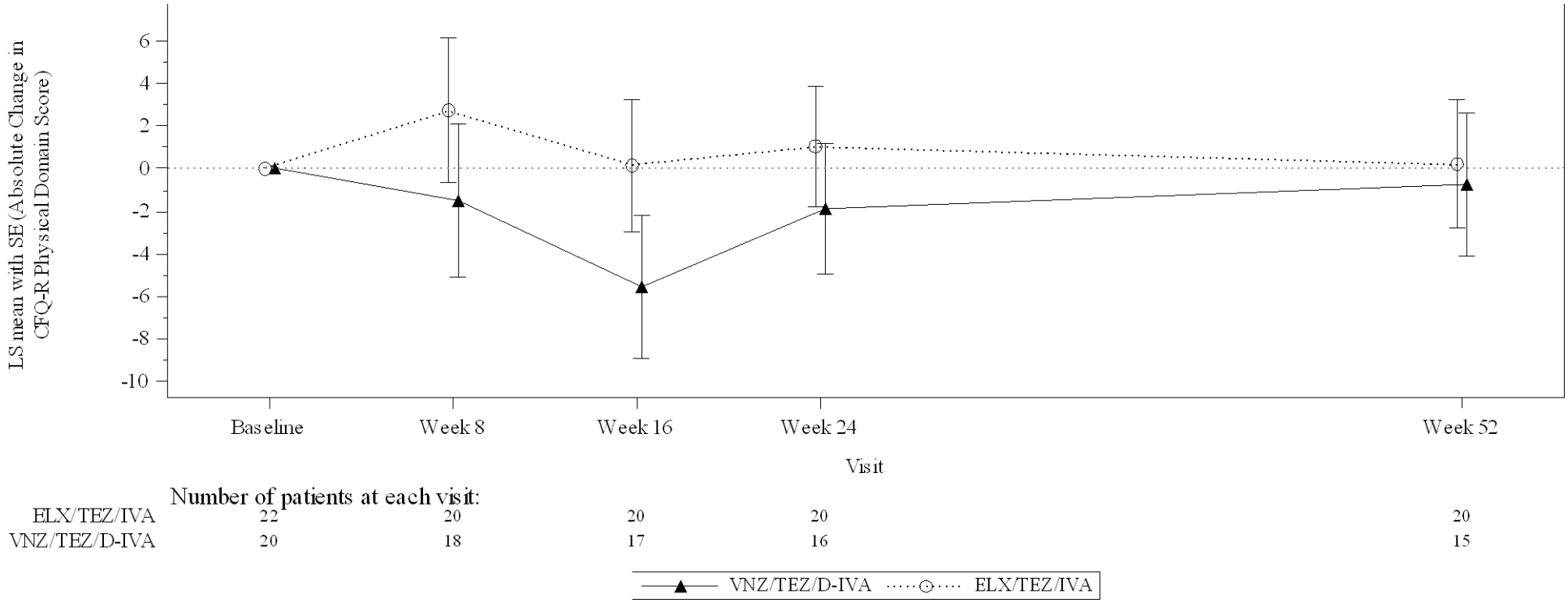
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Domain: Physical
Genotype group: F/RF



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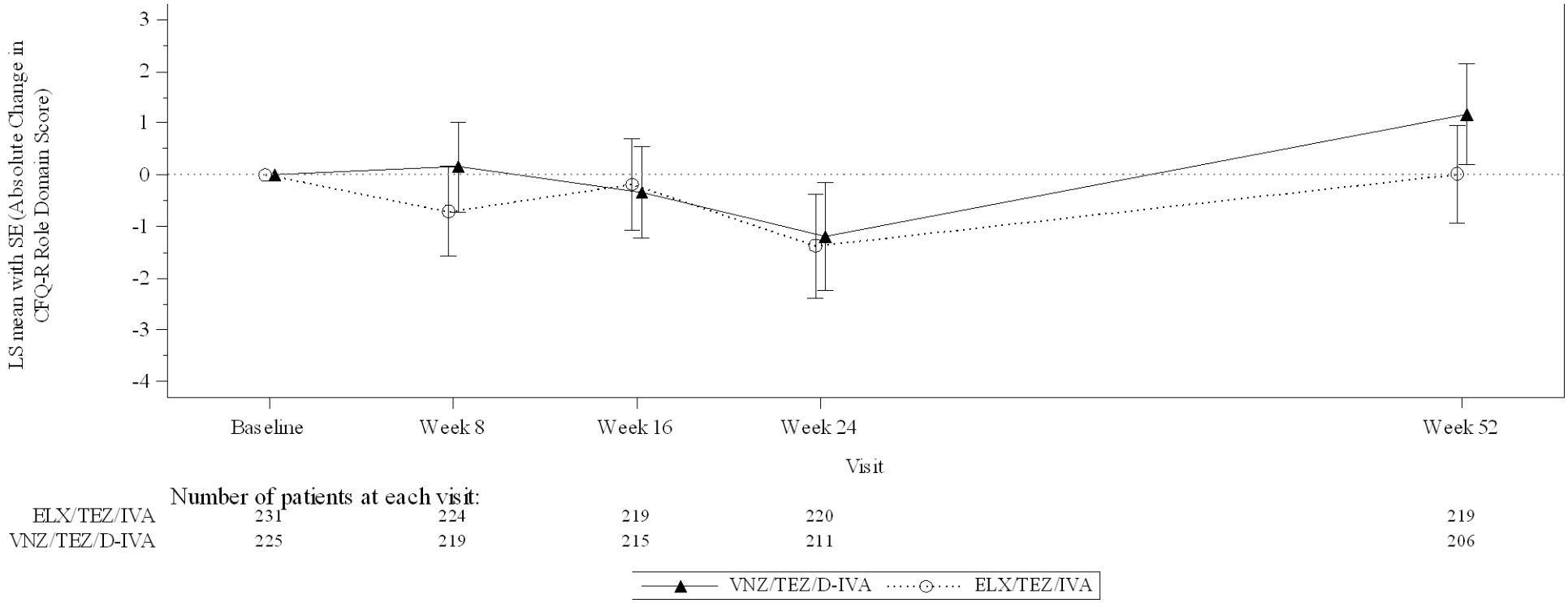
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Domain: Physical
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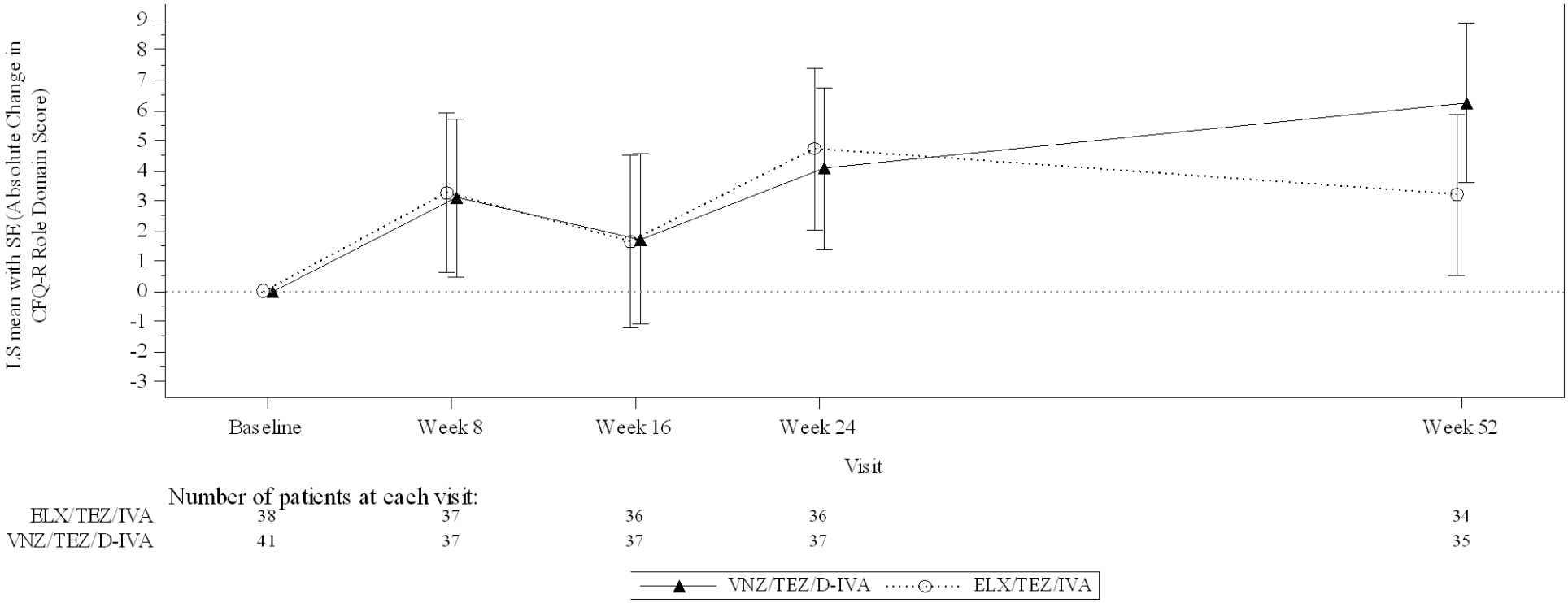
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
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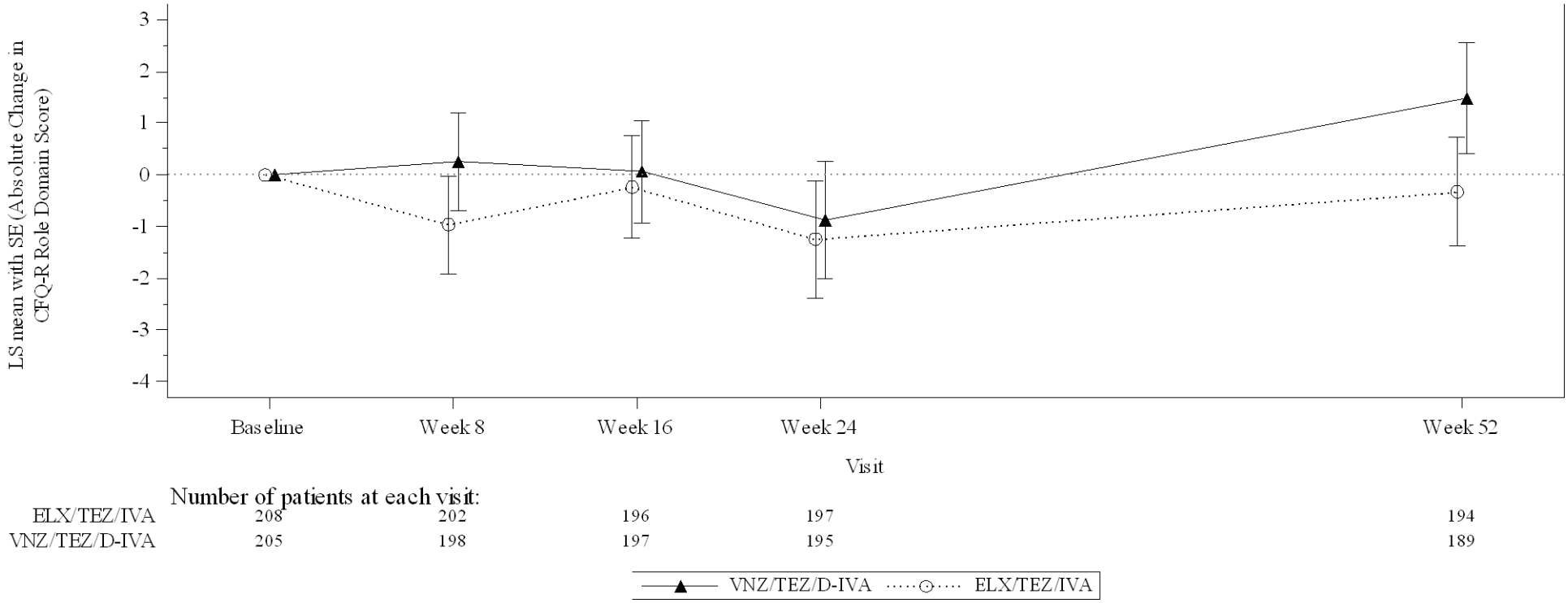
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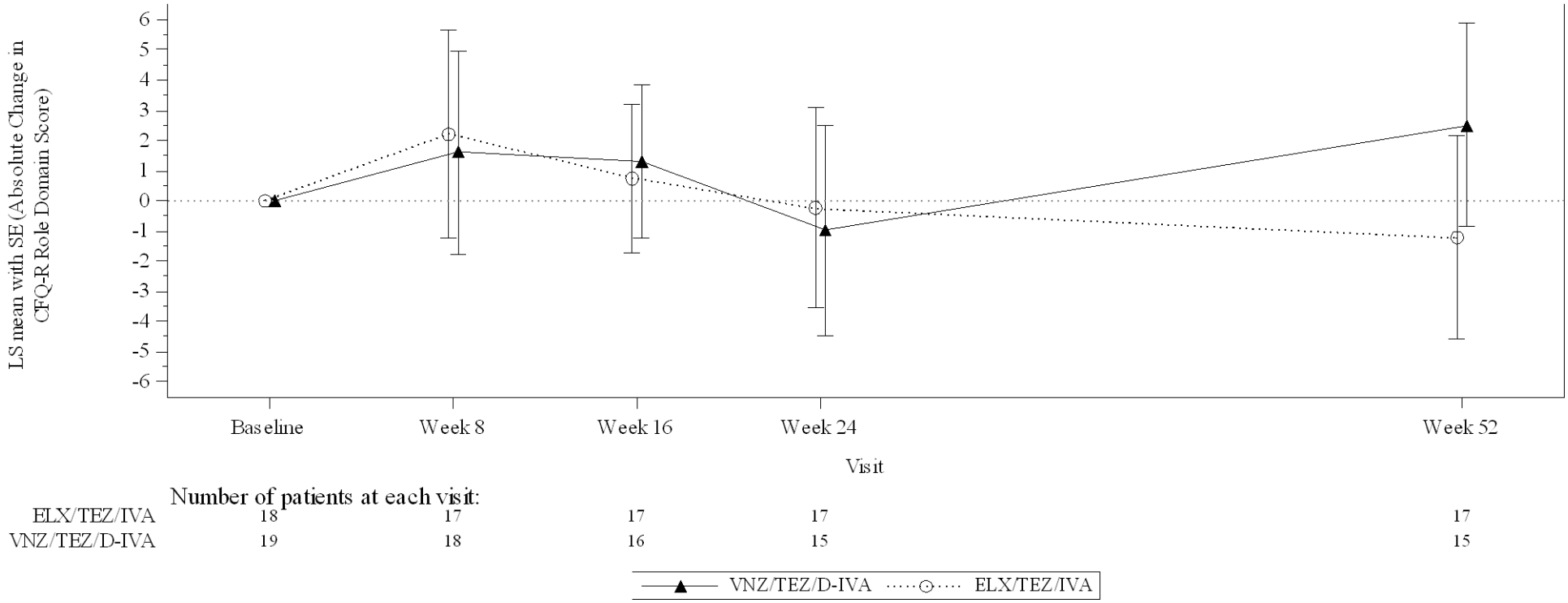
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role
Genotype group: F/F



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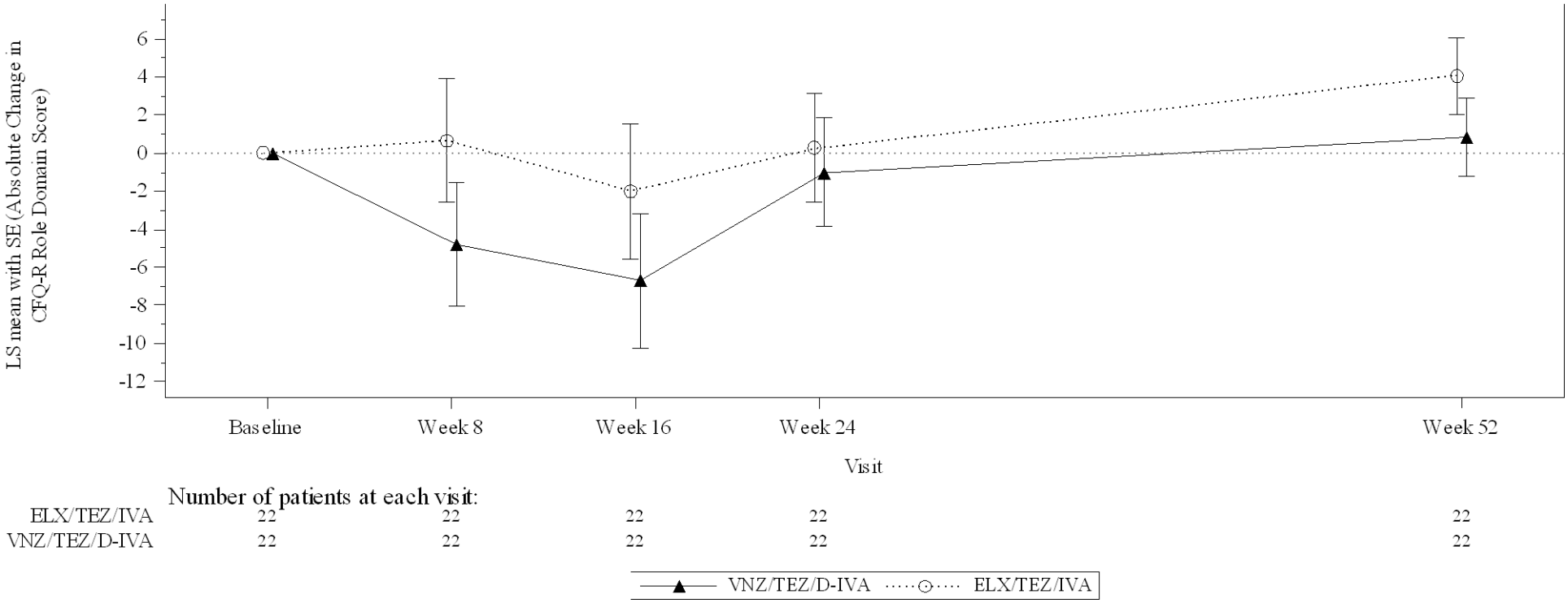
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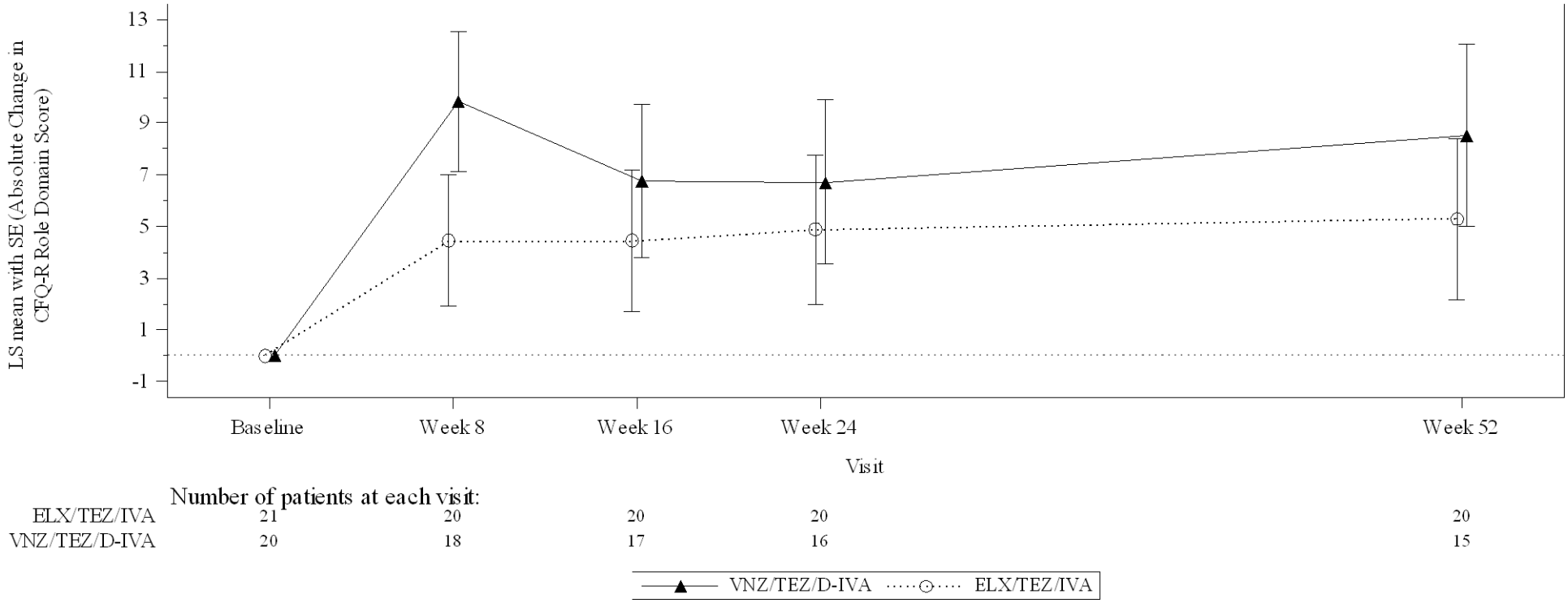
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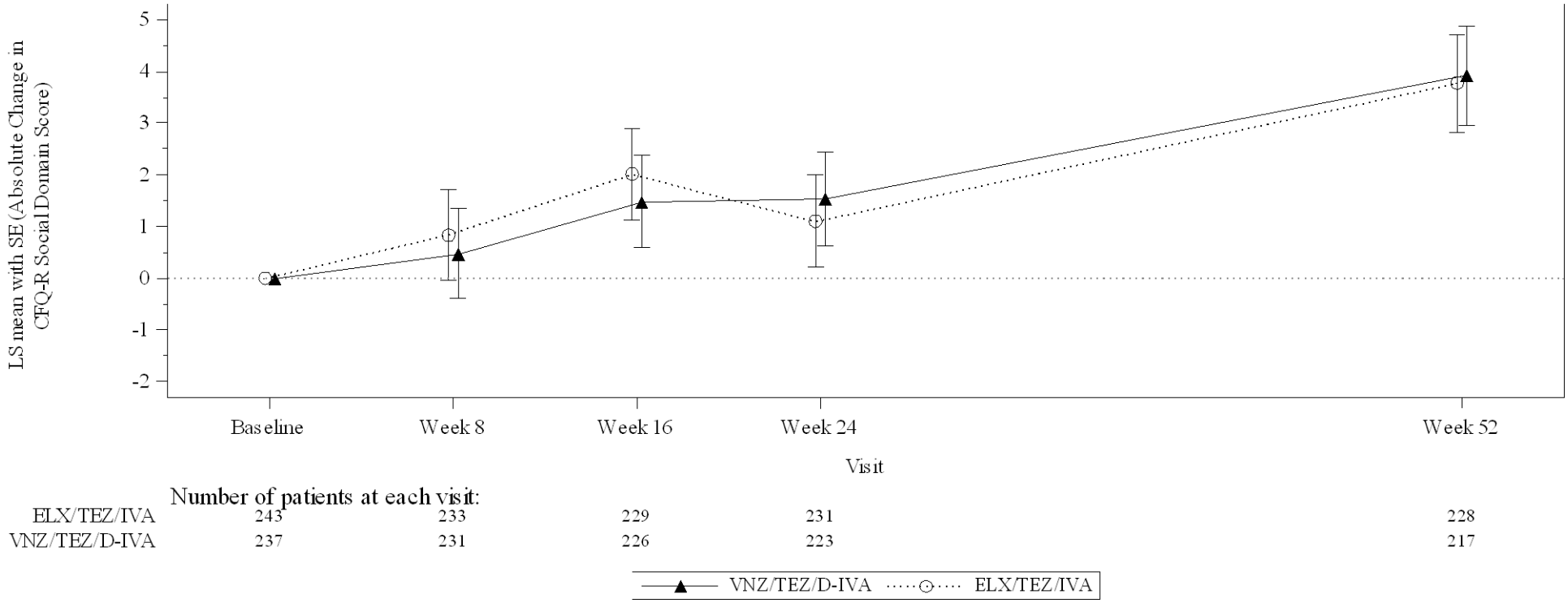
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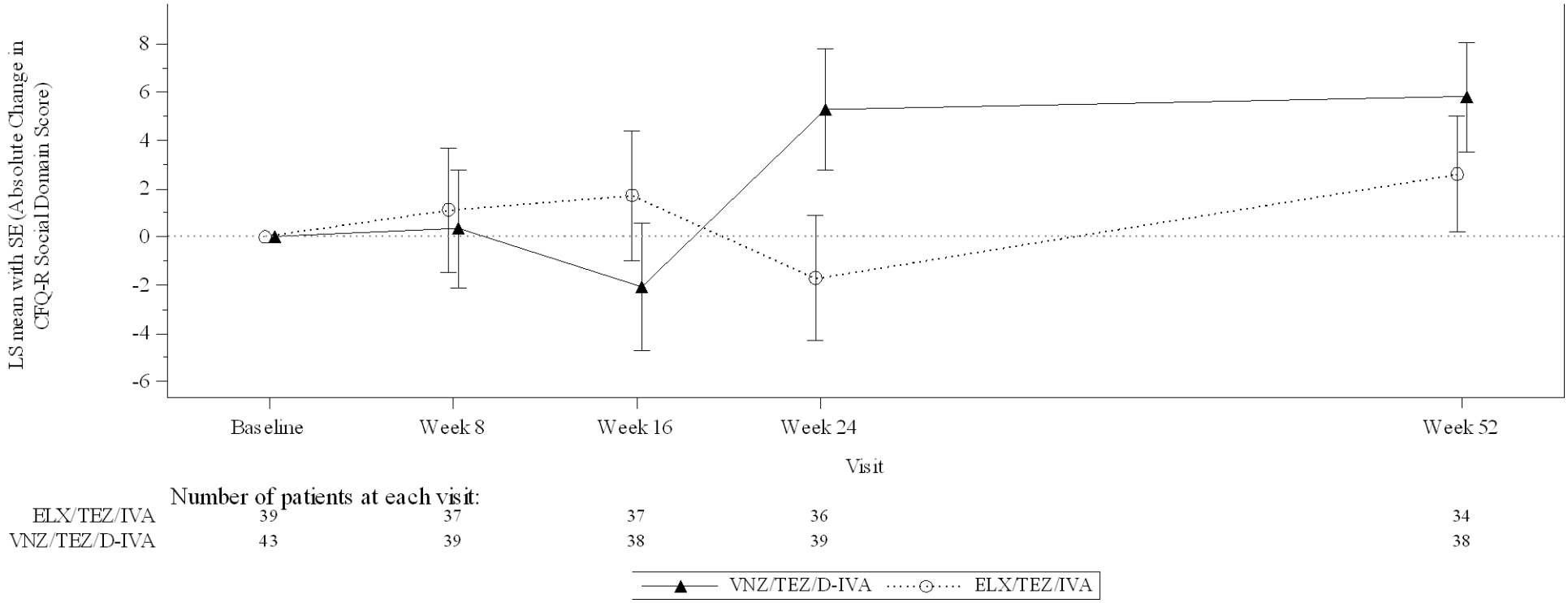
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social
Prior CFTR modulator use: Yes



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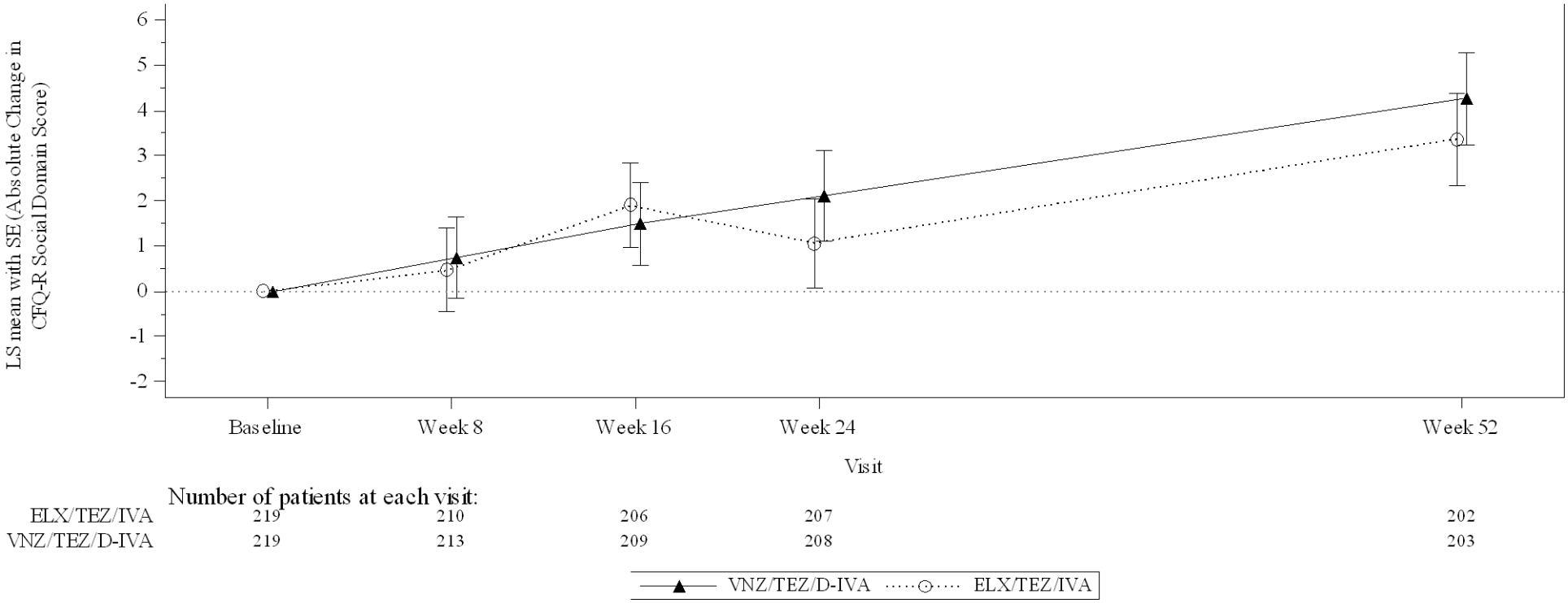
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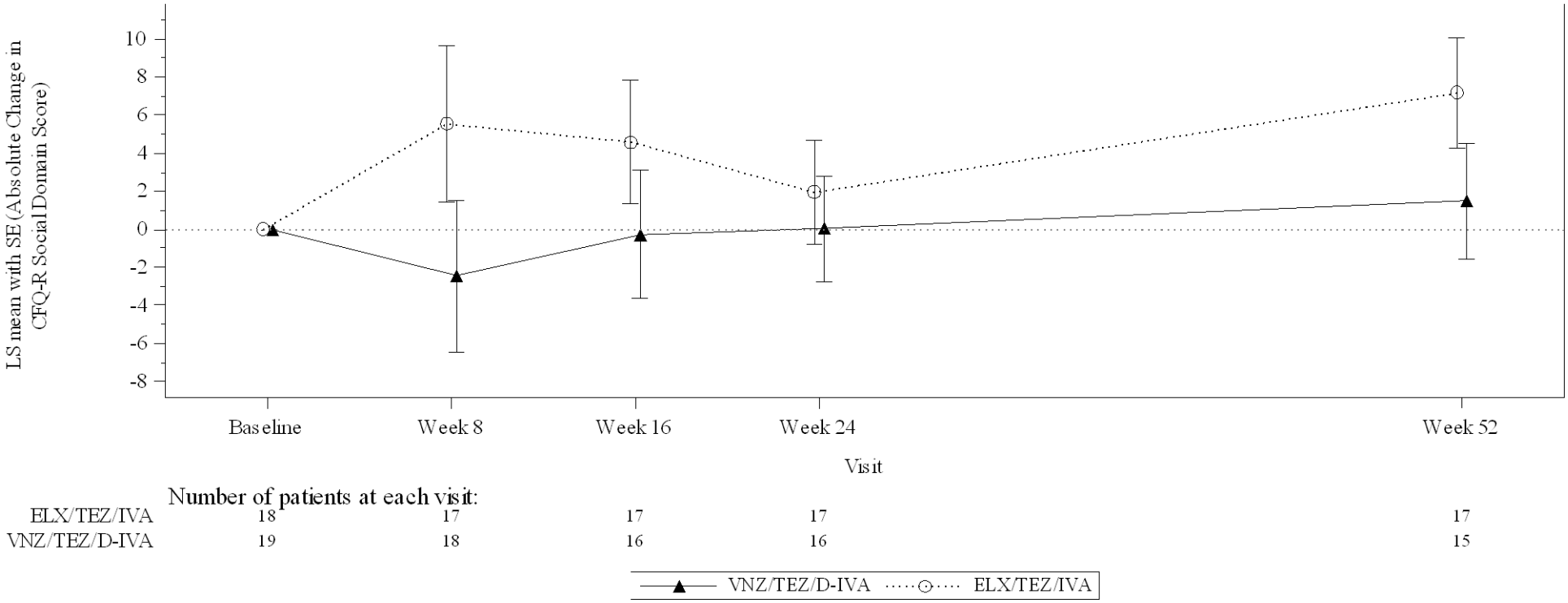
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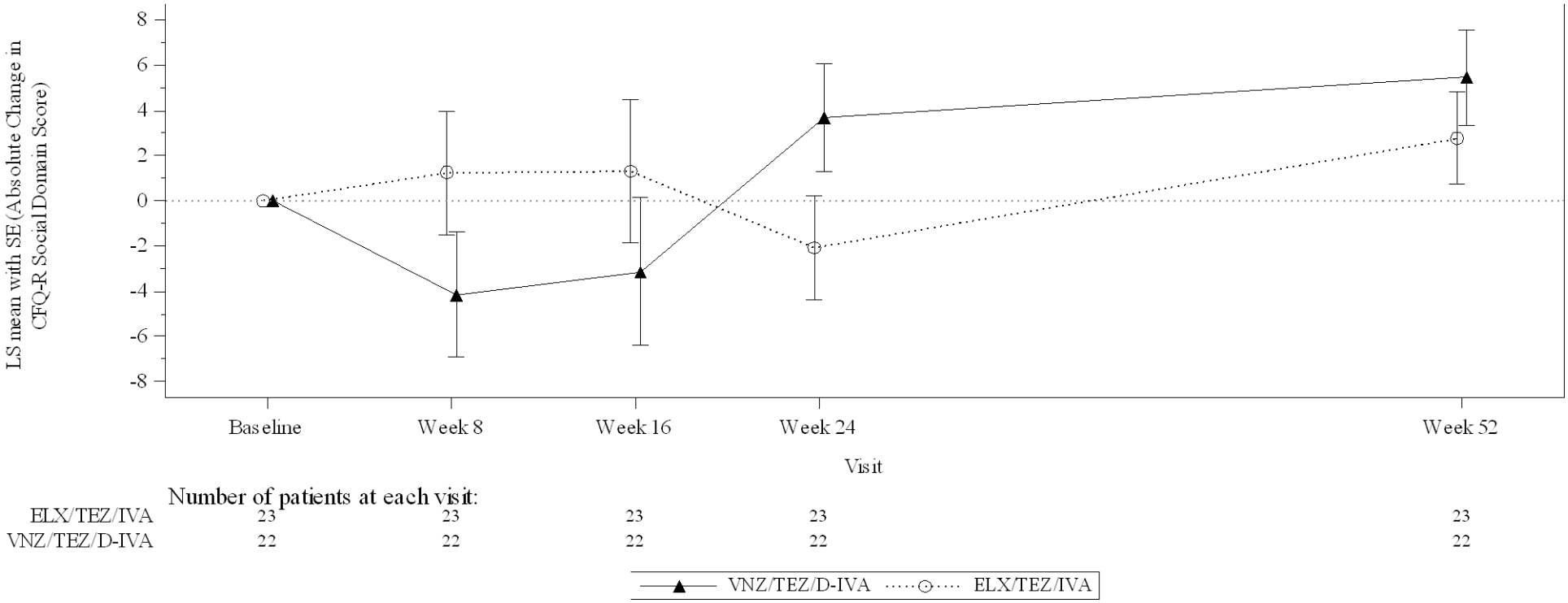
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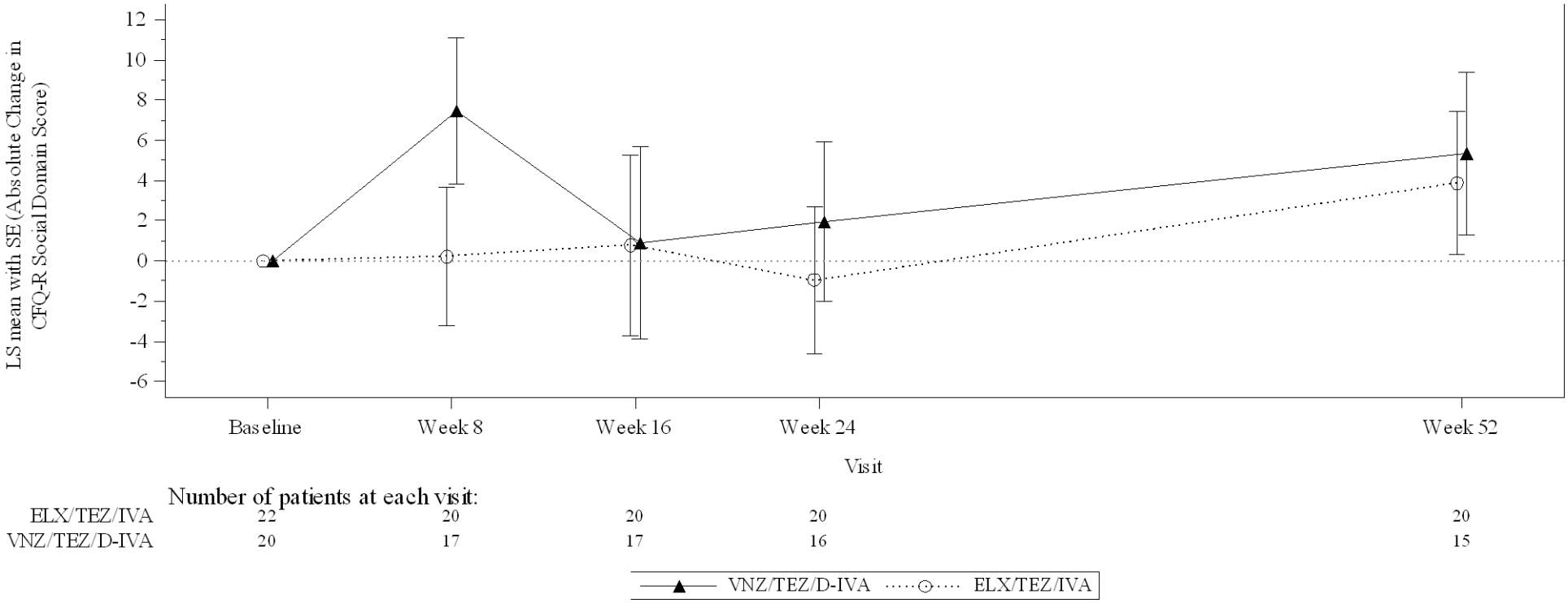
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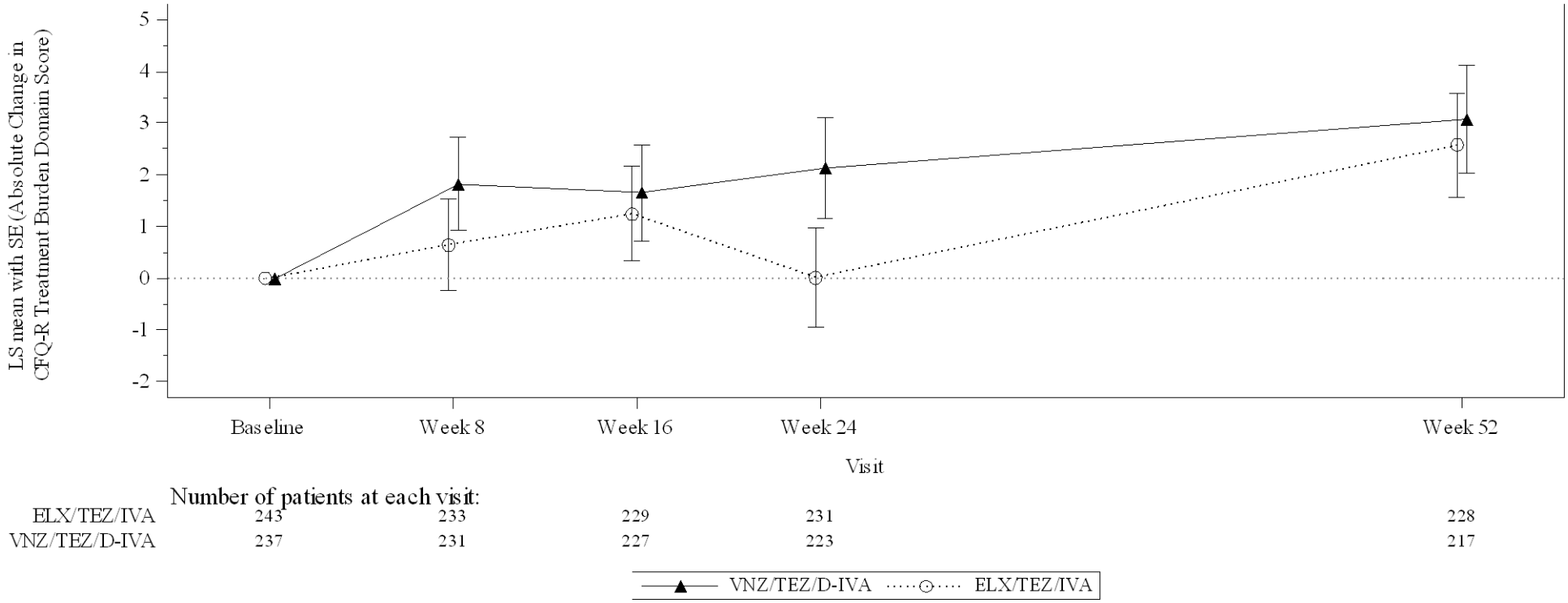
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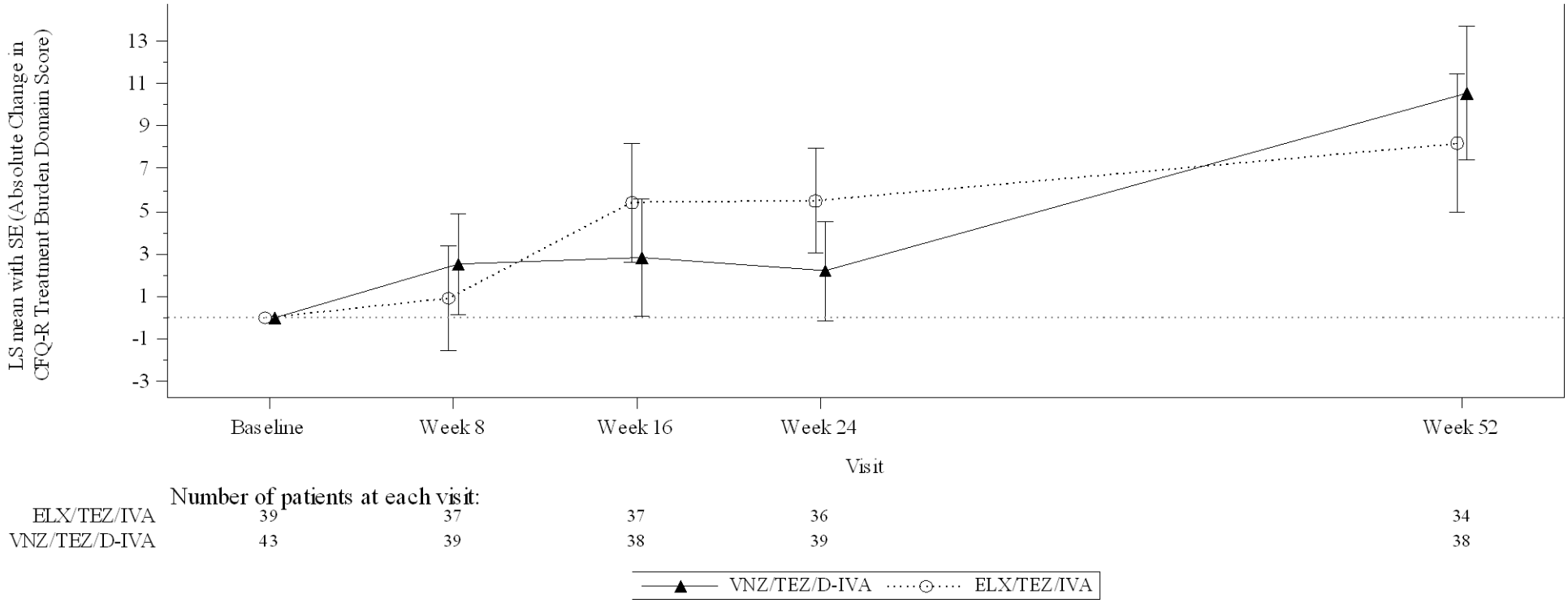
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Prior CFTR modulator use: Yes



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Figure 2.2.2.9.5.1
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups for Additional Subgroups
Full Analysis Set

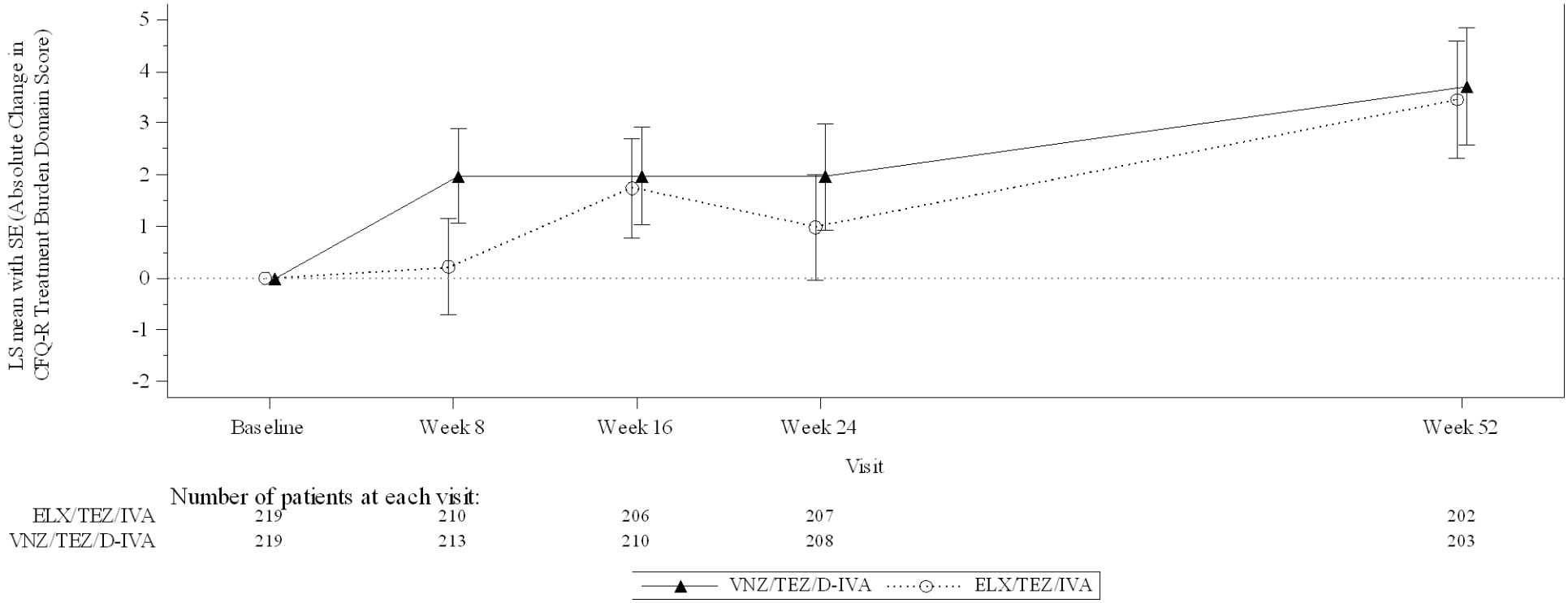
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Prior CFTR modulator use: No



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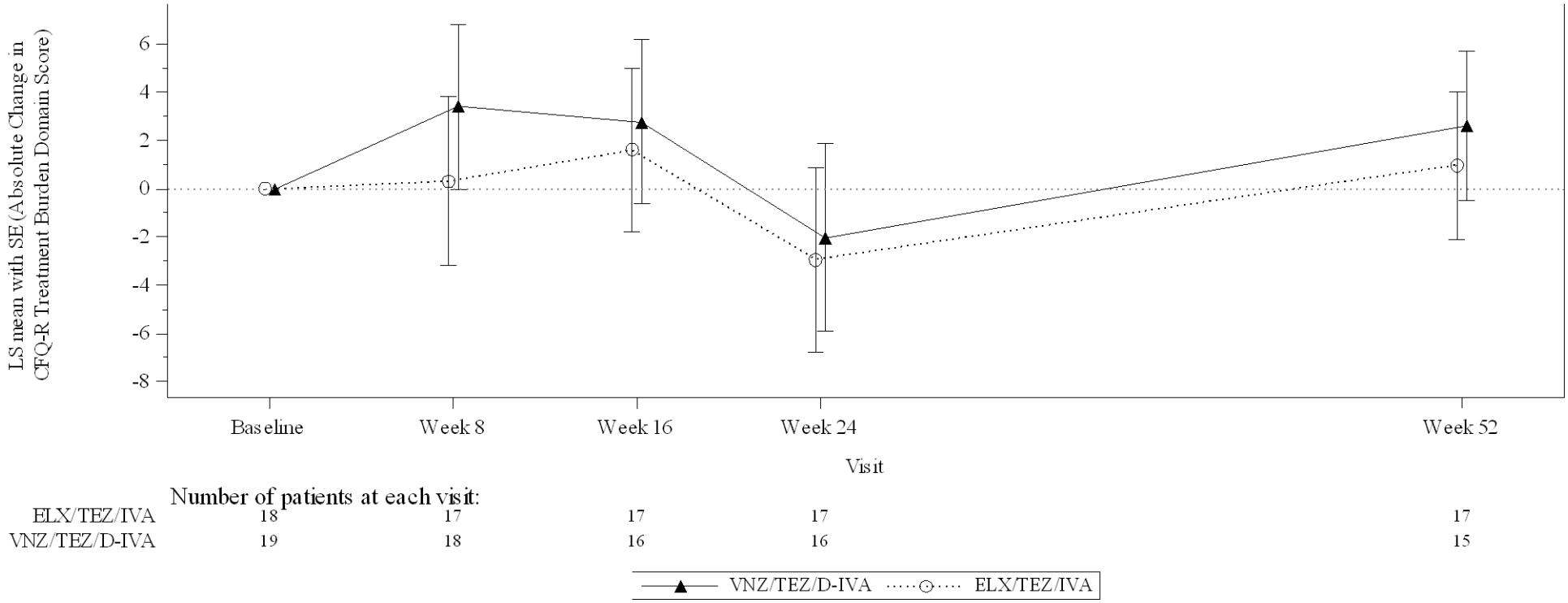
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Genotype group: F/F



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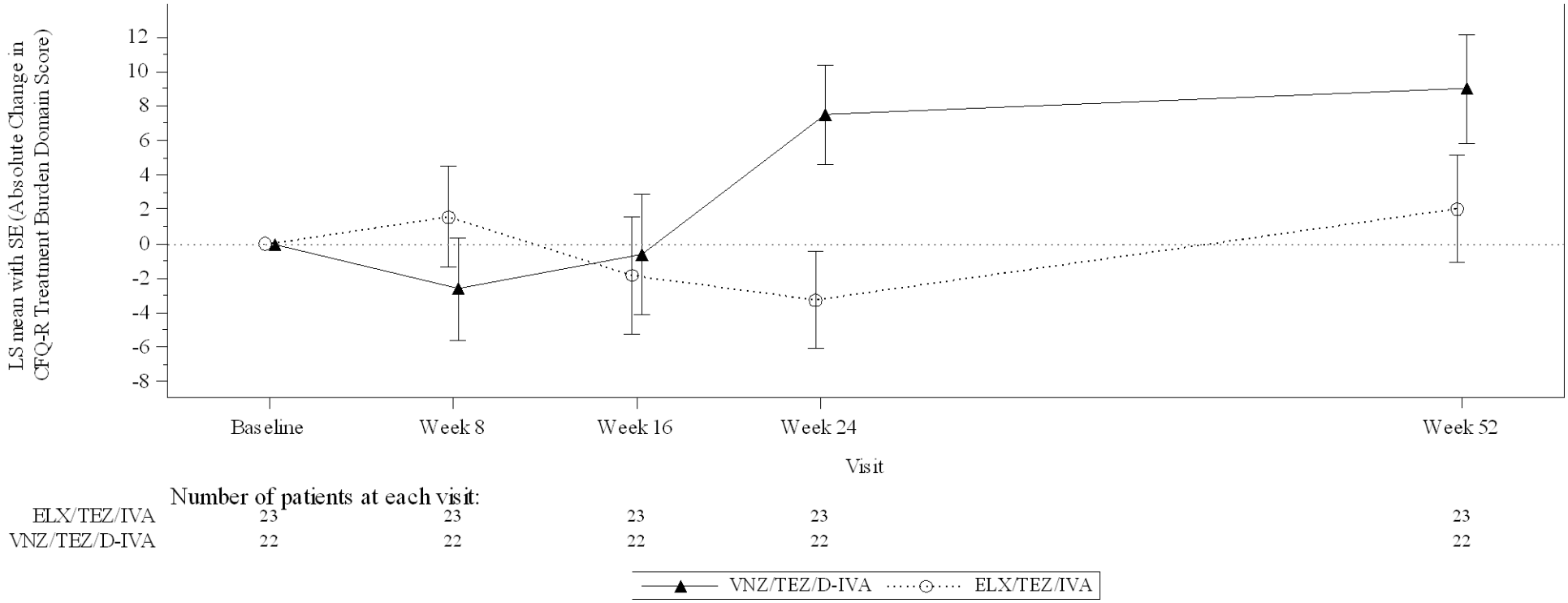
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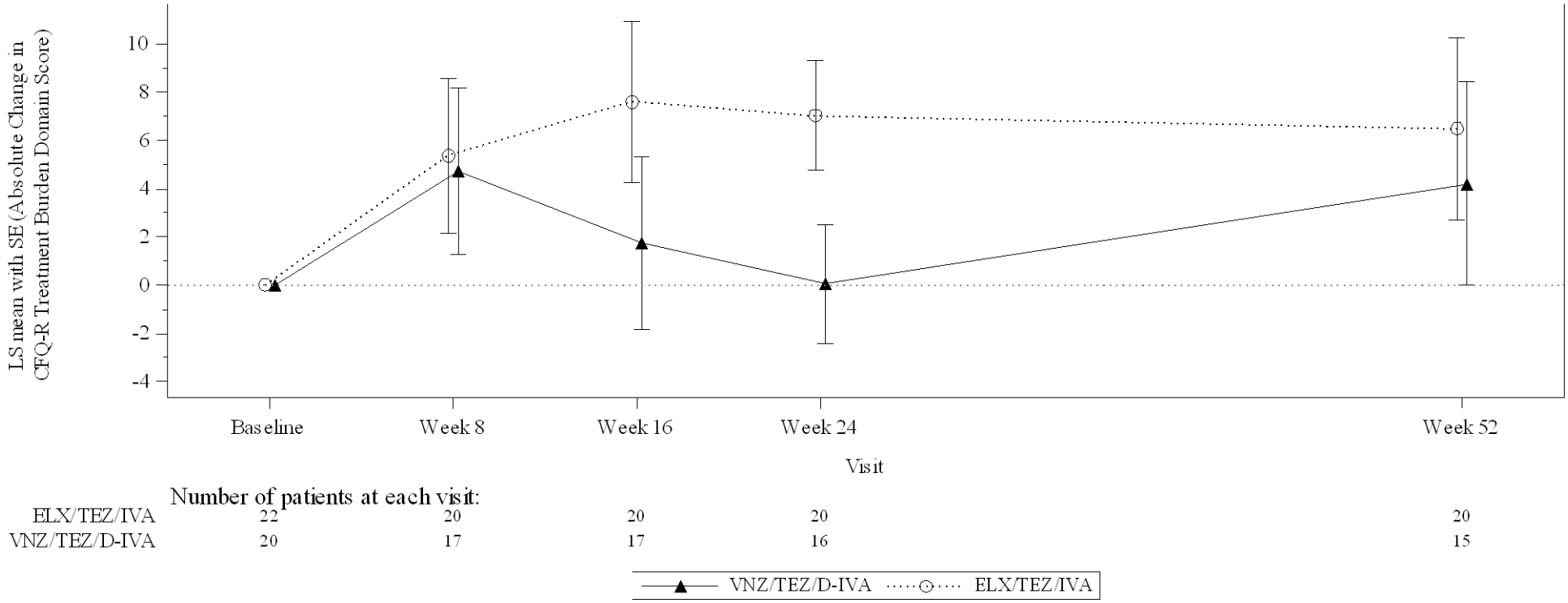
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
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Genotype group: F/RF



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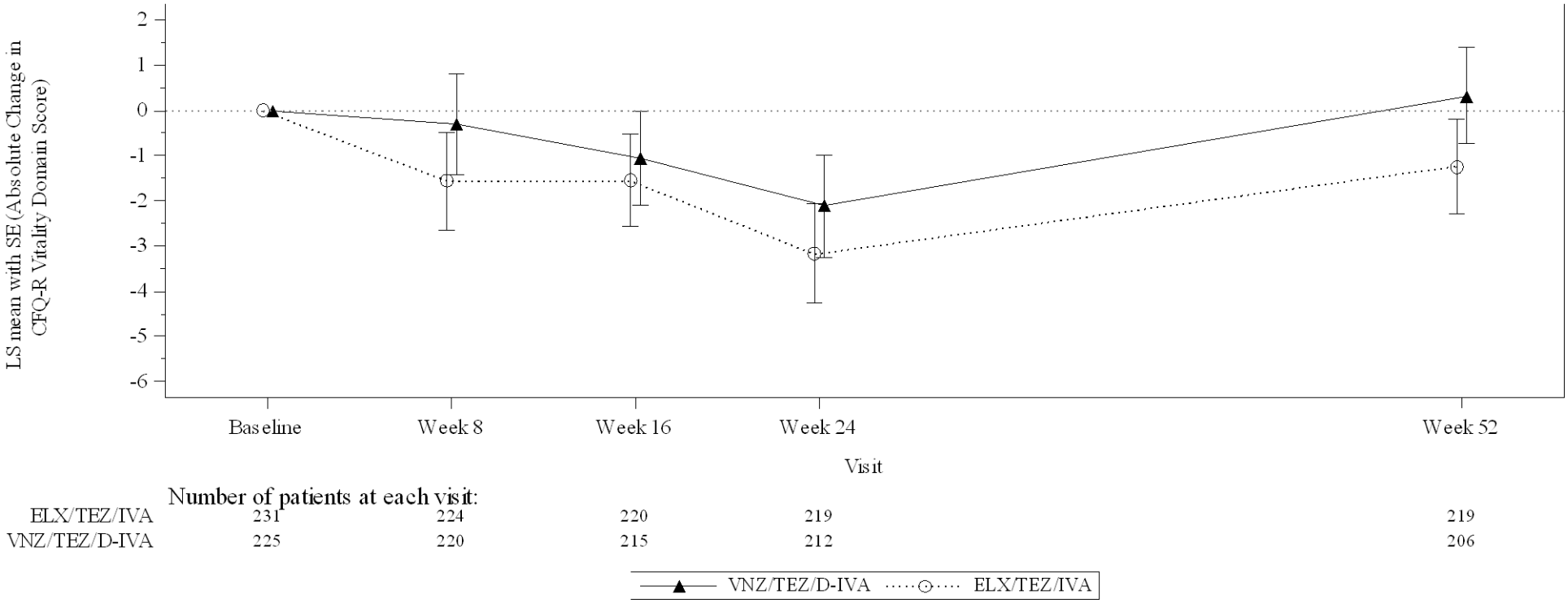
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden
Genotype group: TCR/non-F



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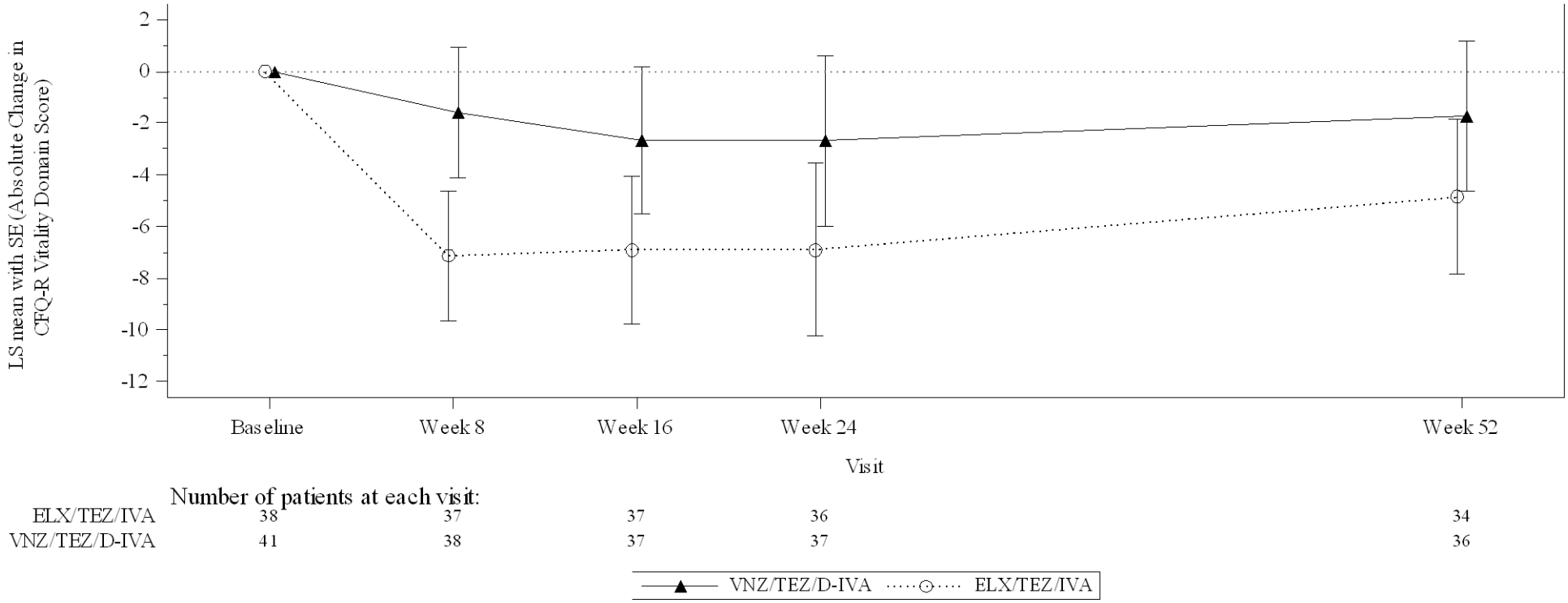
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality
Prior CFTR modulator use: Yes



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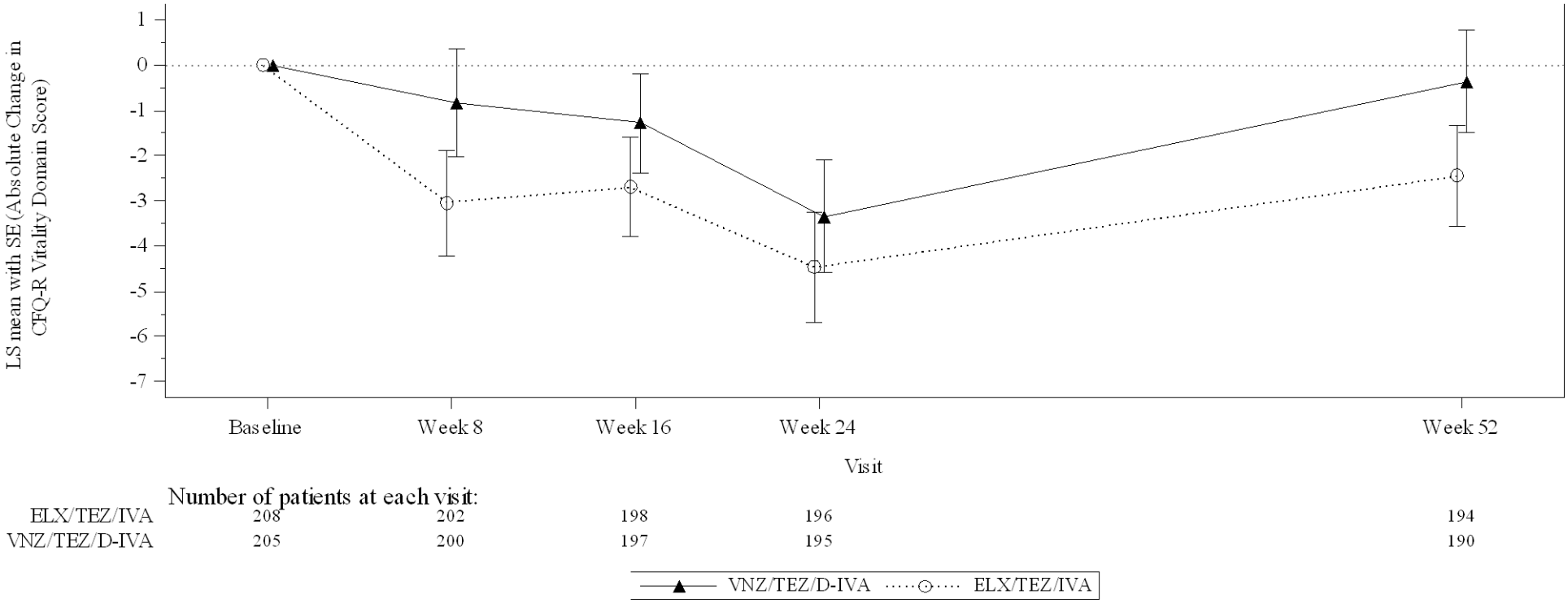
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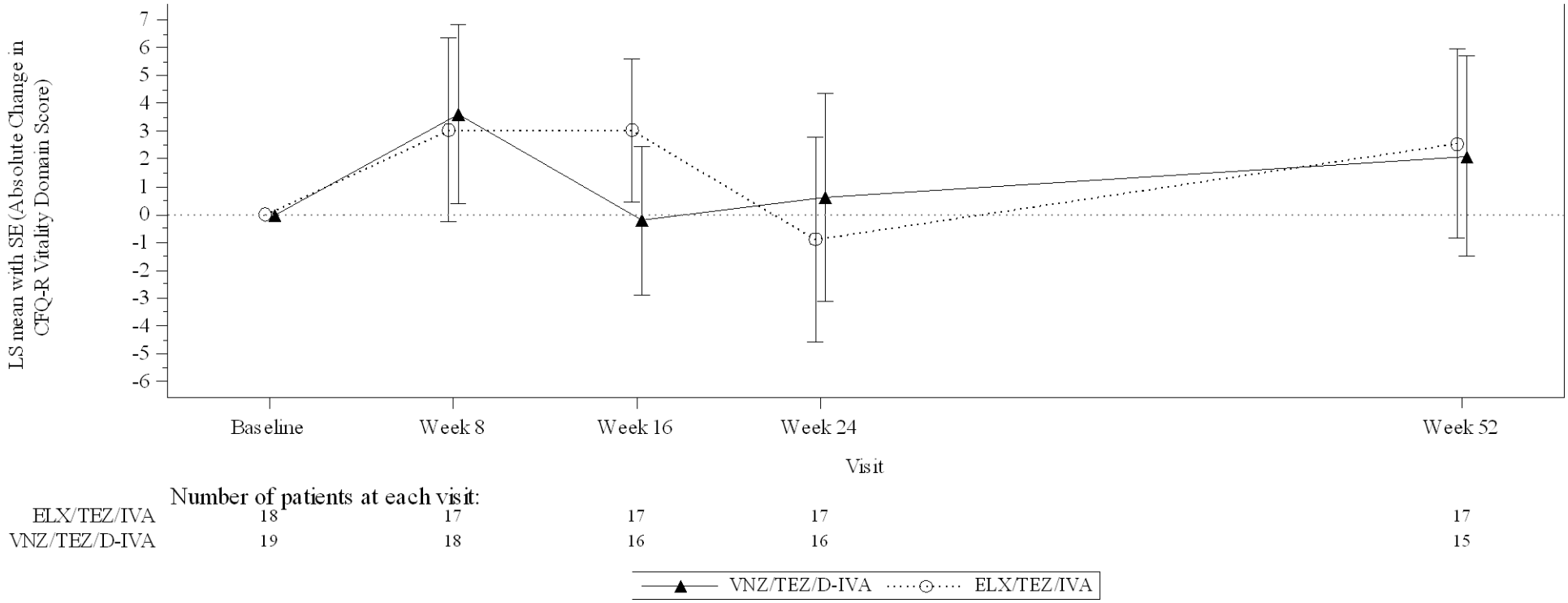
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Domain: Vitality
Genotype group: F/F



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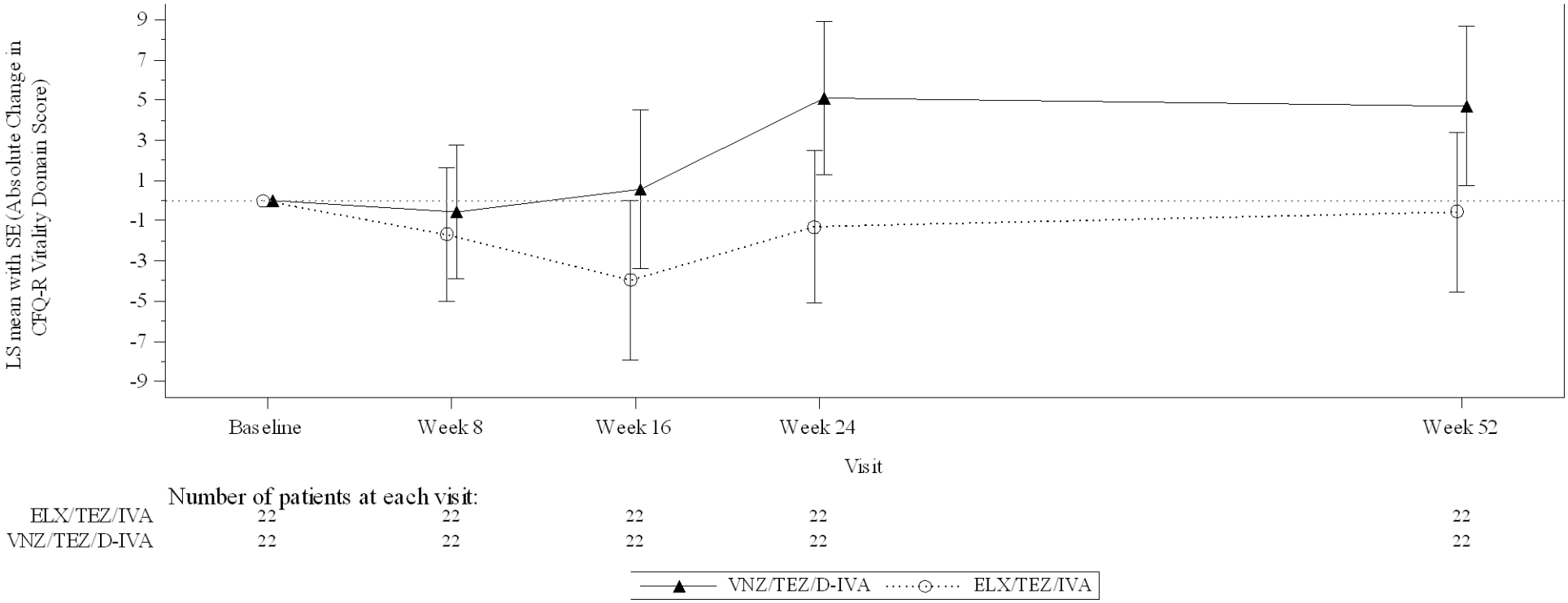
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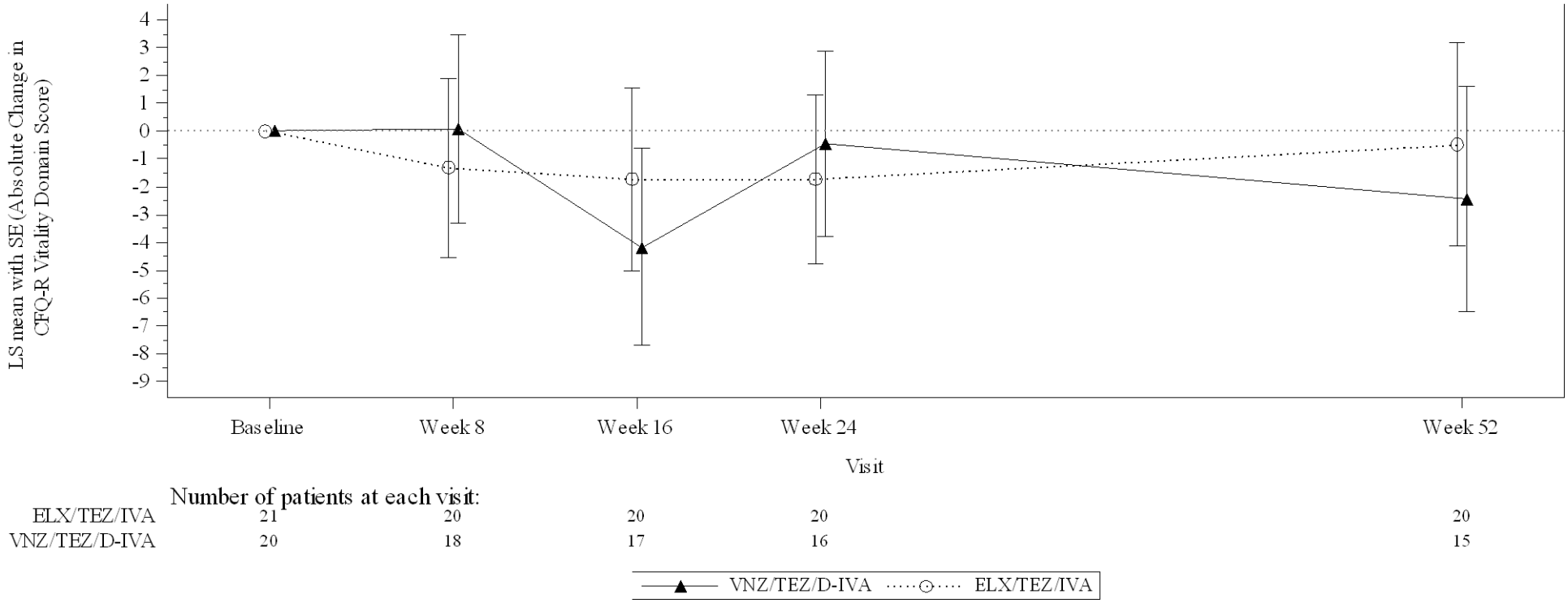
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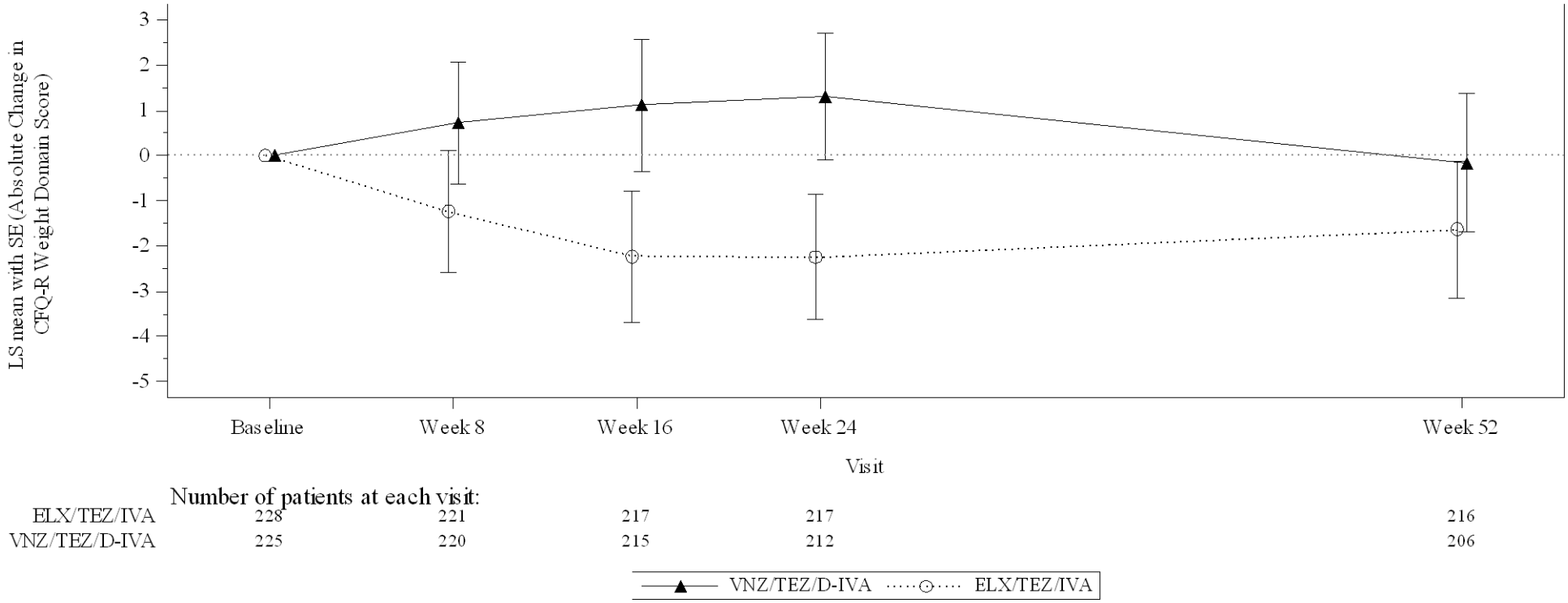
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Domain: Vitality
Genotype group: TCR/non-F



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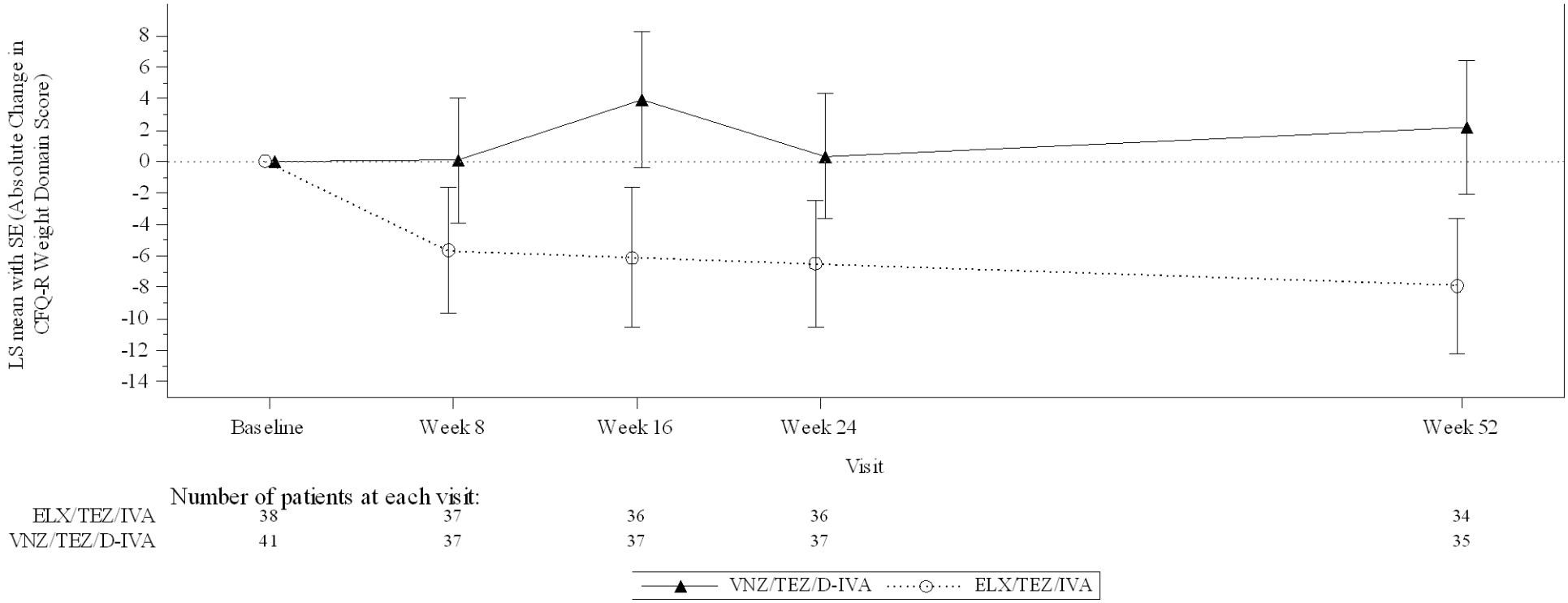
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Prior CFTR modulator use: Yes



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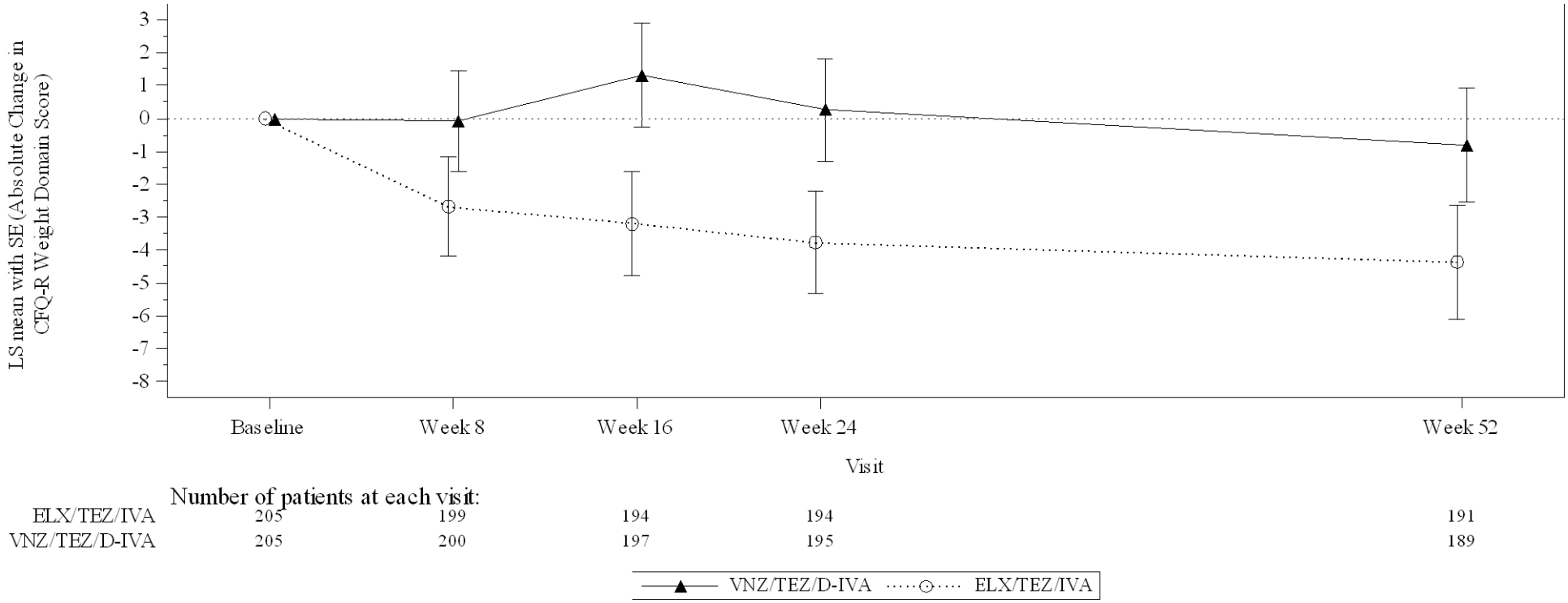
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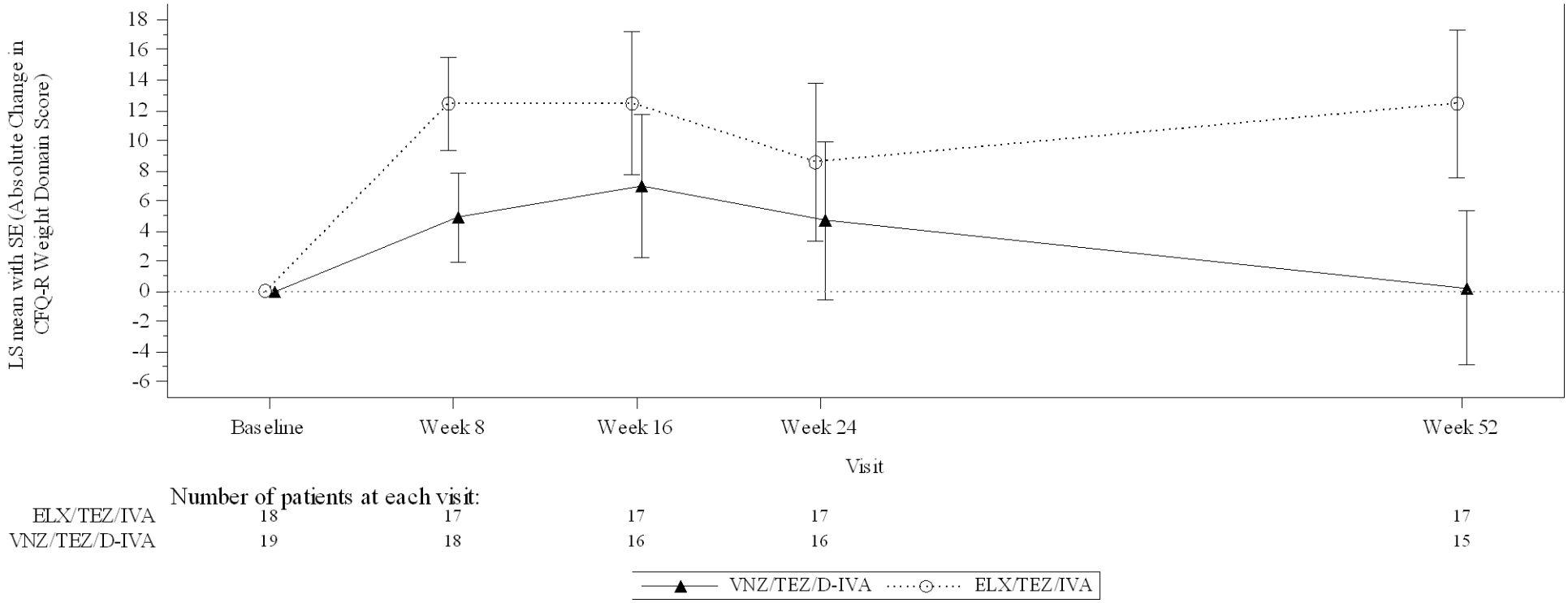
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight
Genotype group: F/F



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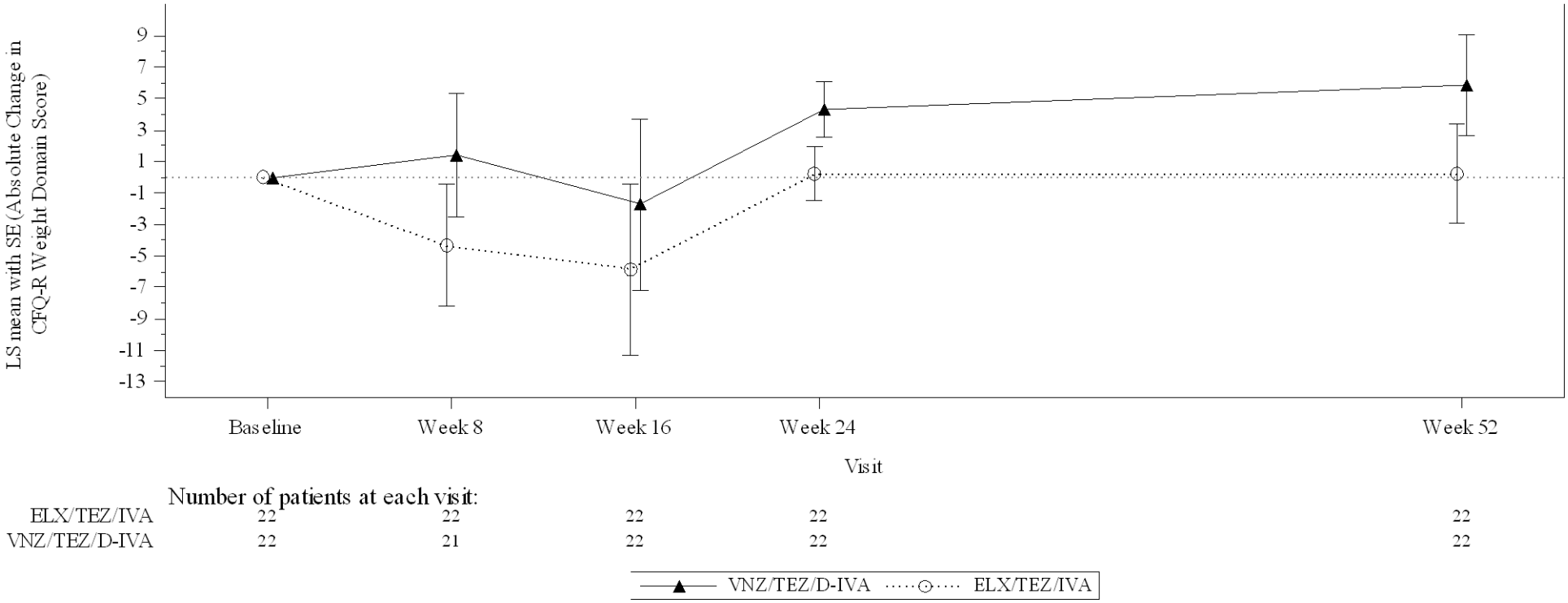
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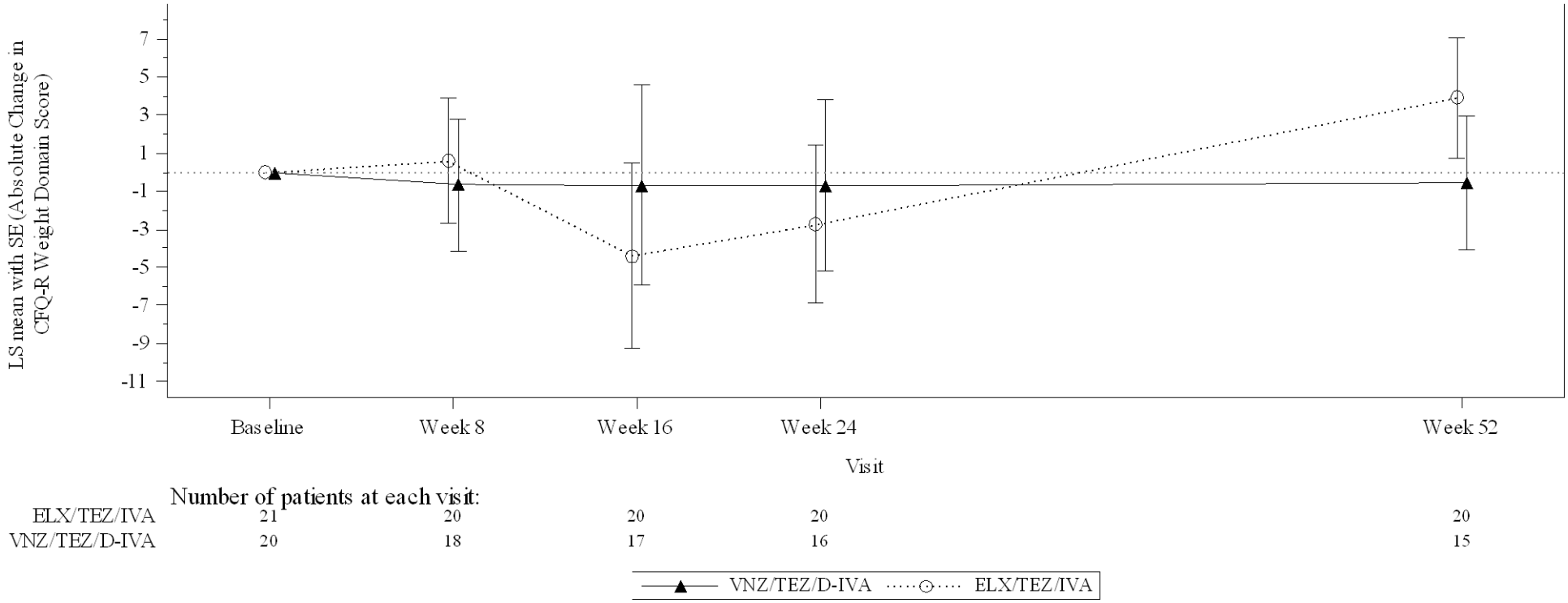
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Full Analysis Set

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Domain: Weight
Genotype group: TCR/non-F



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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

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Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

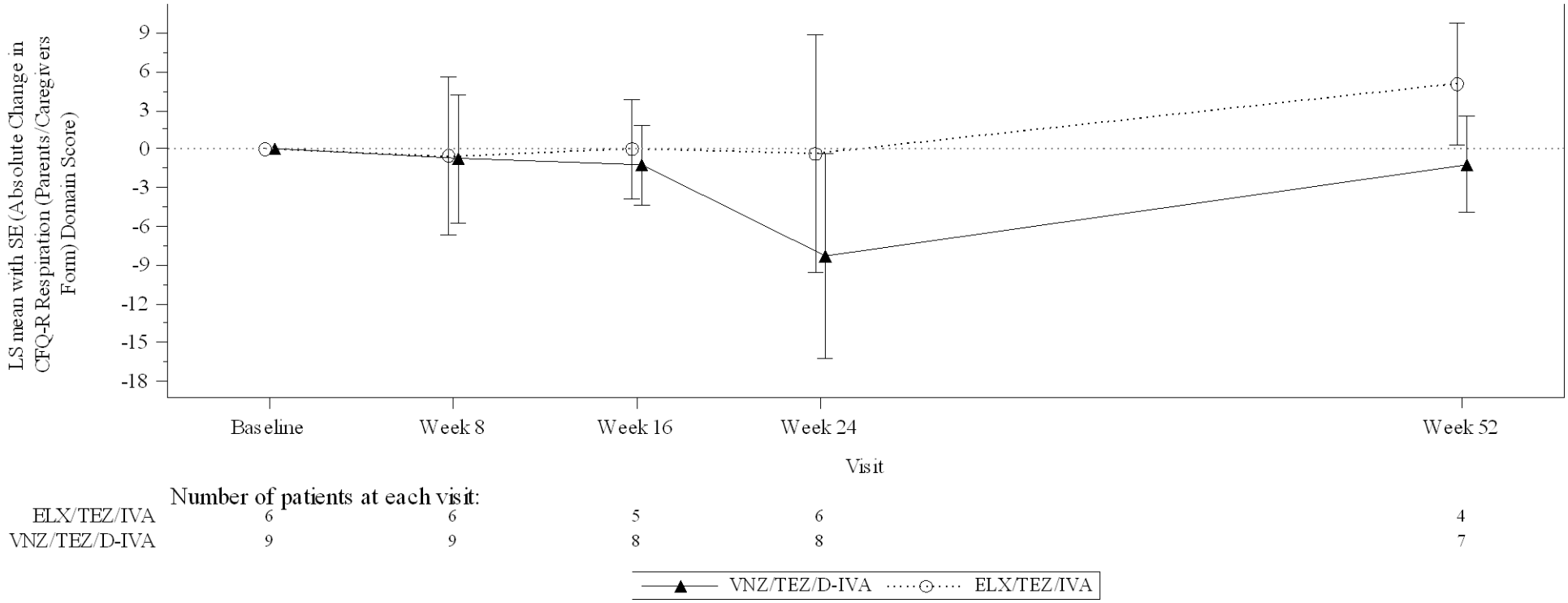
Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Respiration (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

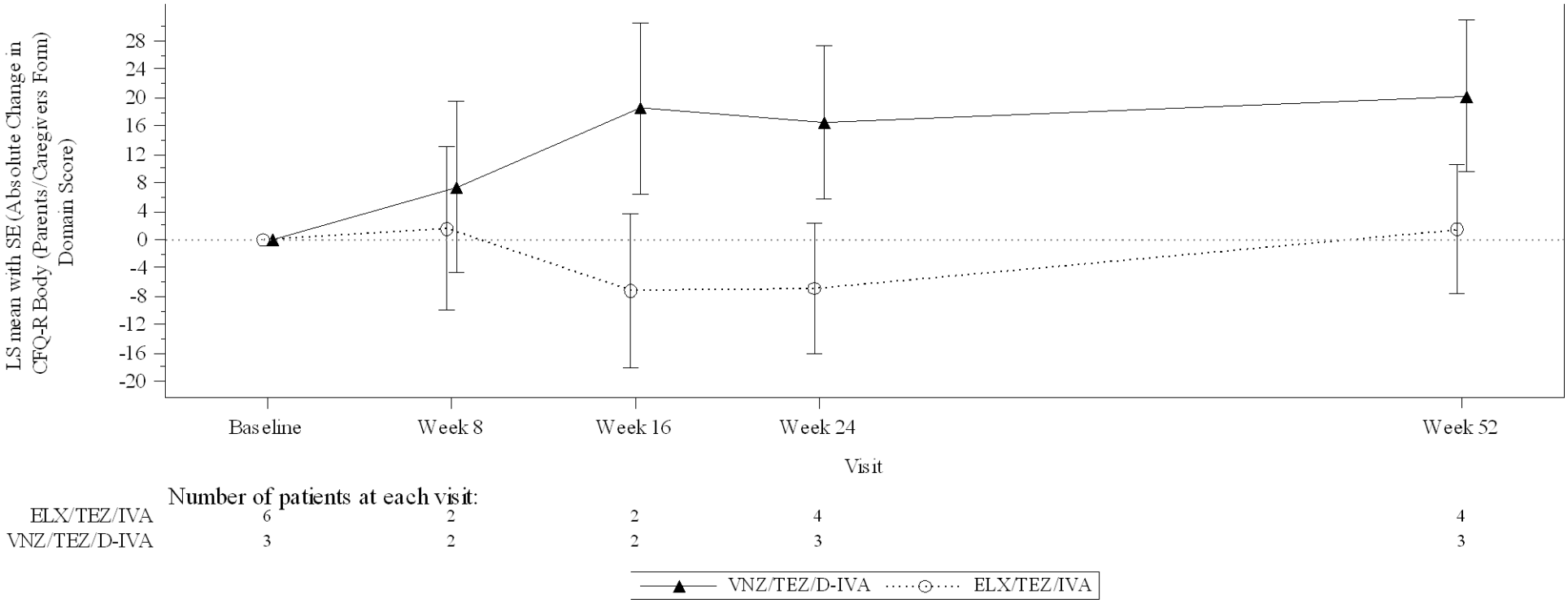
Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

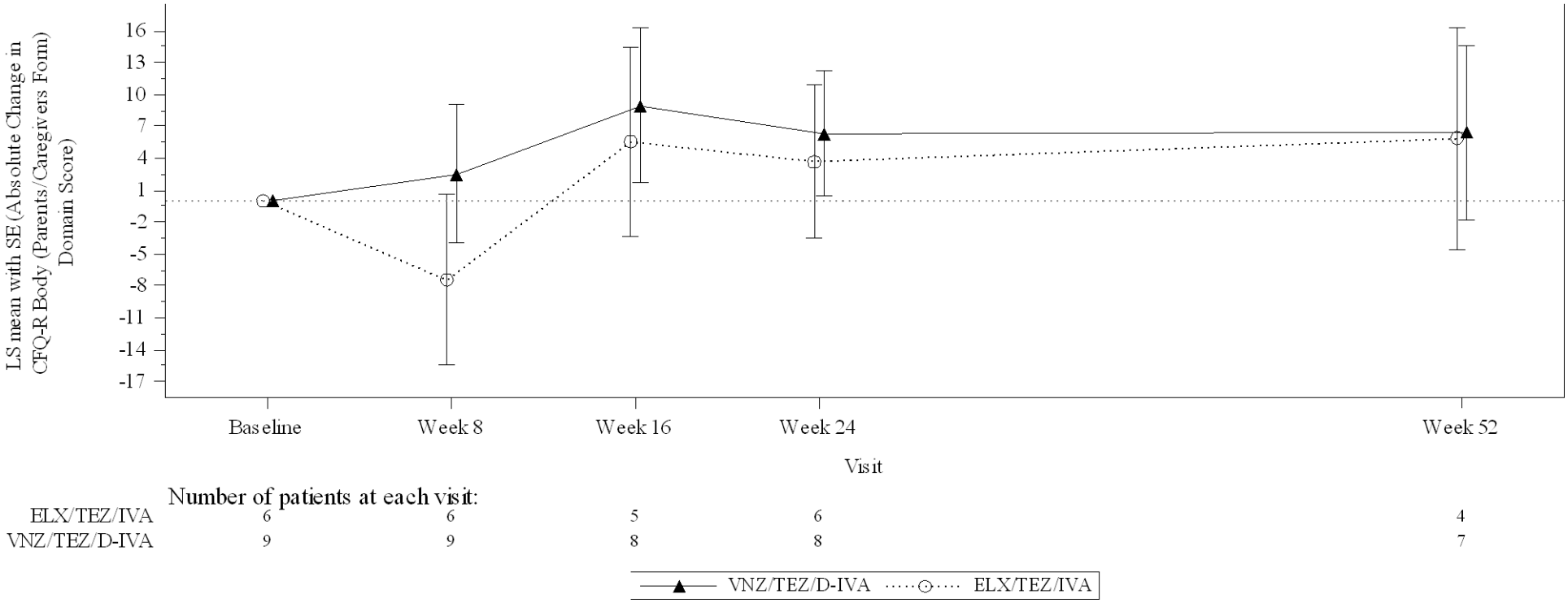
Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Body (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

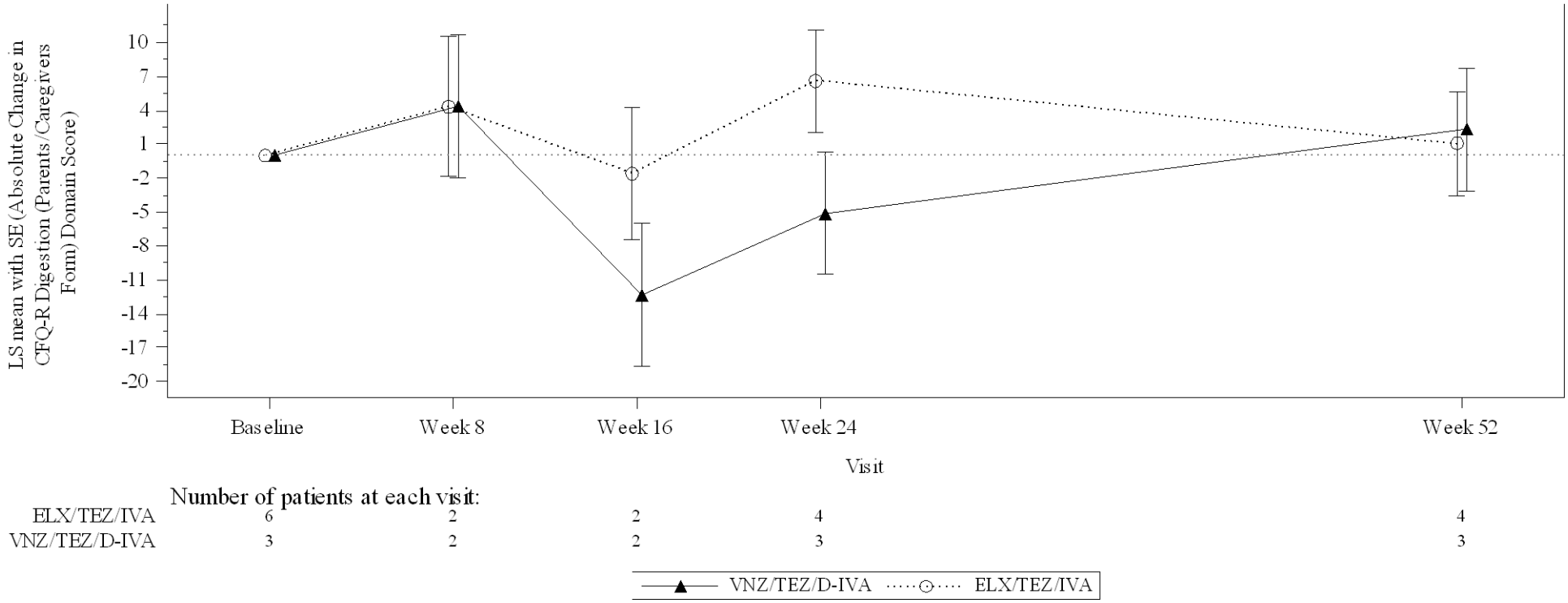
Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

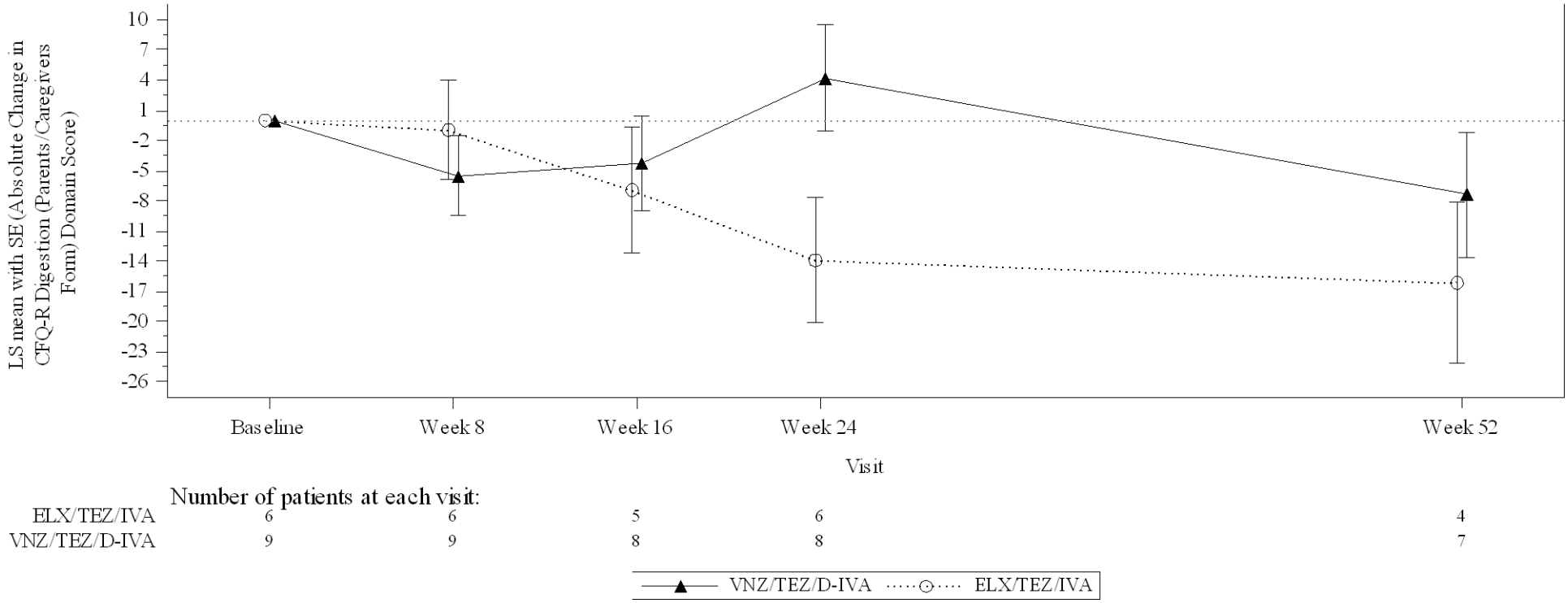
Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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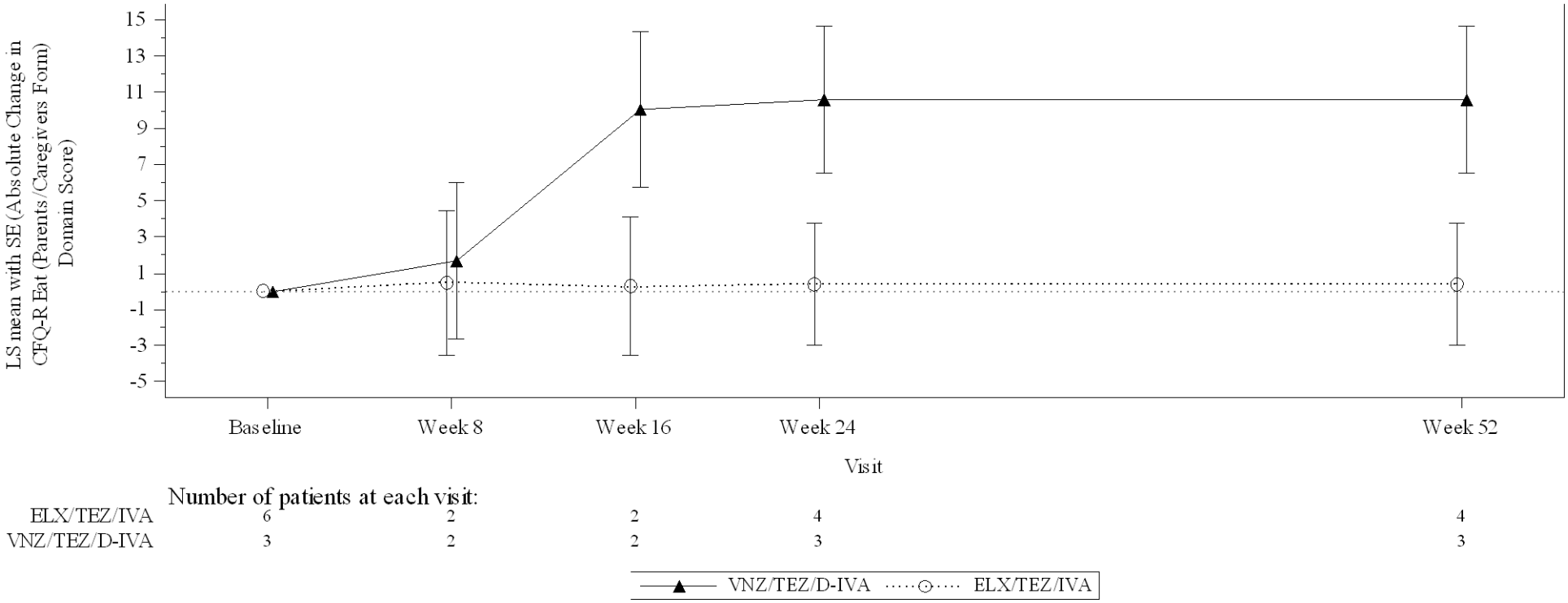
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Domain: Eat (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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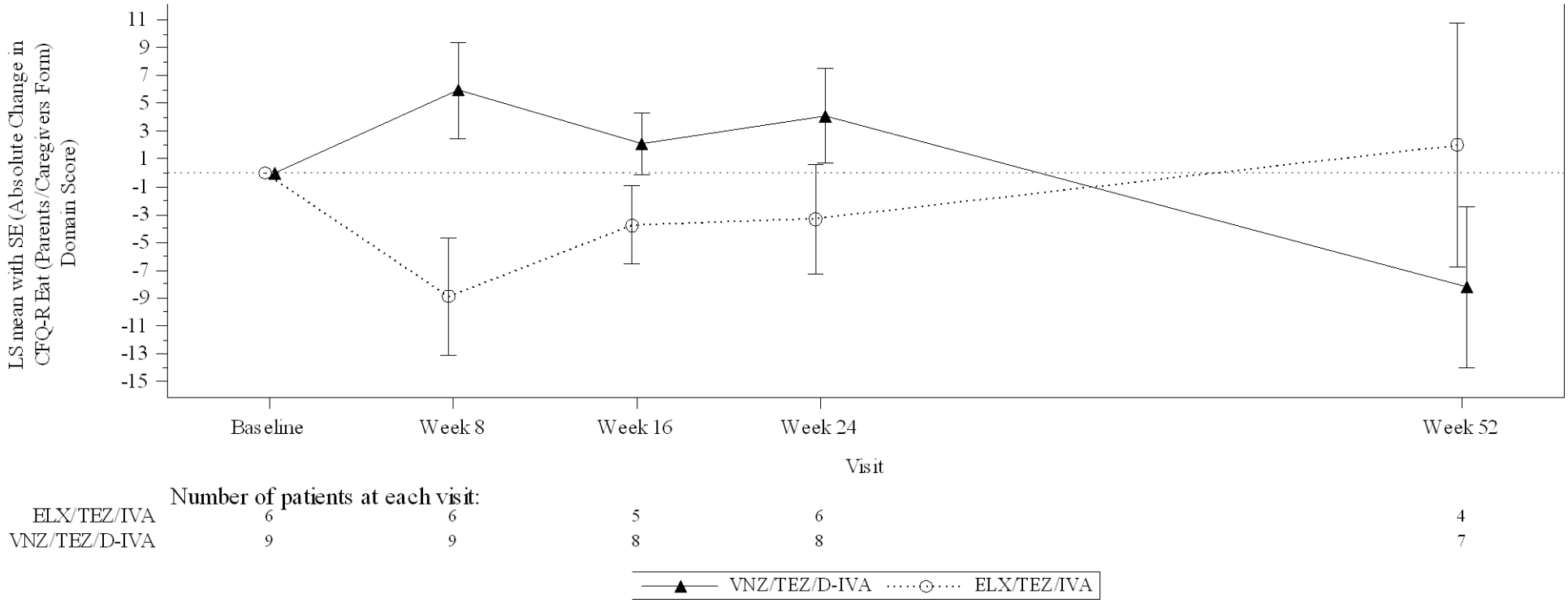
Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
Sex = Male



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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
Sex = Female



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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

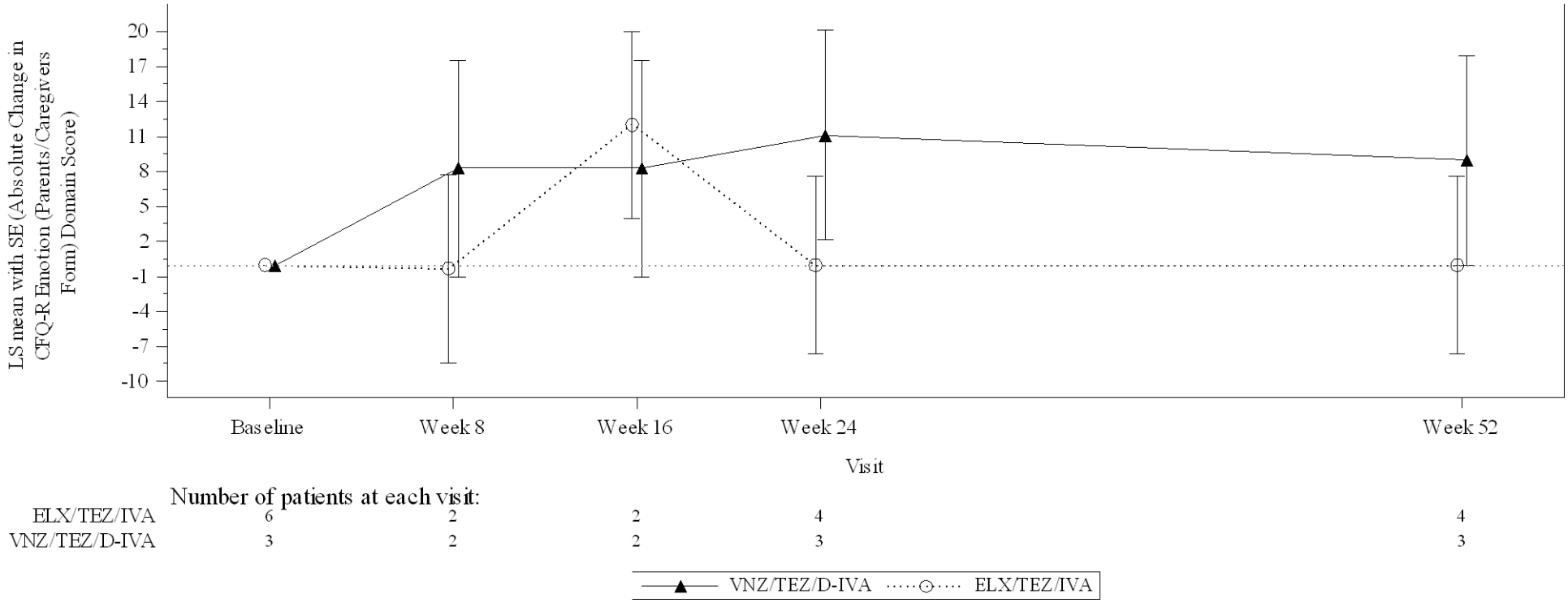
Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

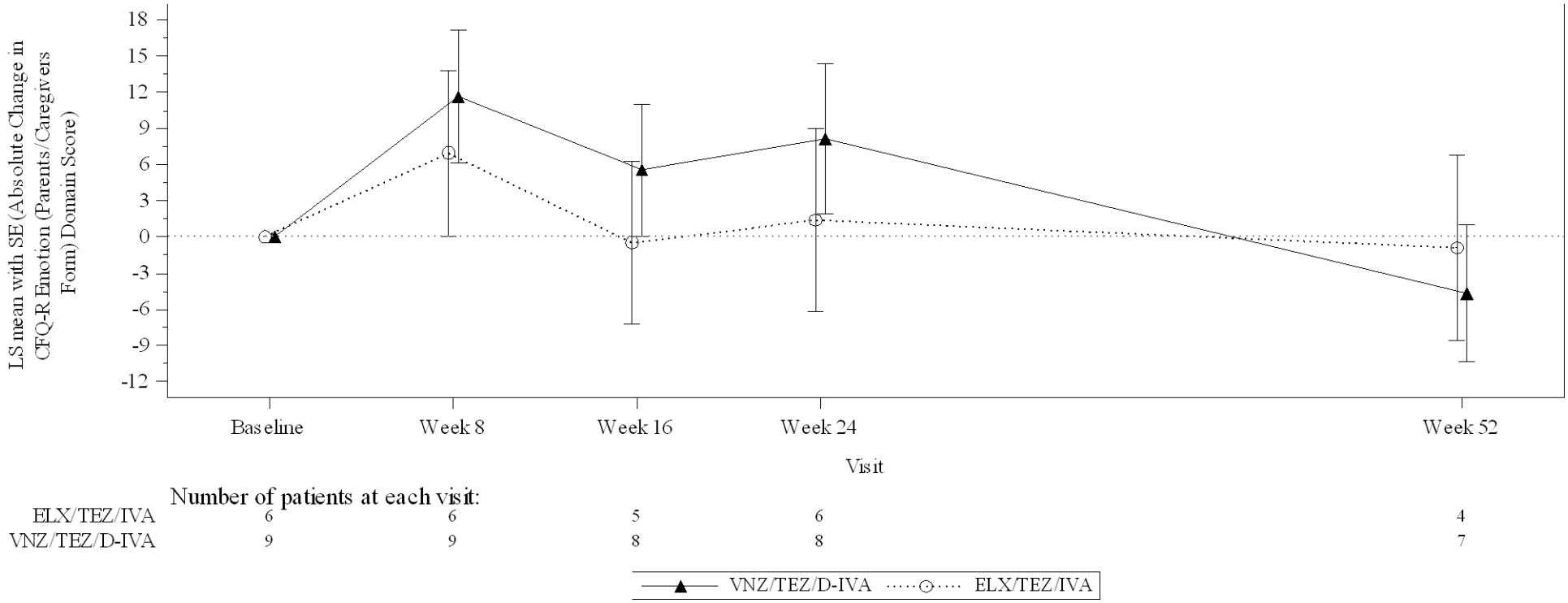
Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

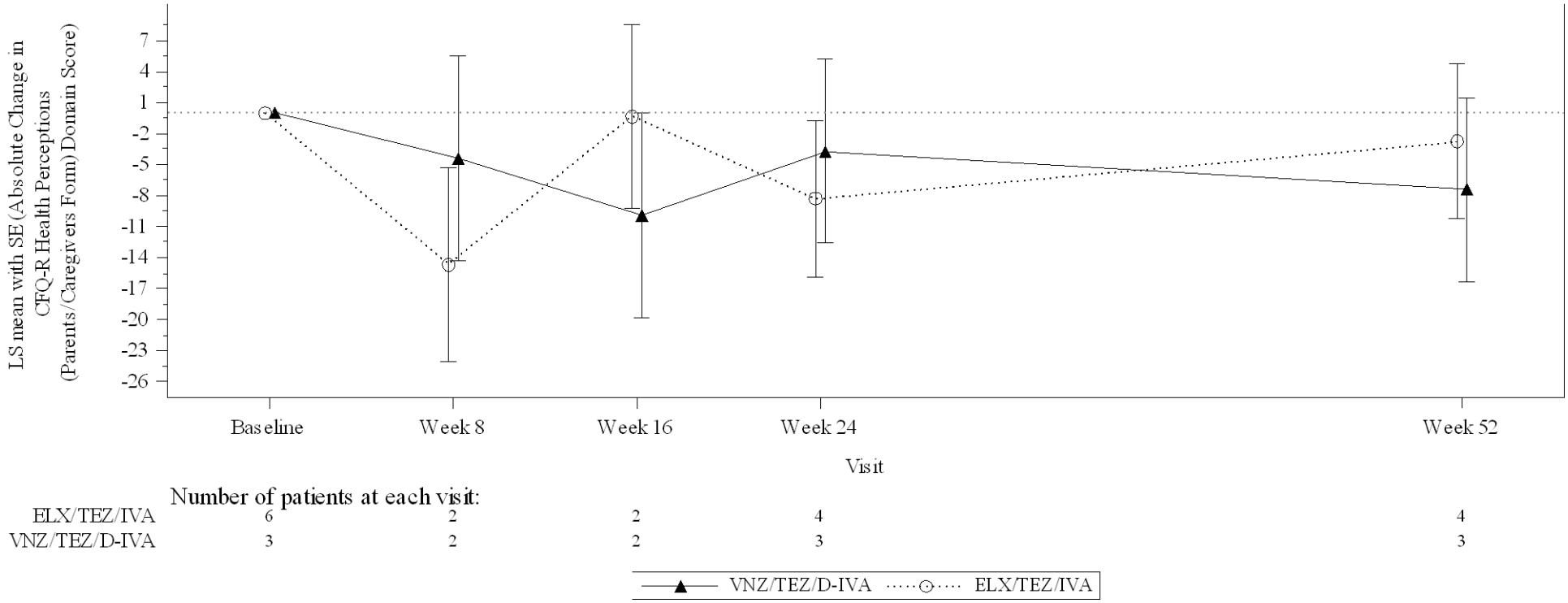
Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

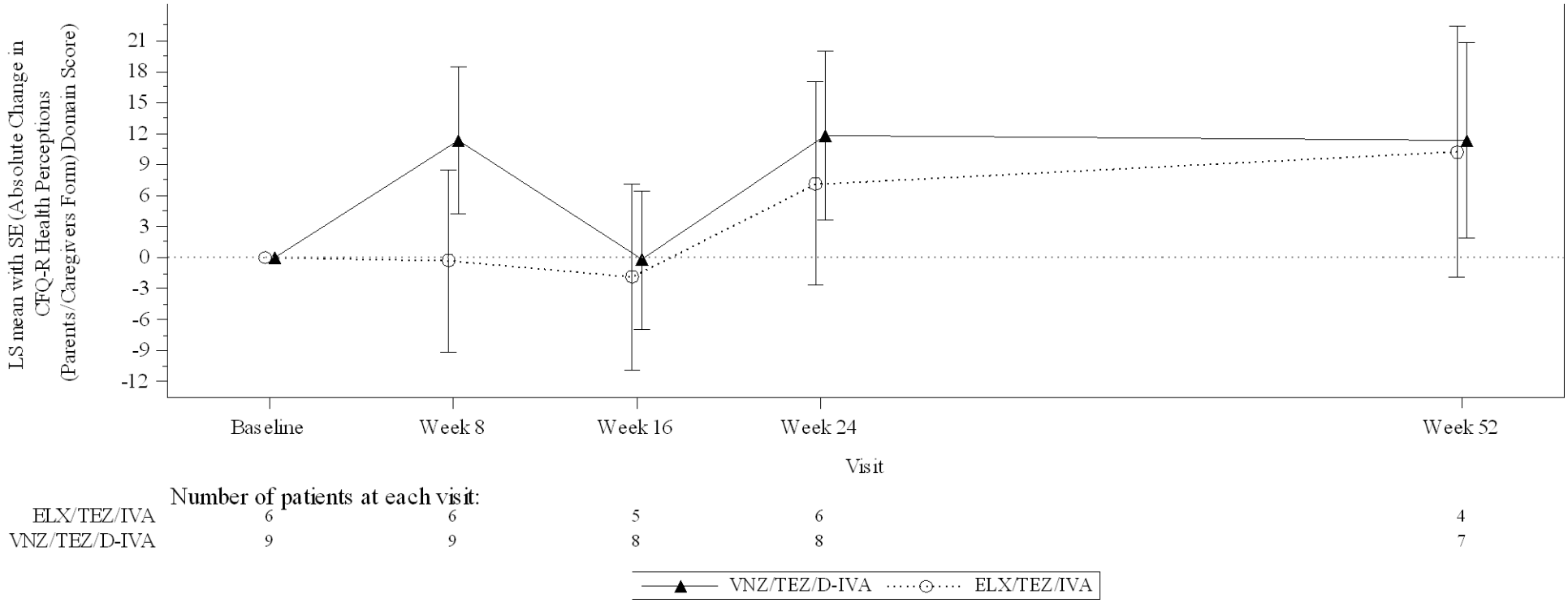
Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

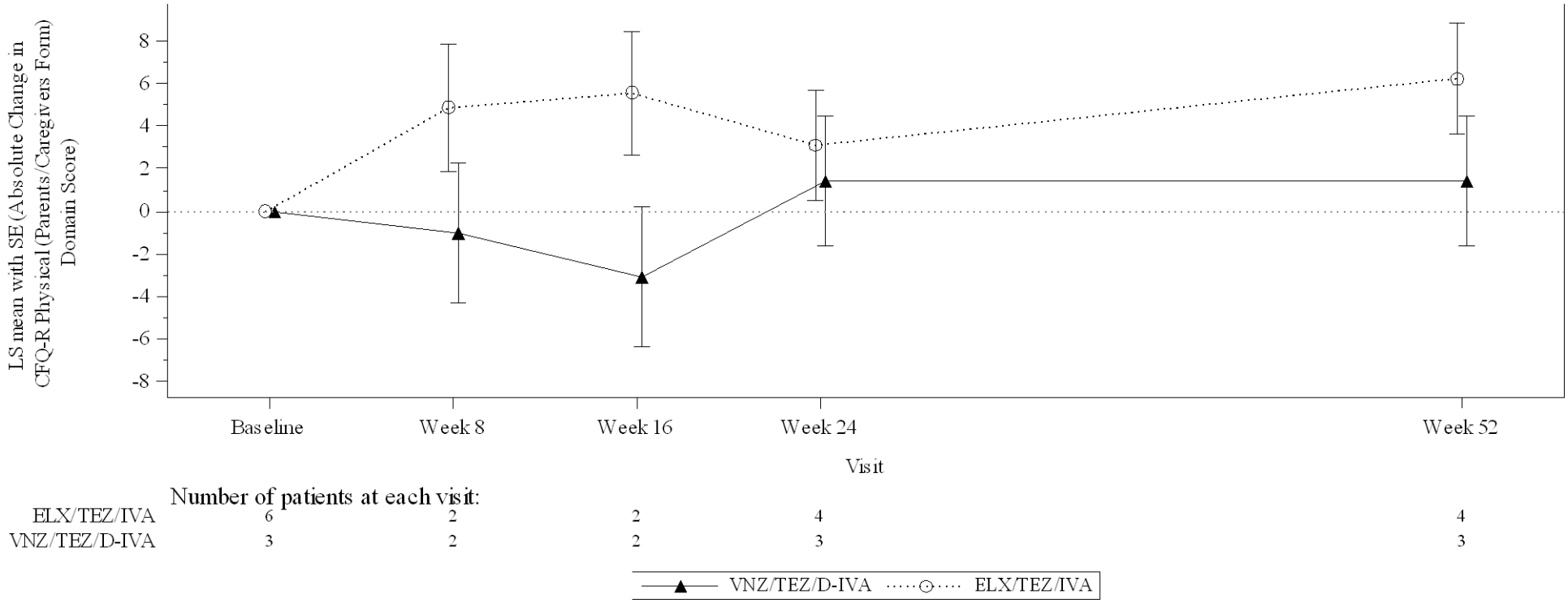
Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

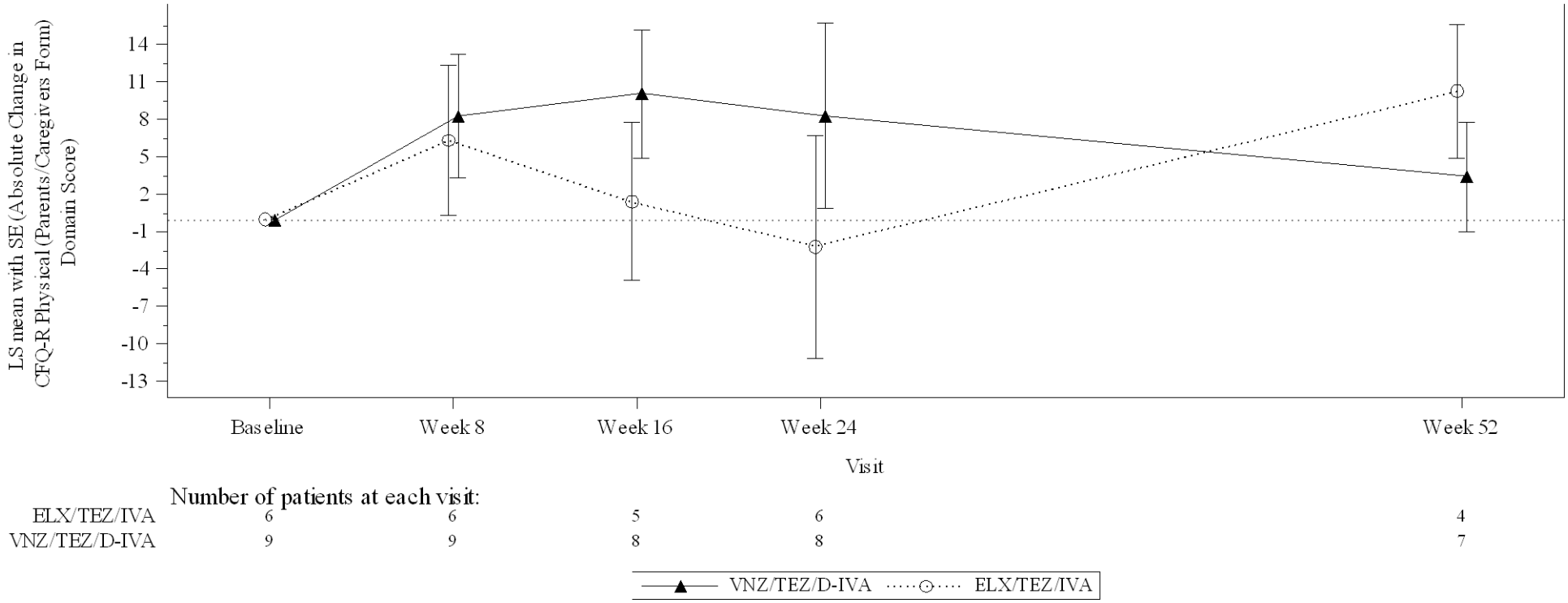
Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

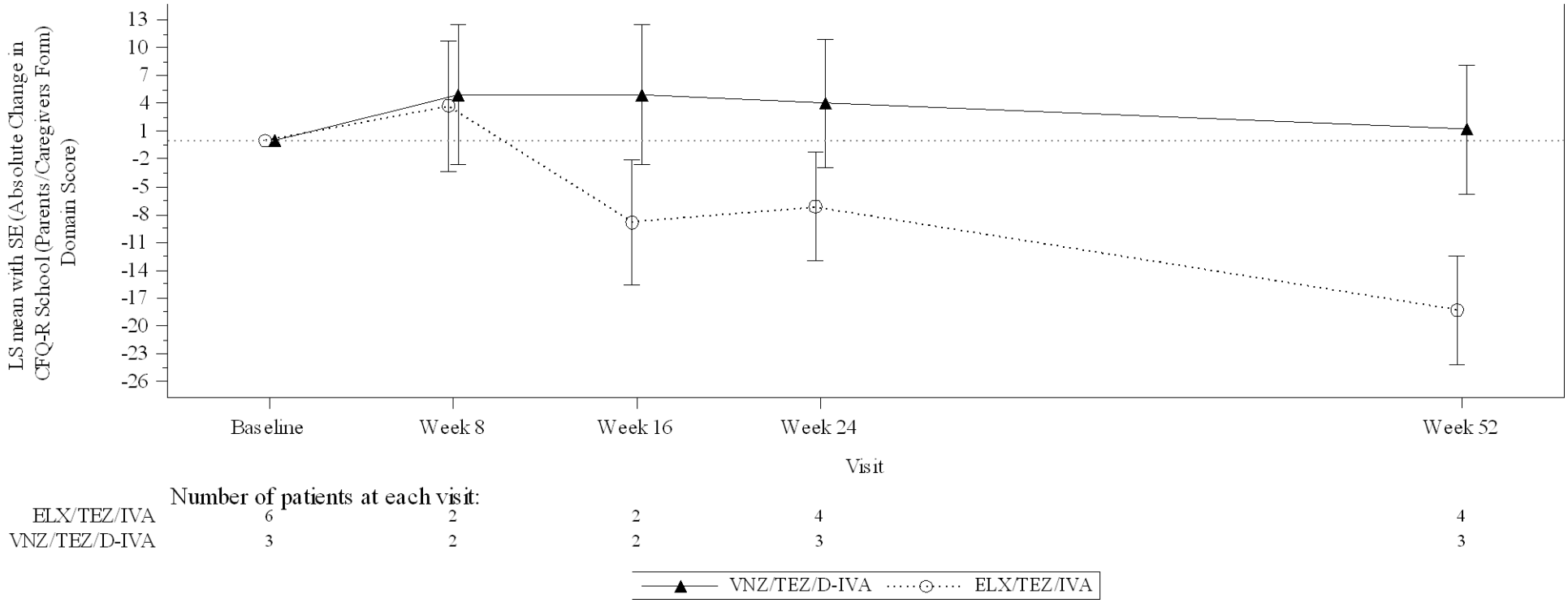
Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

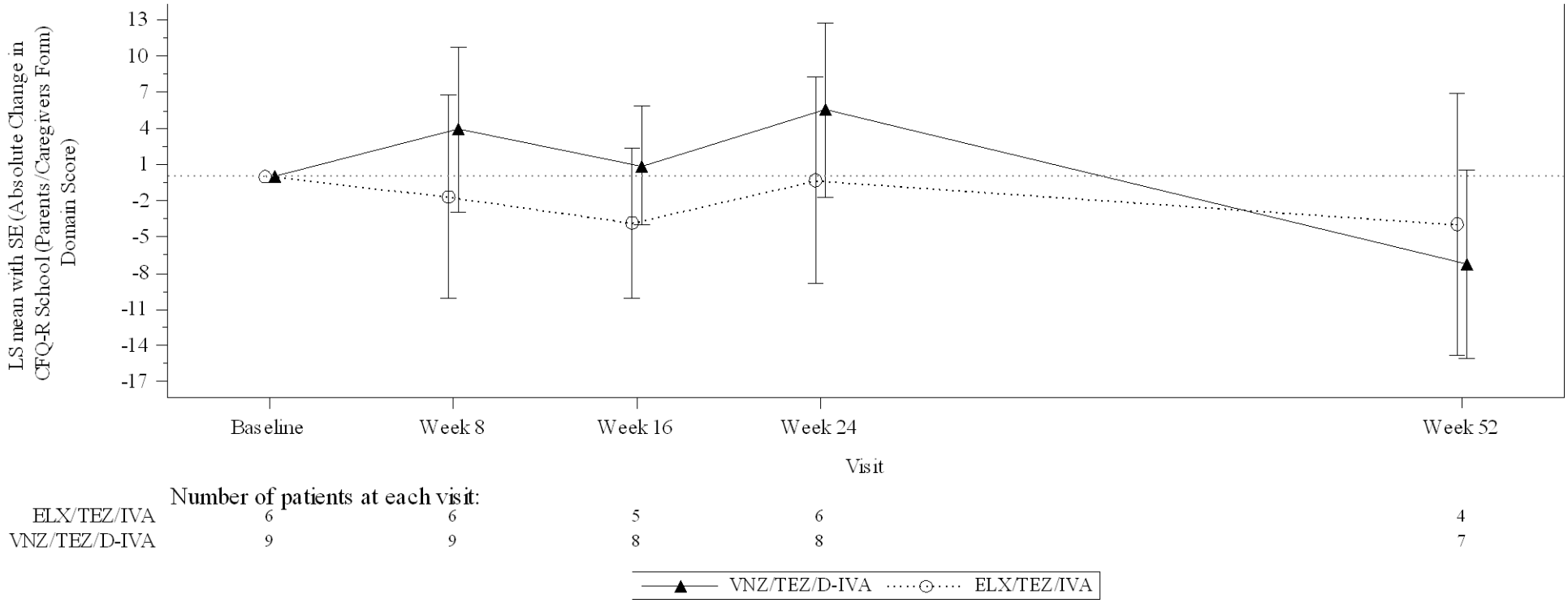
Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
Sex = Female



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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: School (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Full Analysis Set

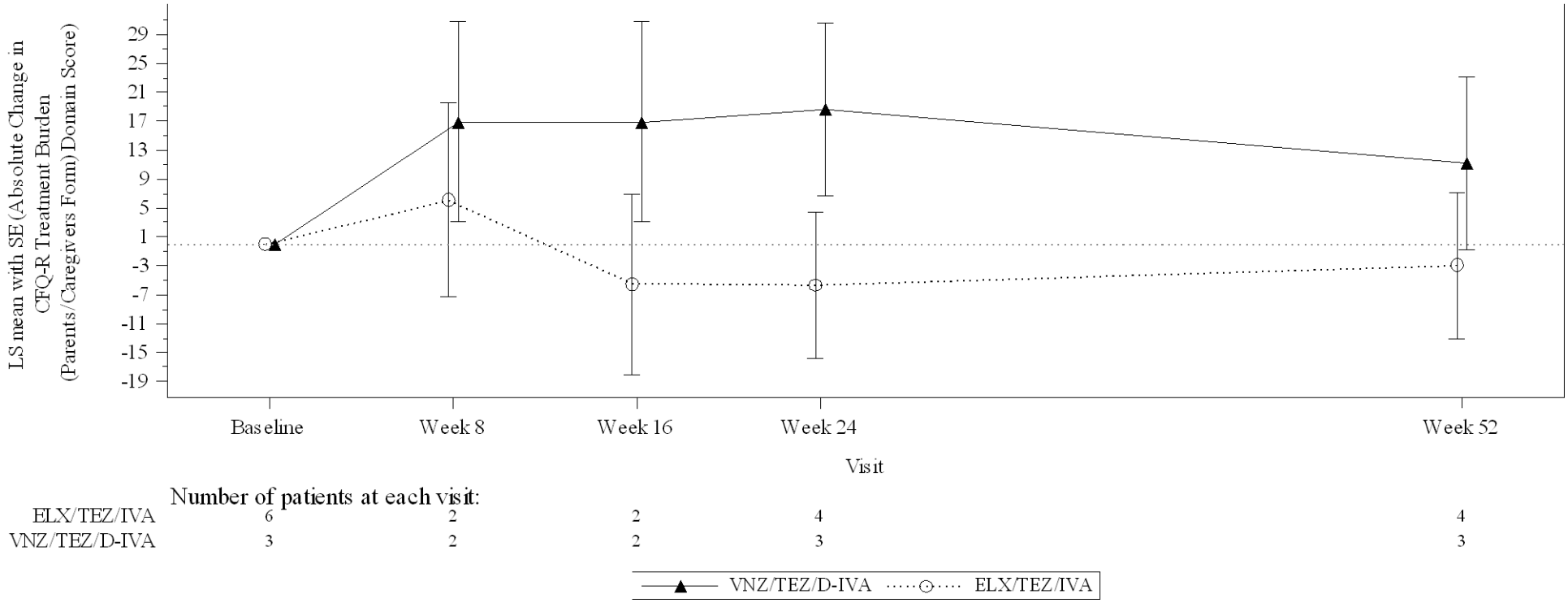
Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

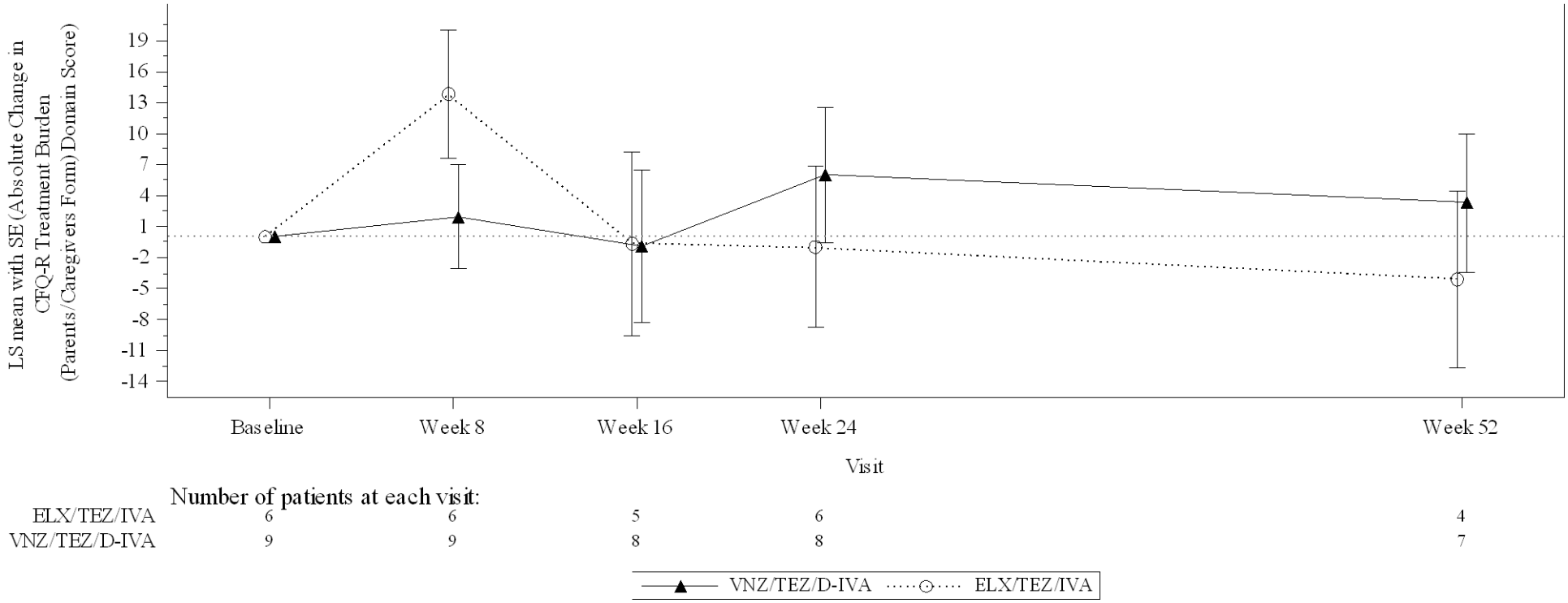
Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female



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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
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Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

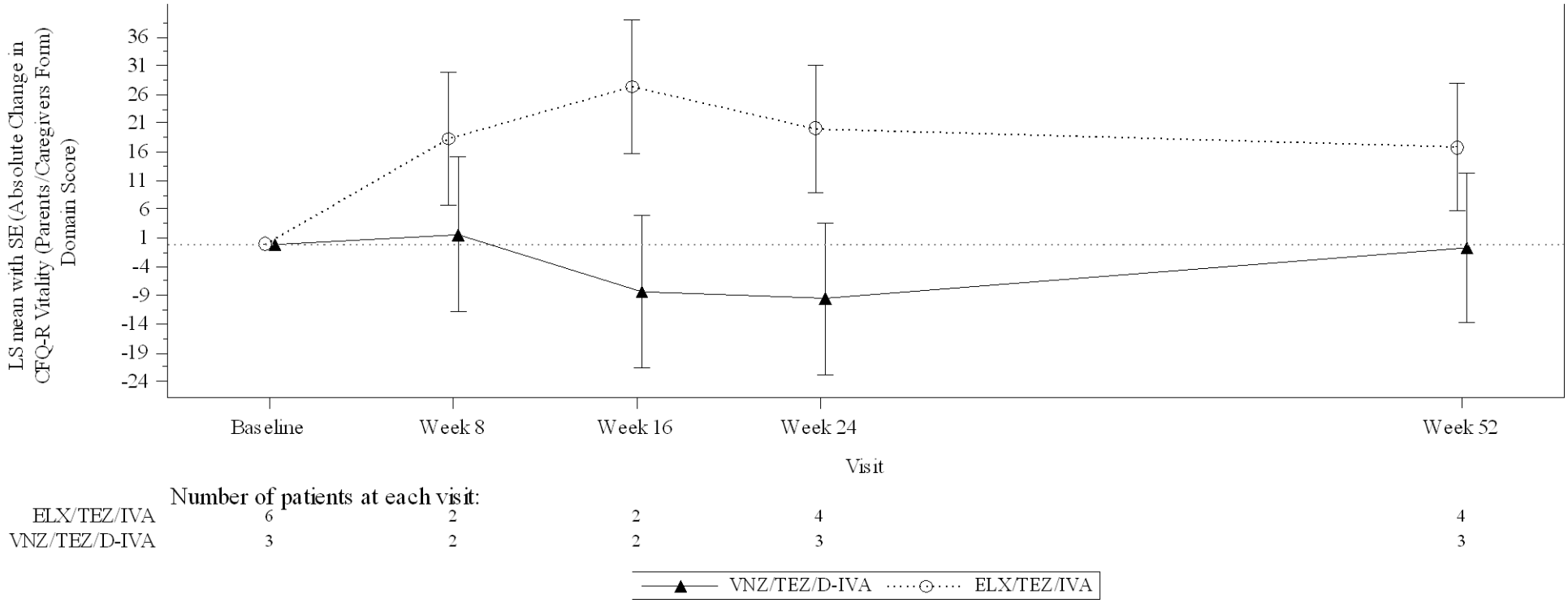
Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

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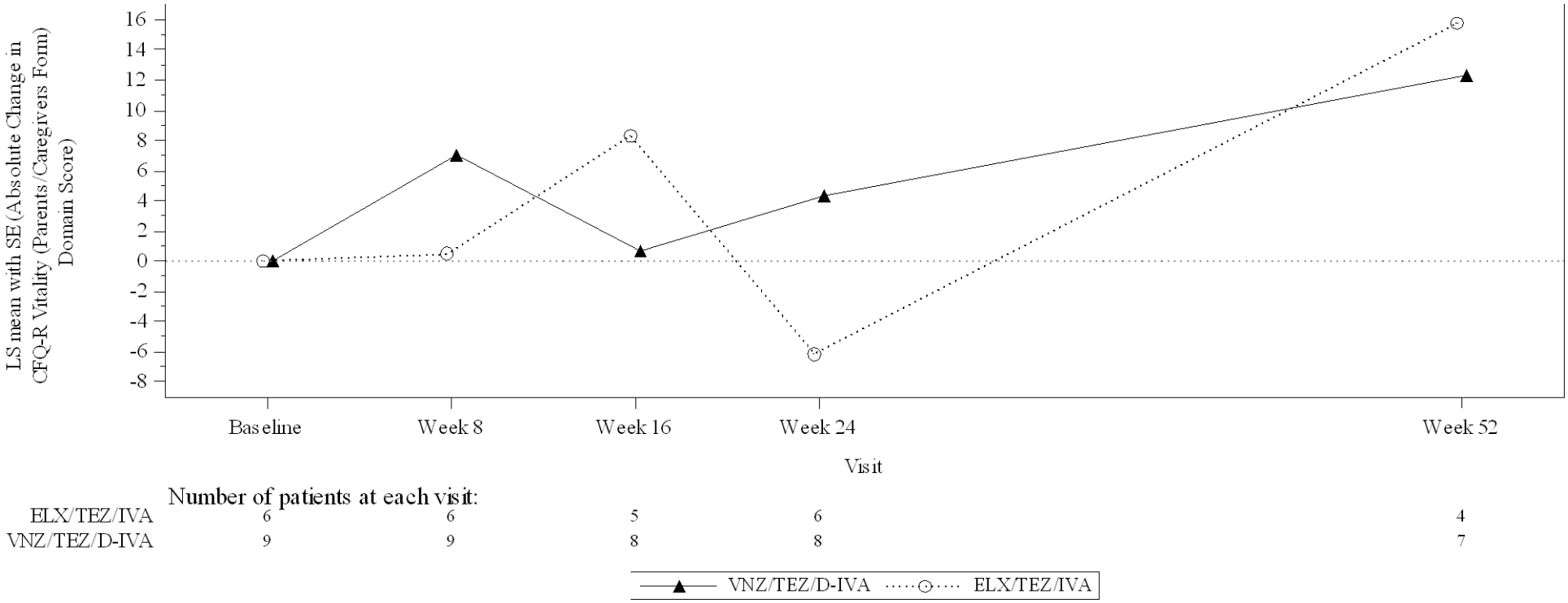
Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
Sex = Male



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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
Sex = Female



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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

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Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
$ppFEV_1$ at baseline <70 %

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
$ppFEV_1$ at baseline ≥70 %

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Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
SwCl at baseline <30 mmol/L

Subgroup criteria are not met for this subgroup factor.

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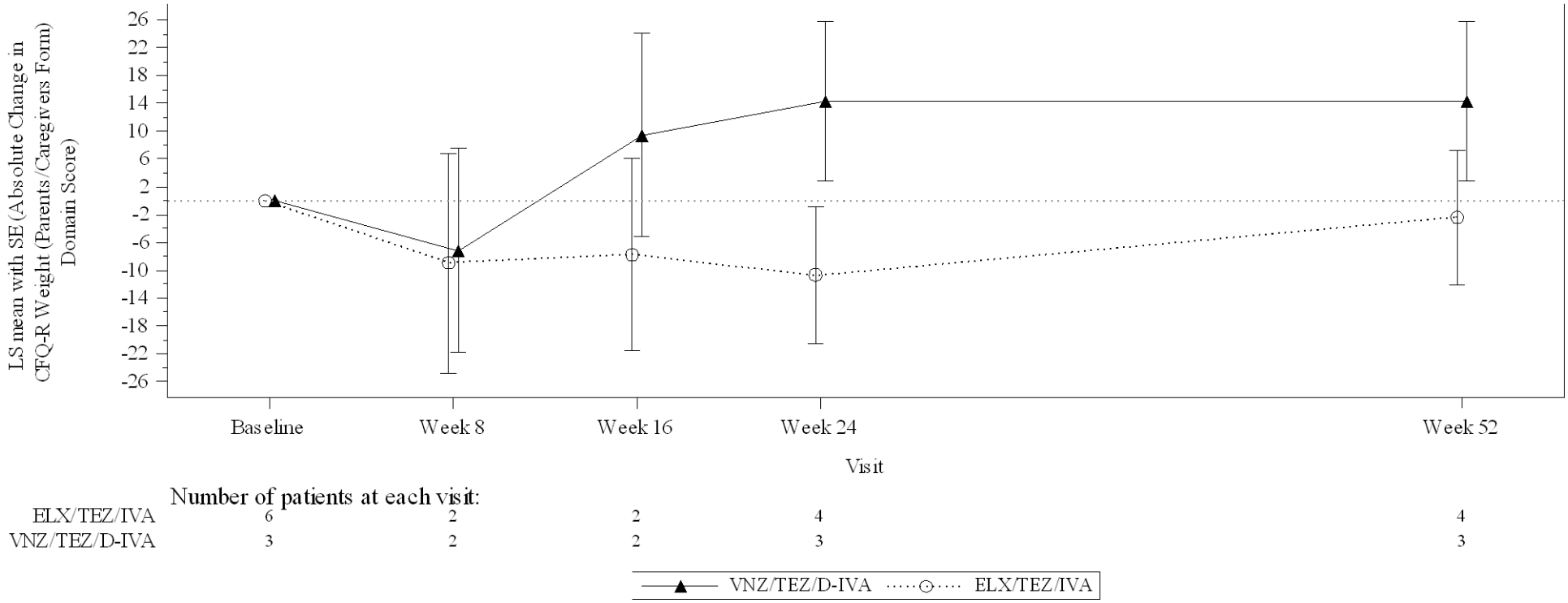
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Domain: Weight (Parents/Caregivers Form)
SwCl at baseline ≥30 mmol/L

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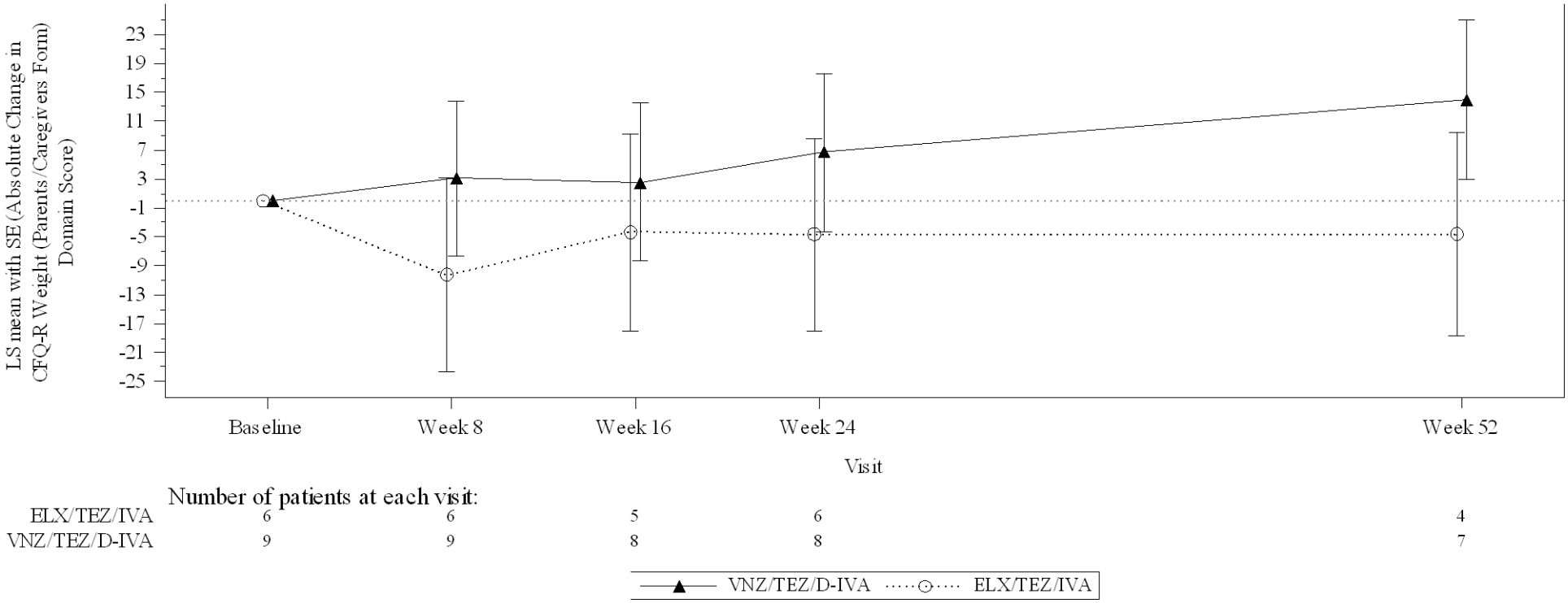
Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
Sex = Male



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Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, genotype group (F/F, non-F/F) and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
Region = North America

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.9.6
Study VX20-121-103: Plot of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit up to Week 52 by Subgroups
Full Analysis Set

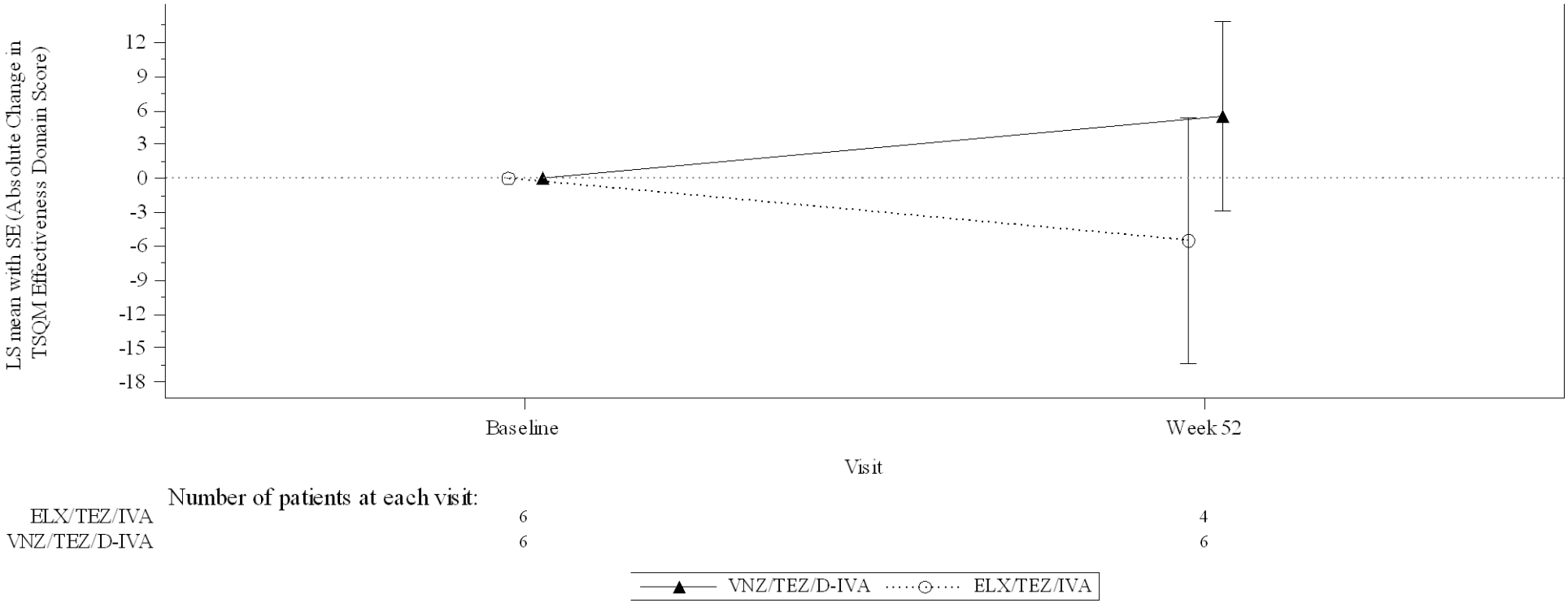
Version: Parents/Caregivers Version
Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from all available visits up to Week 52. The model includes fixed categorical effects for treatment, visit, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

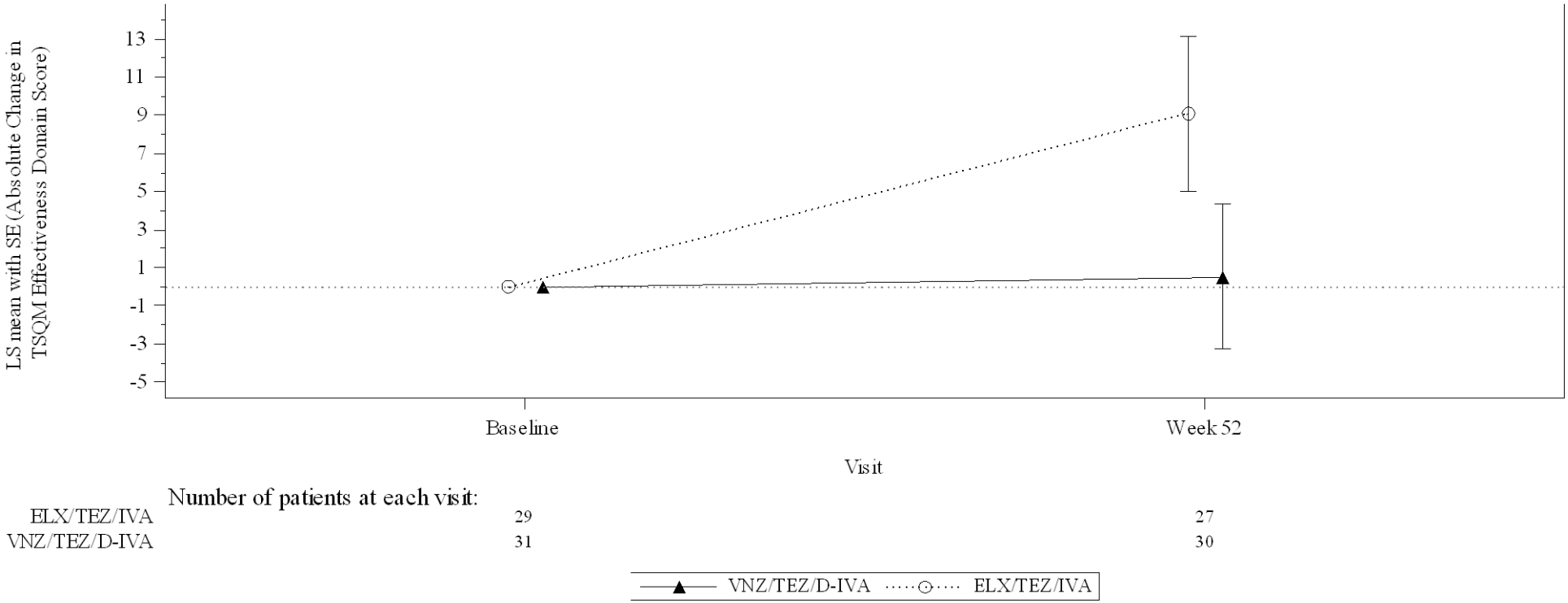
Domain: Effectiveness
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
$ppFEV_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Effectiveness
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

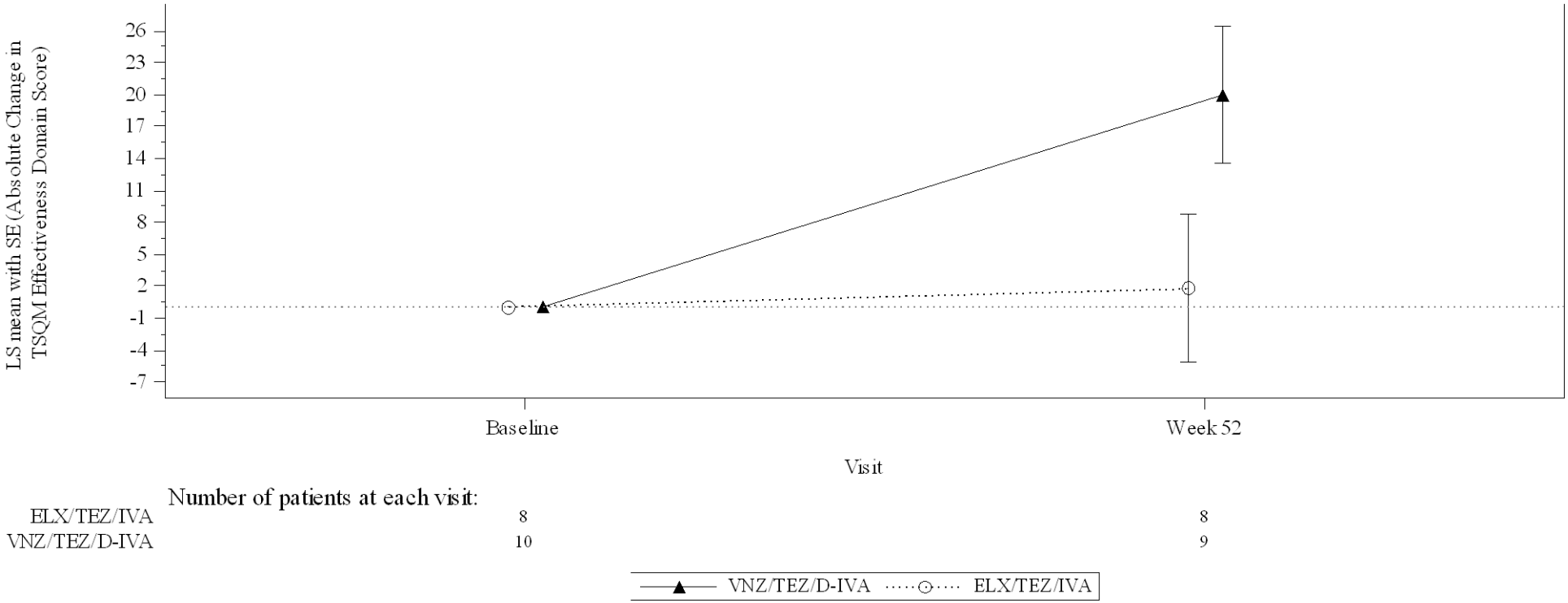
Domain: Effectiveness
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

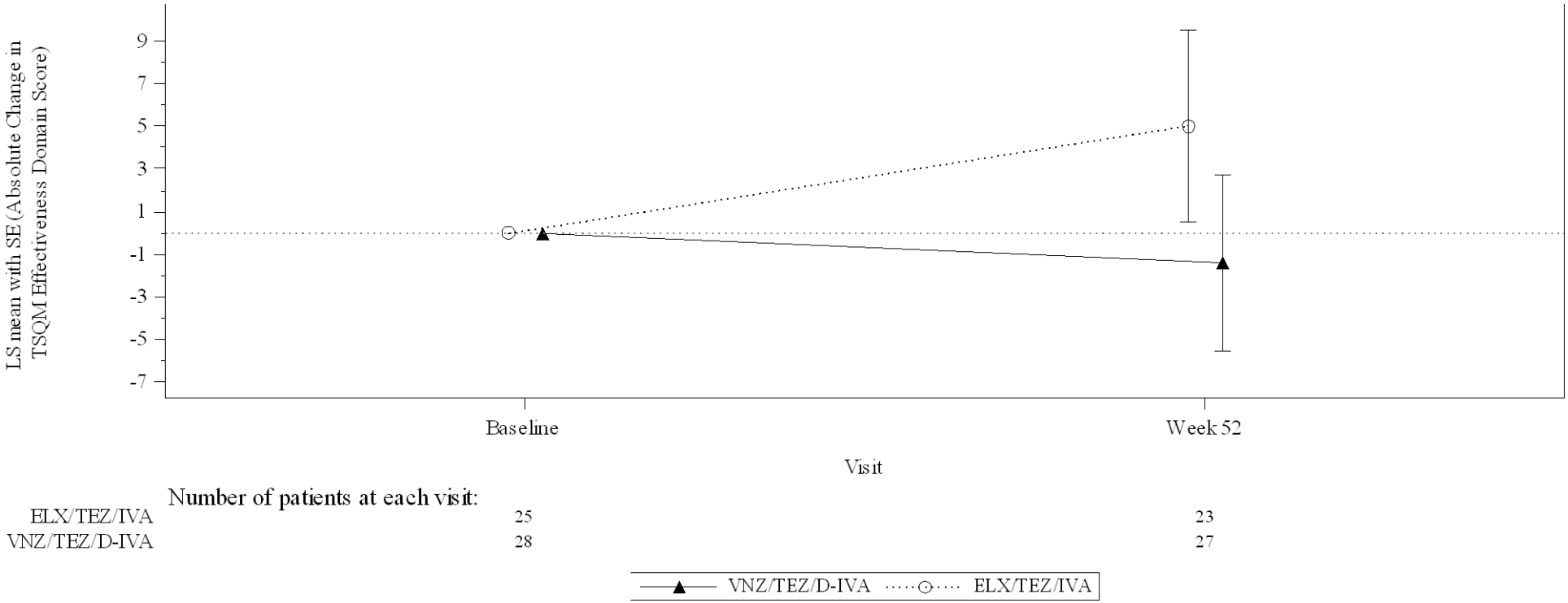
Domain: Effectiveness
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

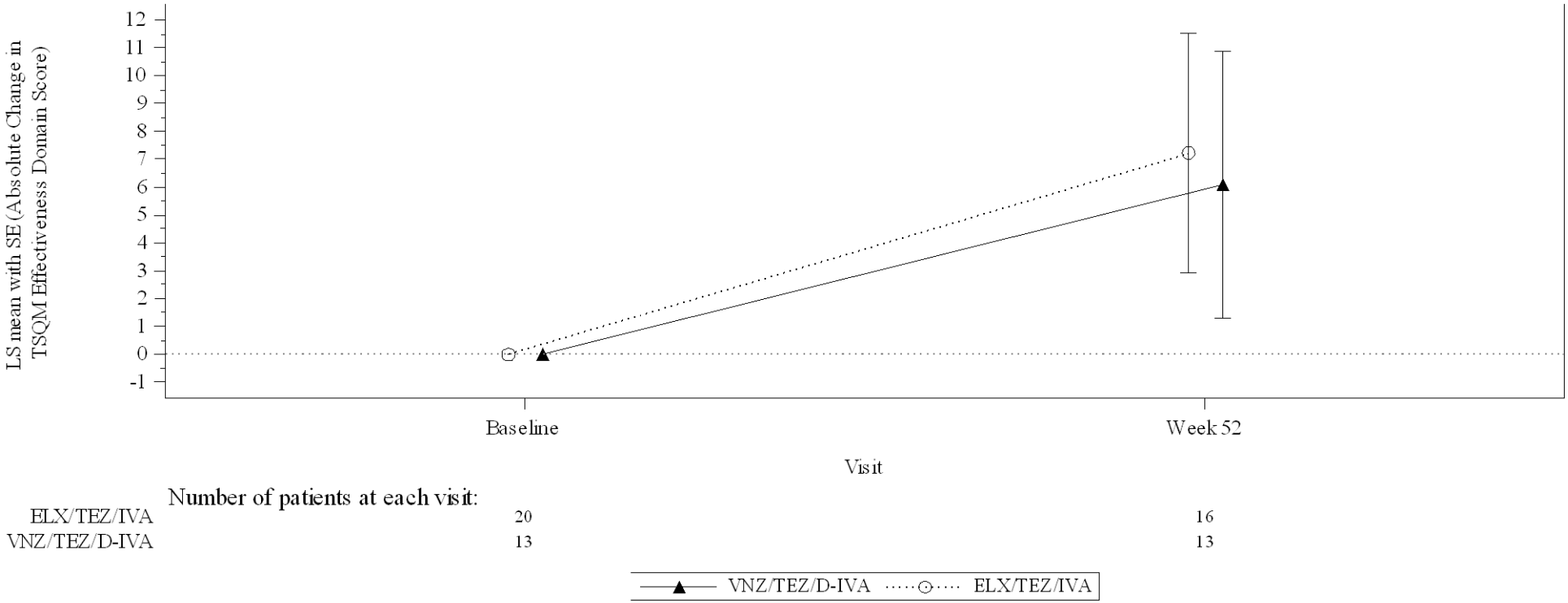
Domain: Effectiveness
SwCl at baseline ≥30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

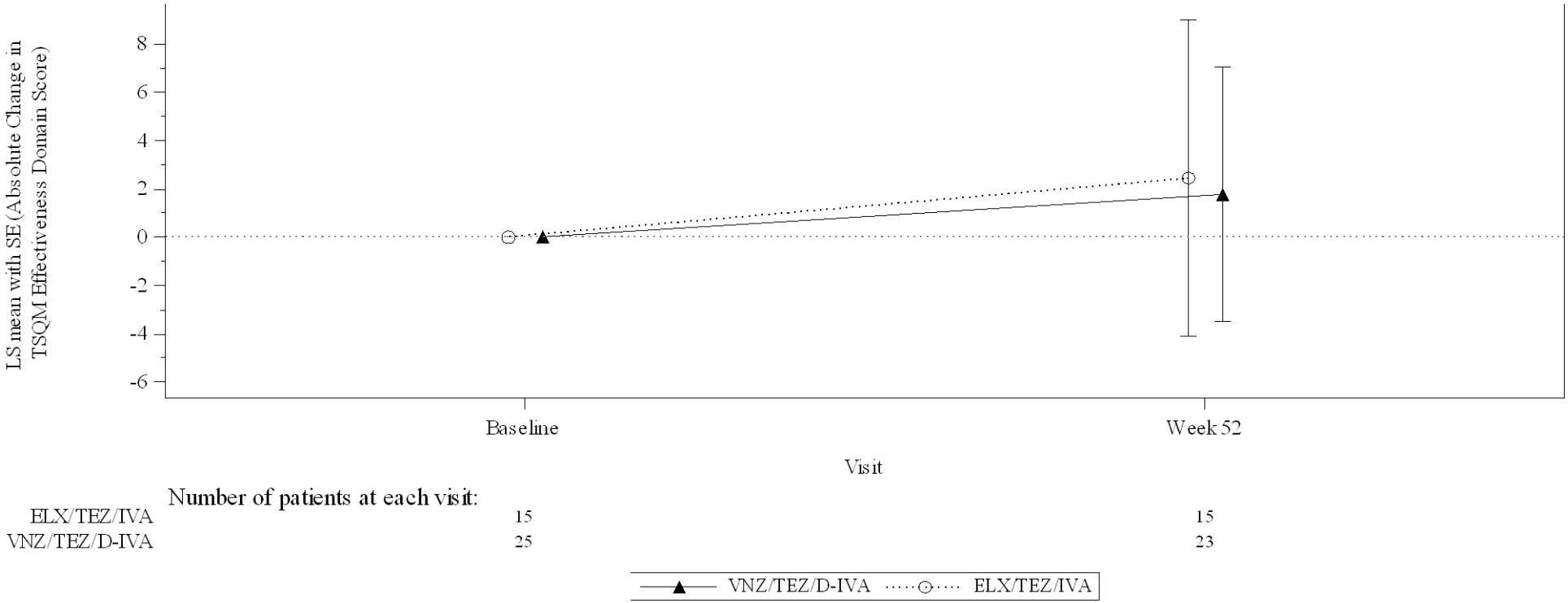
Domain: Effectiveness
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

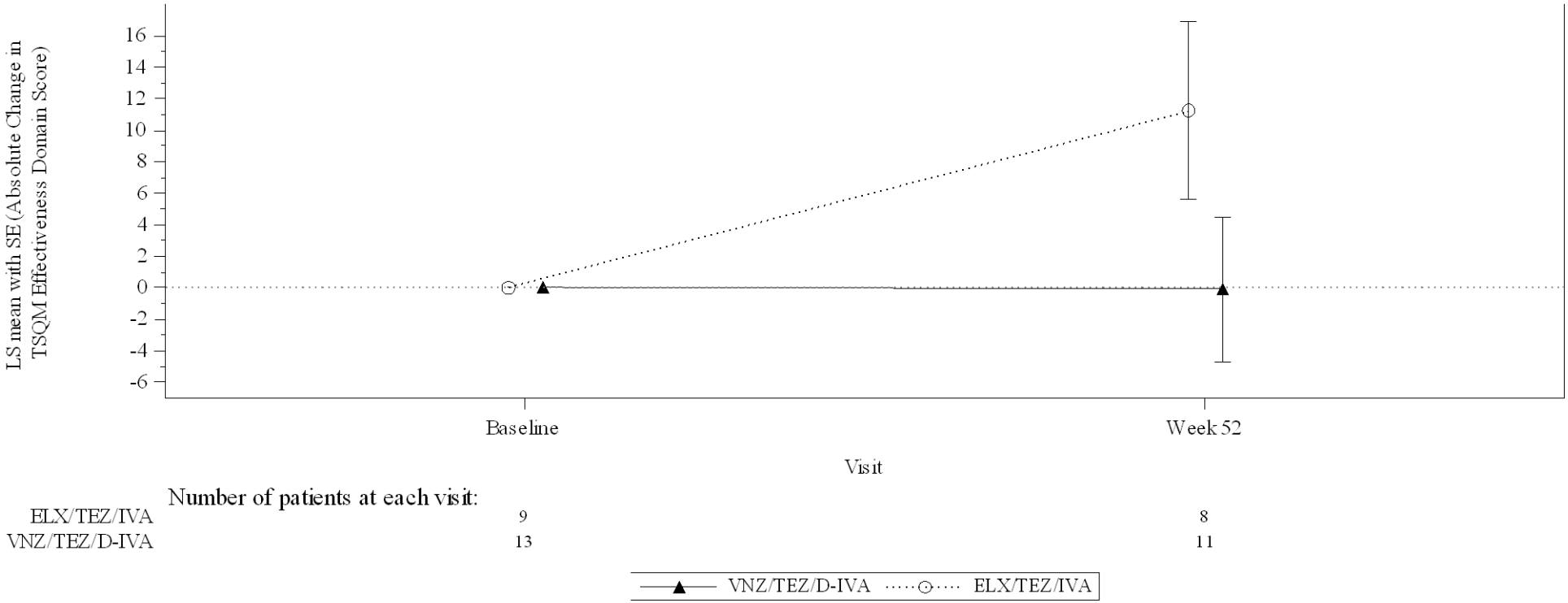
Domain: Effectiveness
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

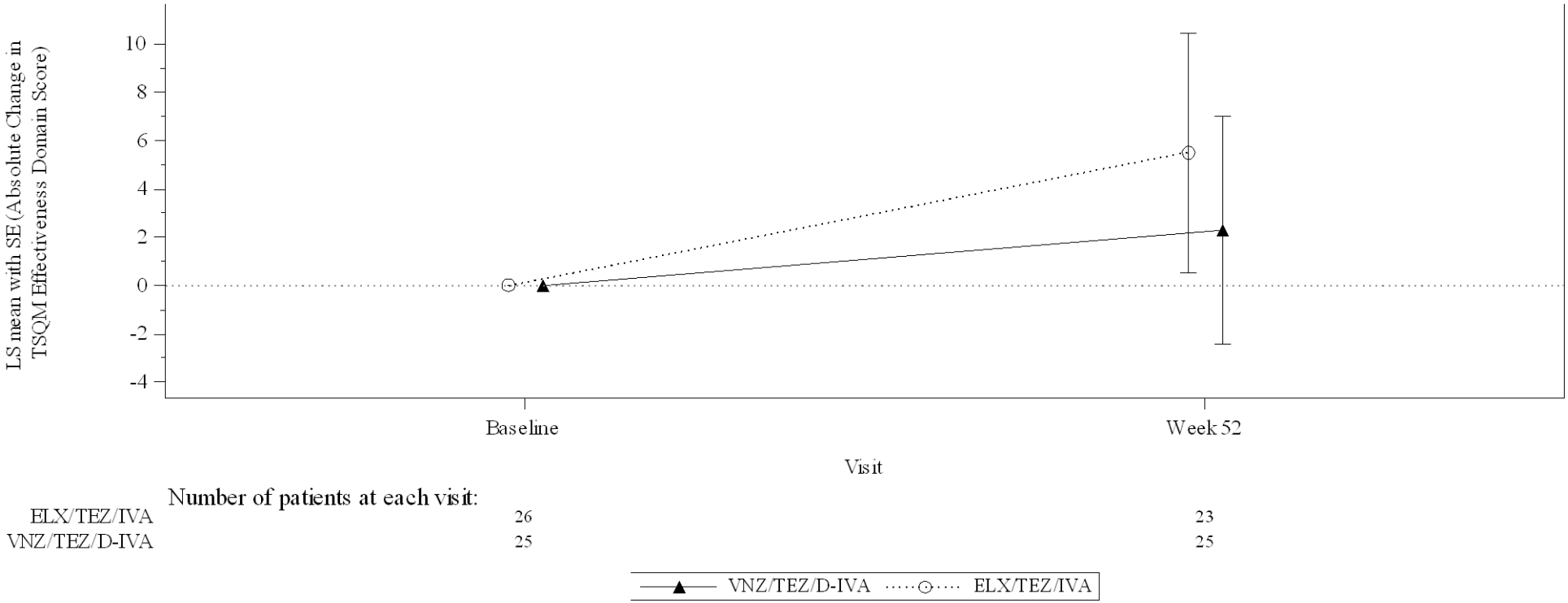
Domain: Effectiveness
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

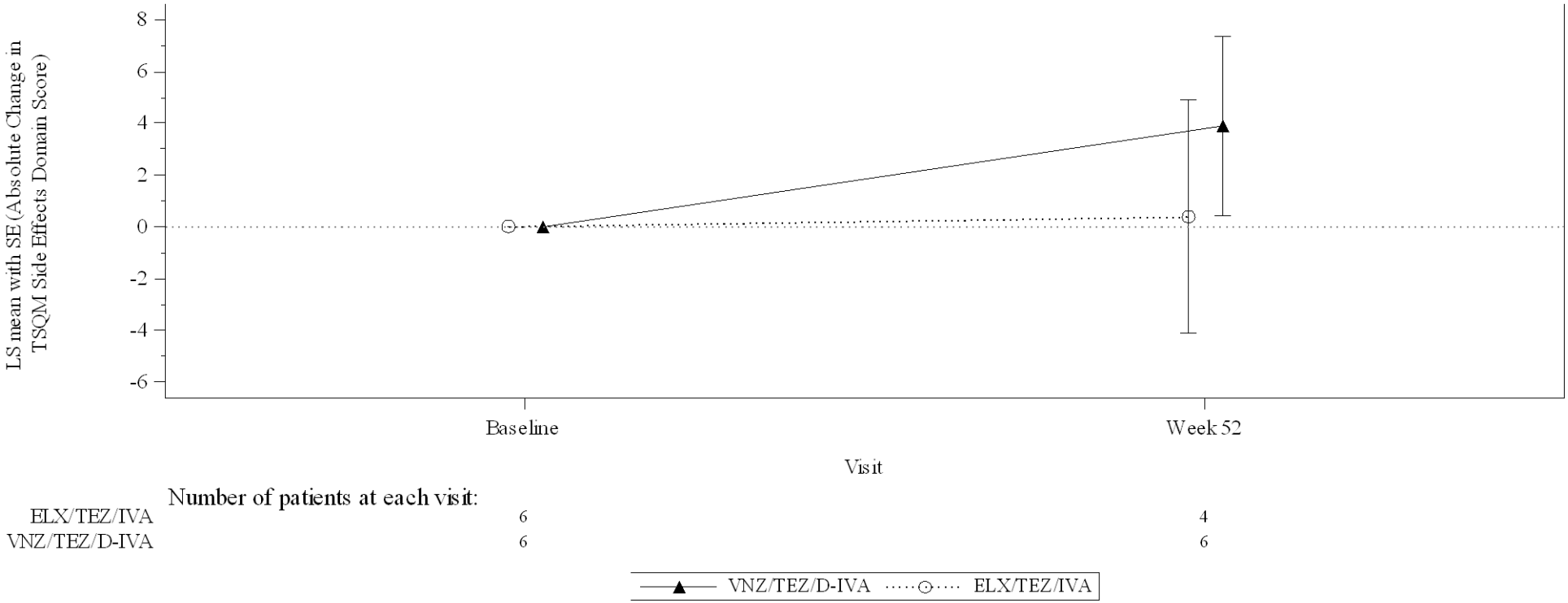
Domain: Effectiveness
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

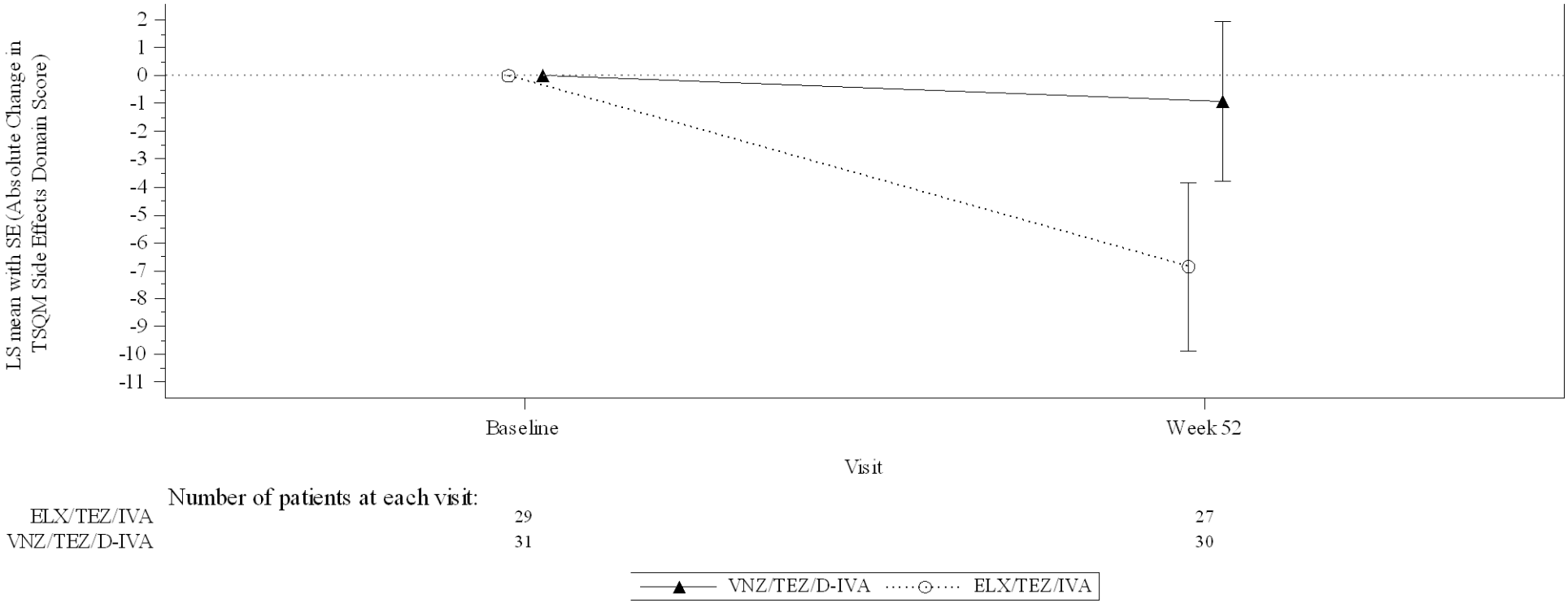
Domain: Side Effects
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
ppFEV$_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Side Effects
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

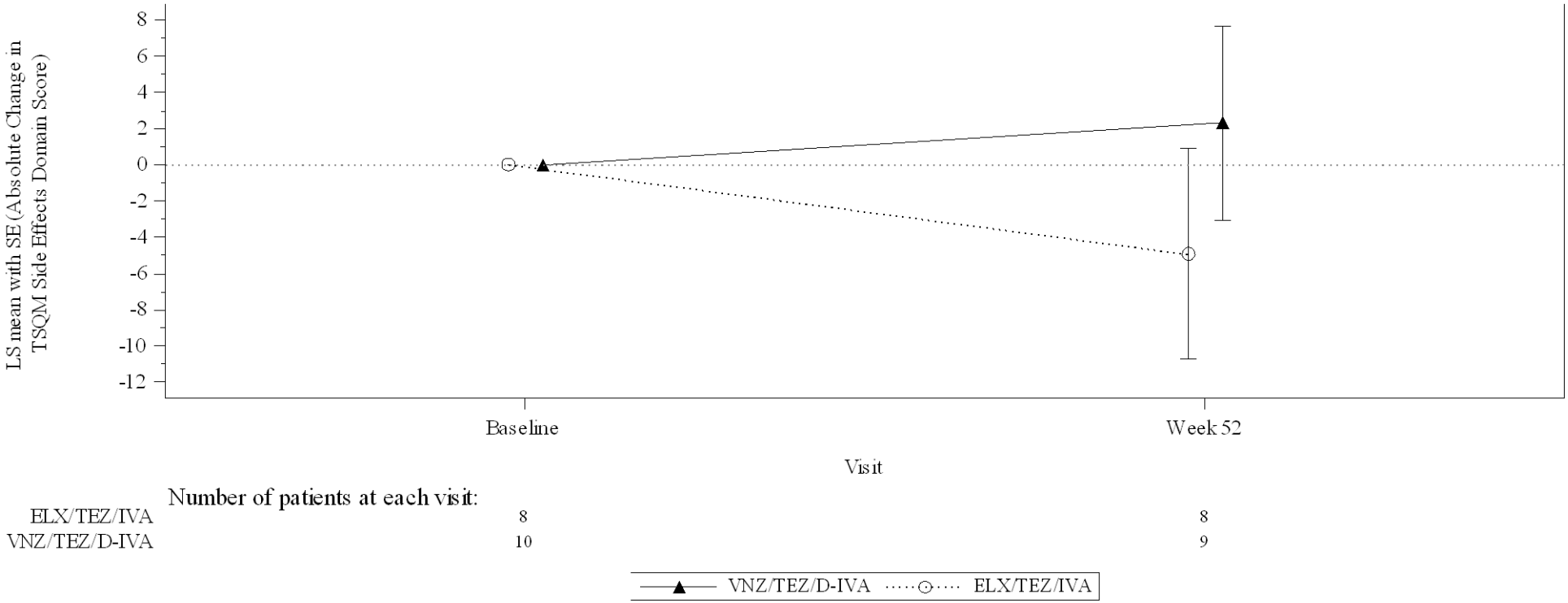
Domain: Side Effects
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

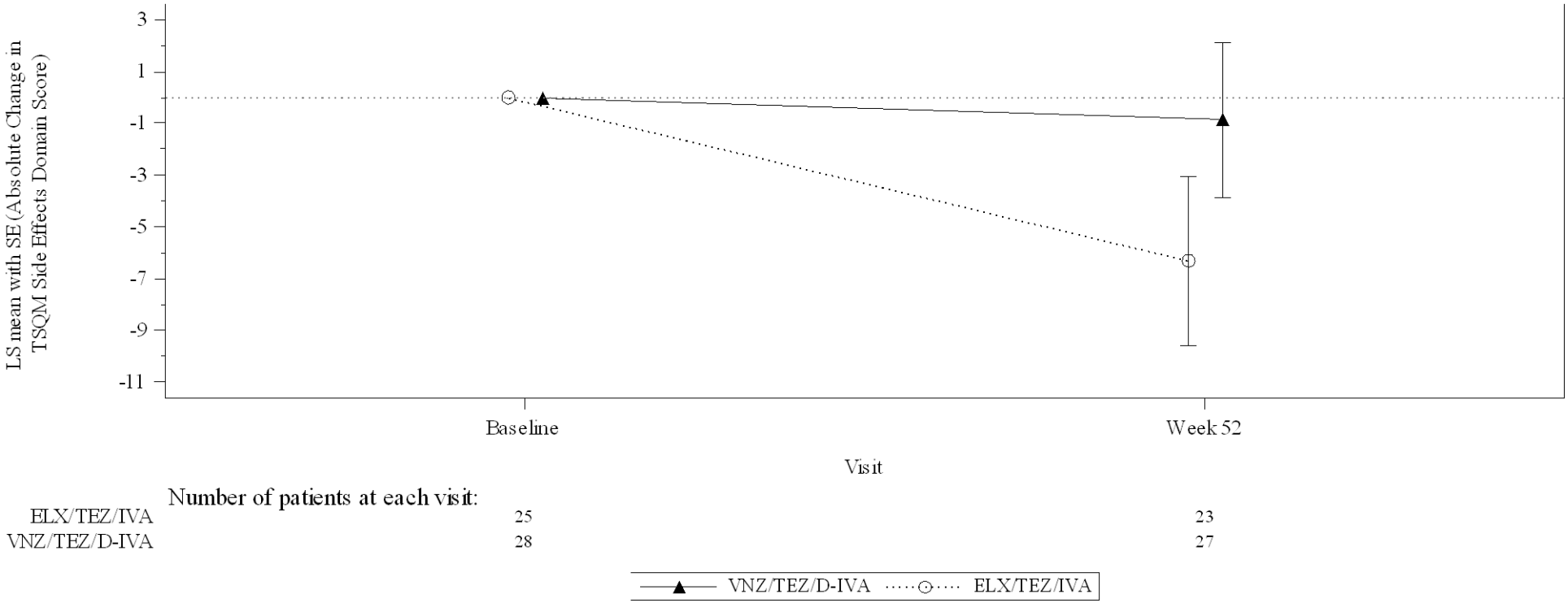
Domain: Side Effects
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, F/G, F/RF, TCR/non-F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

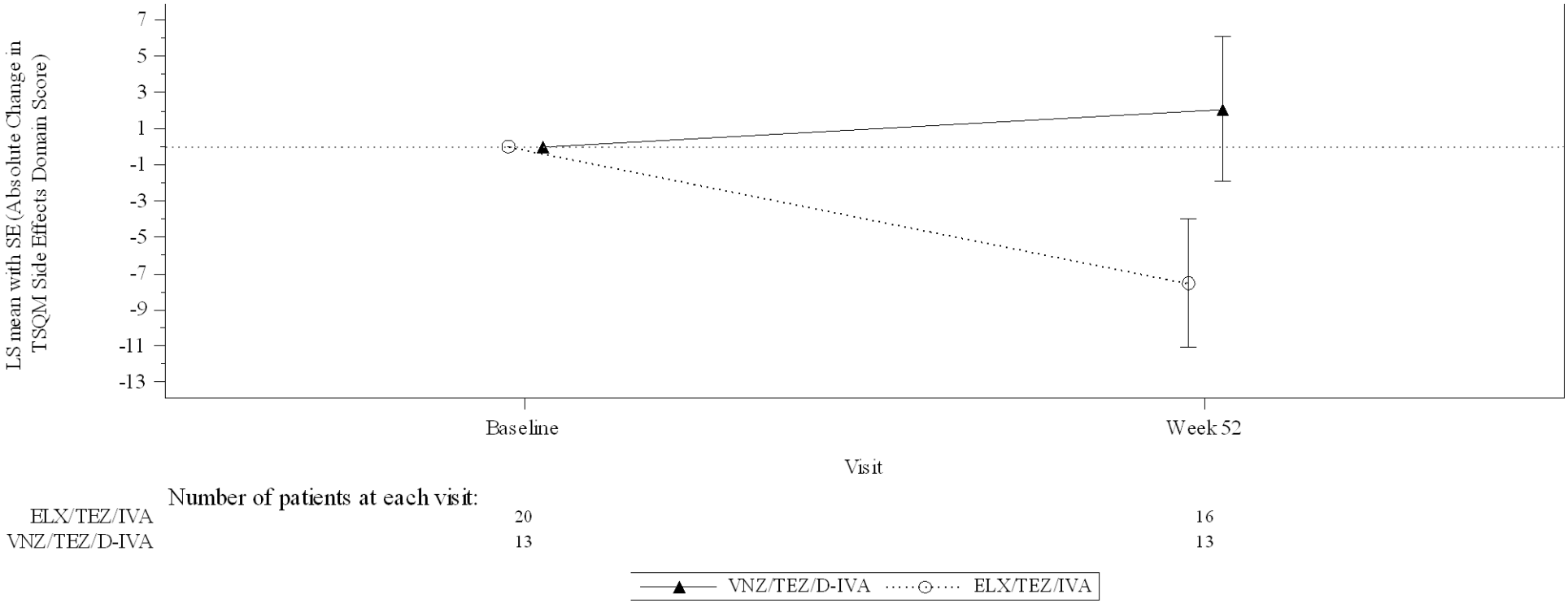
Domain: Side Effects
SwCl at baseline ≥30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

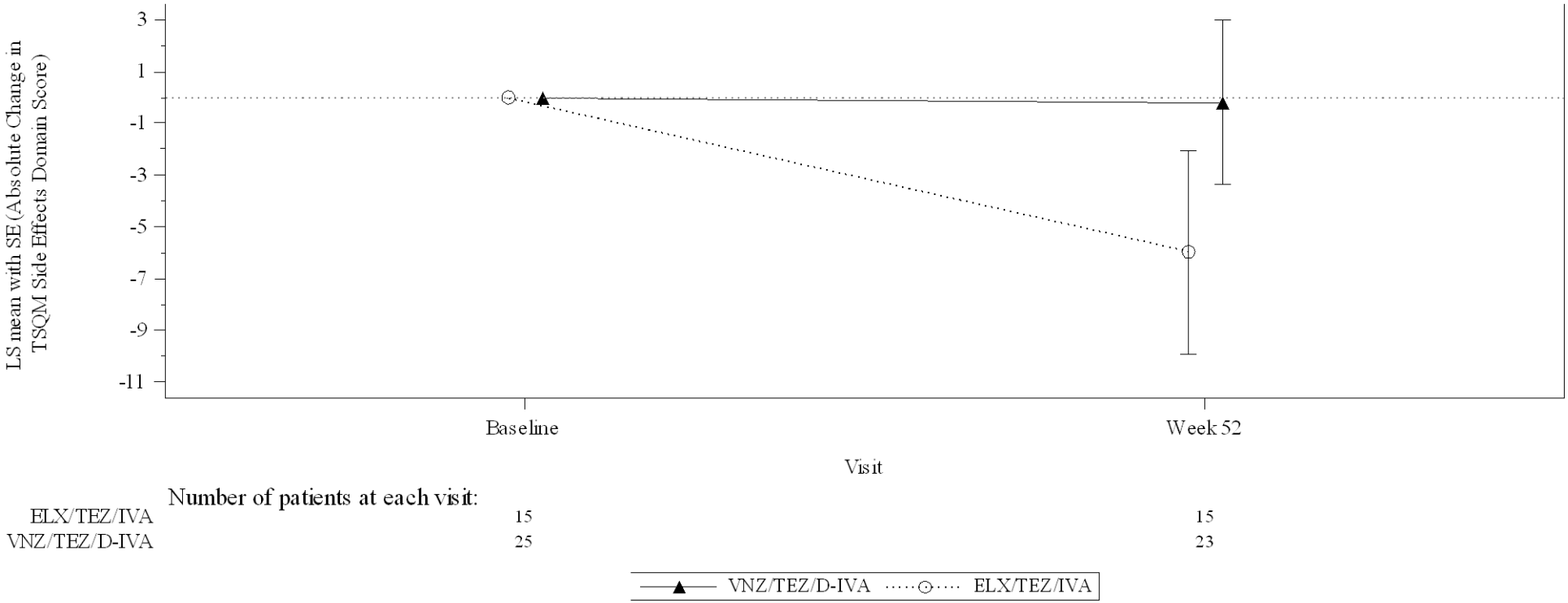
Domain: Side Effects
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

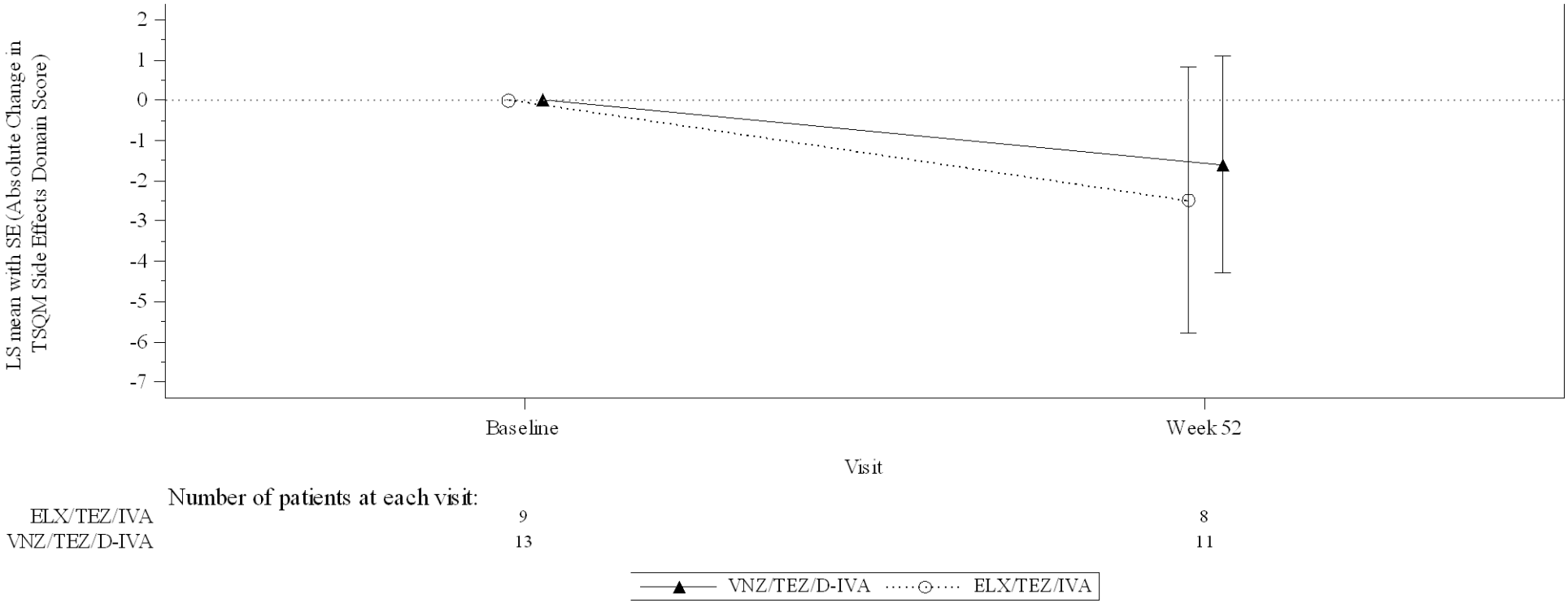
Domain: Side Effects
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

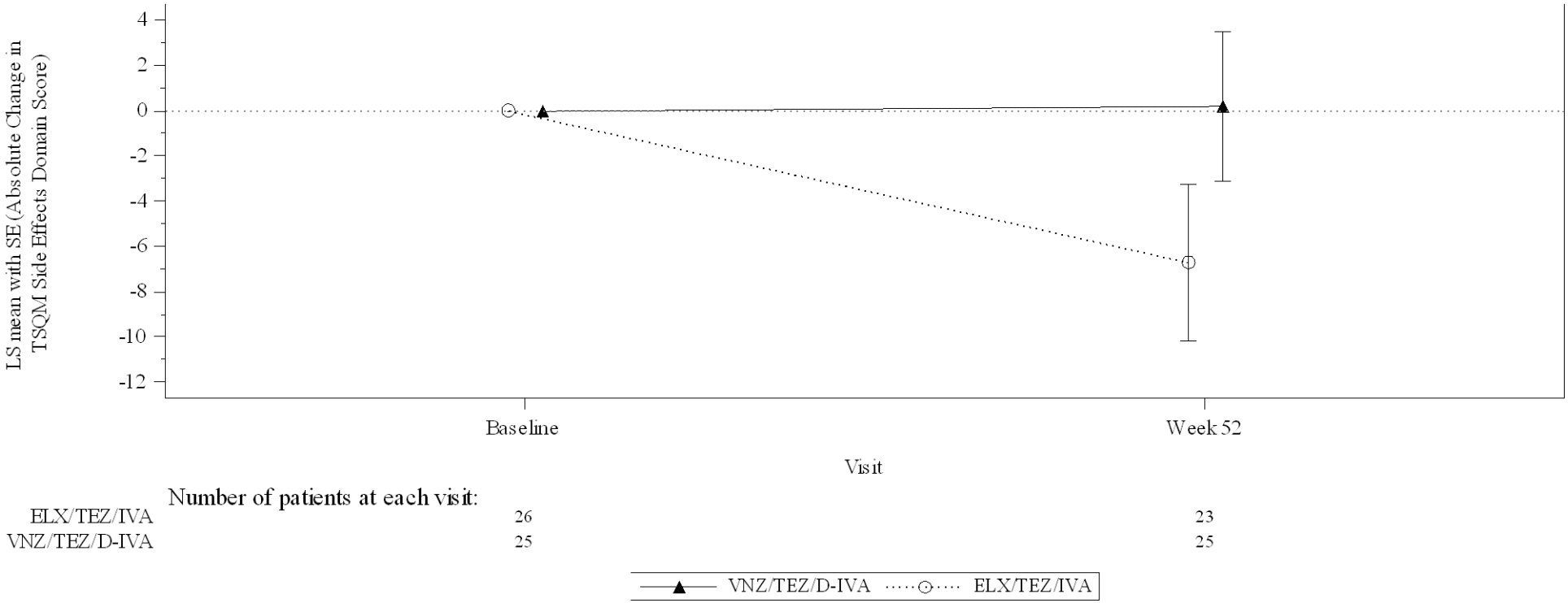
Domain: Side Effects
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

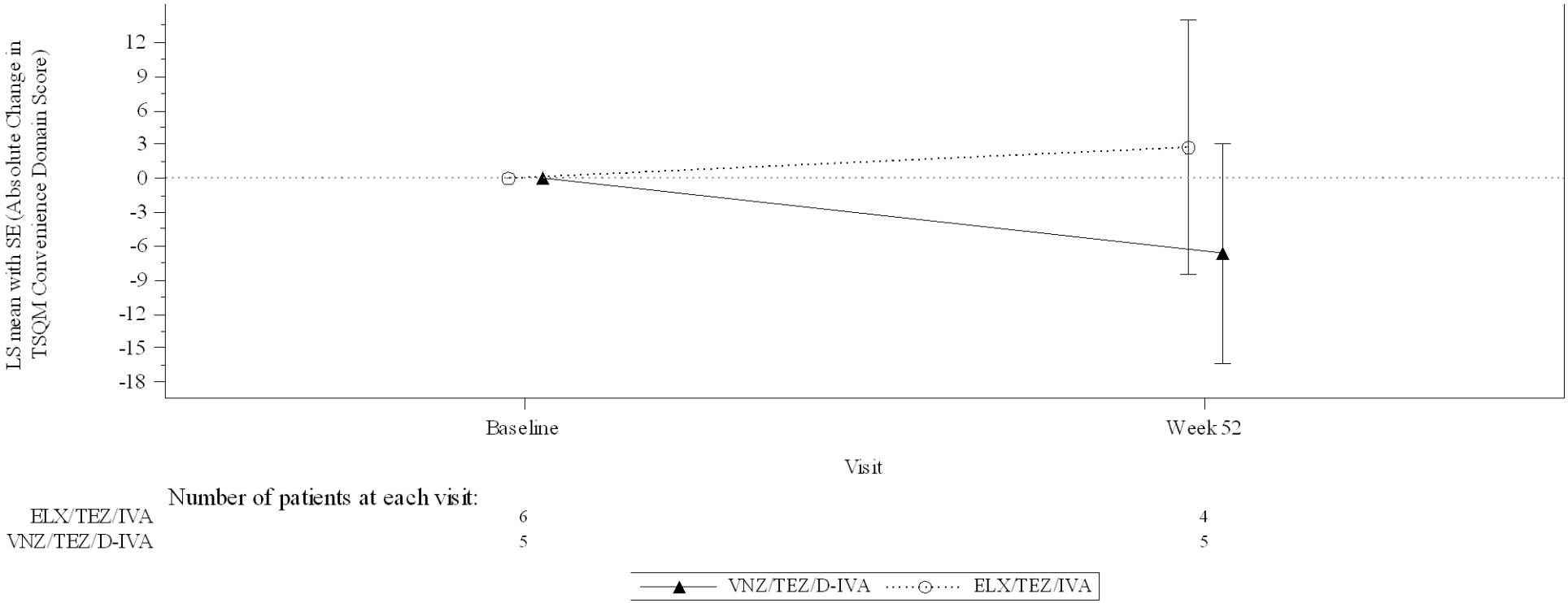
Domain: Side Effects
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

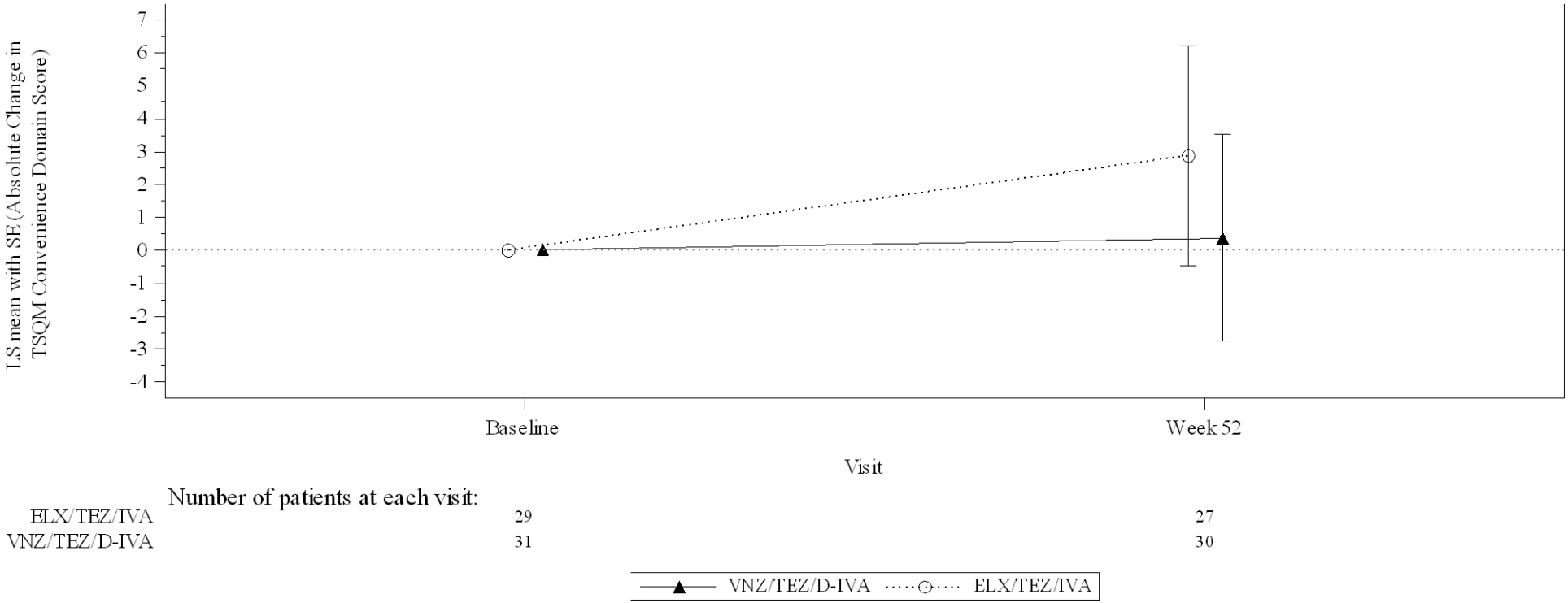
Domain: Convenience
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from Week 52. The model includes fixed categorical effects for treatment, genotype group (F/F, non-F/F), with baseline $ppFEV_1$ and baseline sweat chloride as continuous covariates.

Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
ppFEV$_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Convenience
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

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Figure 2.2.2.12.2
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Full Analysis Set

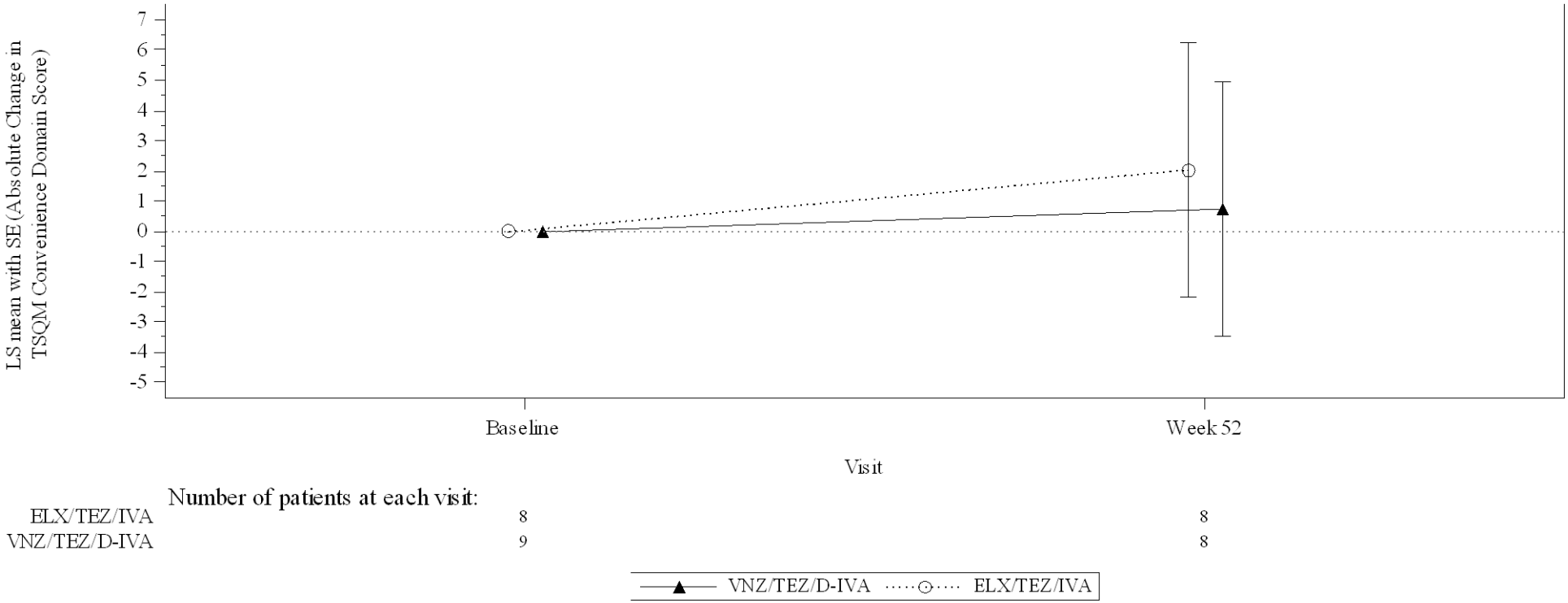
Domain: Convenience
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Full Analysis Set

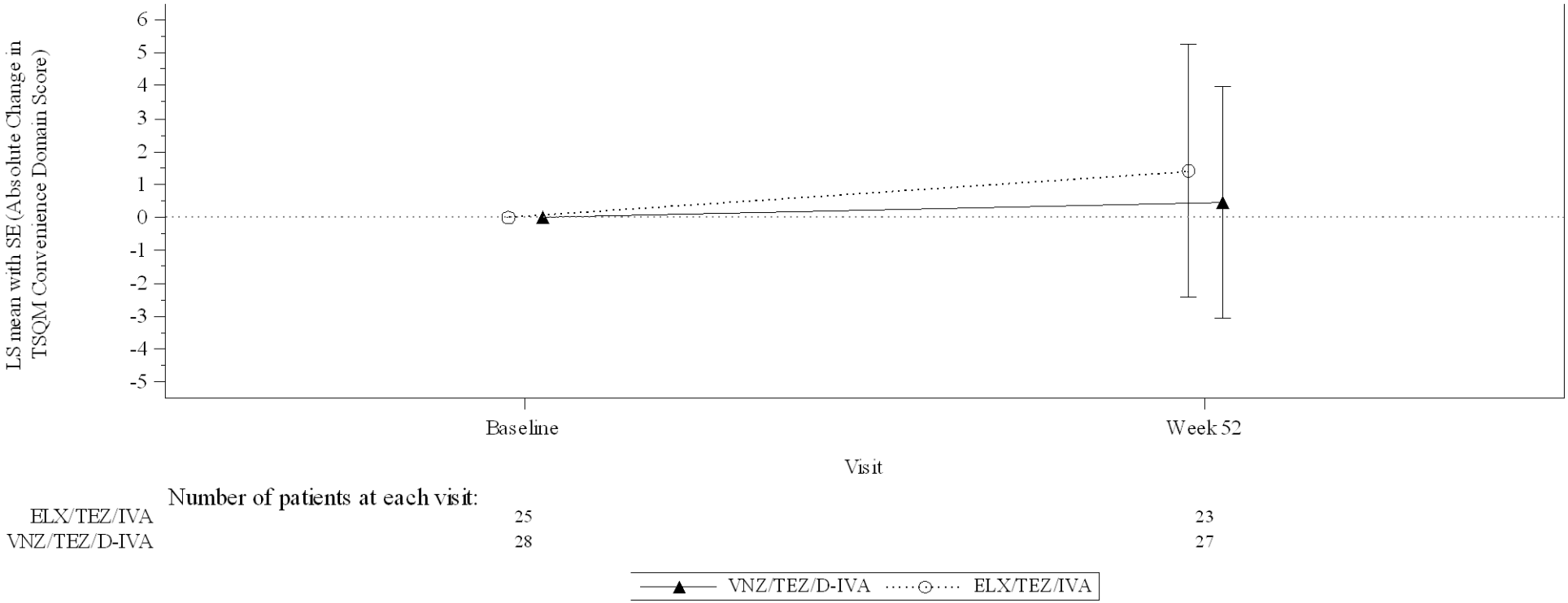
Domain: Convenience
SwCl at baseline <30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Full Analysis Set

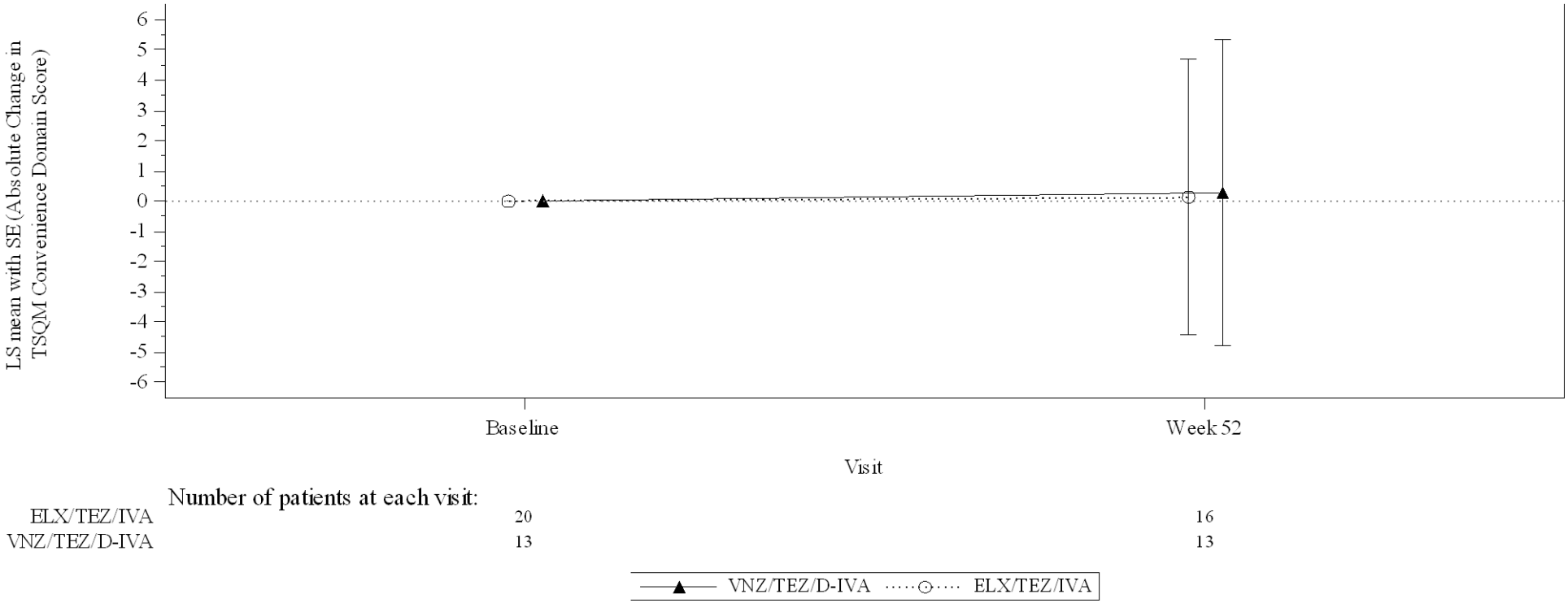
Domain: Convenience
SwCl at baseline ≥30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Full Analysis Set

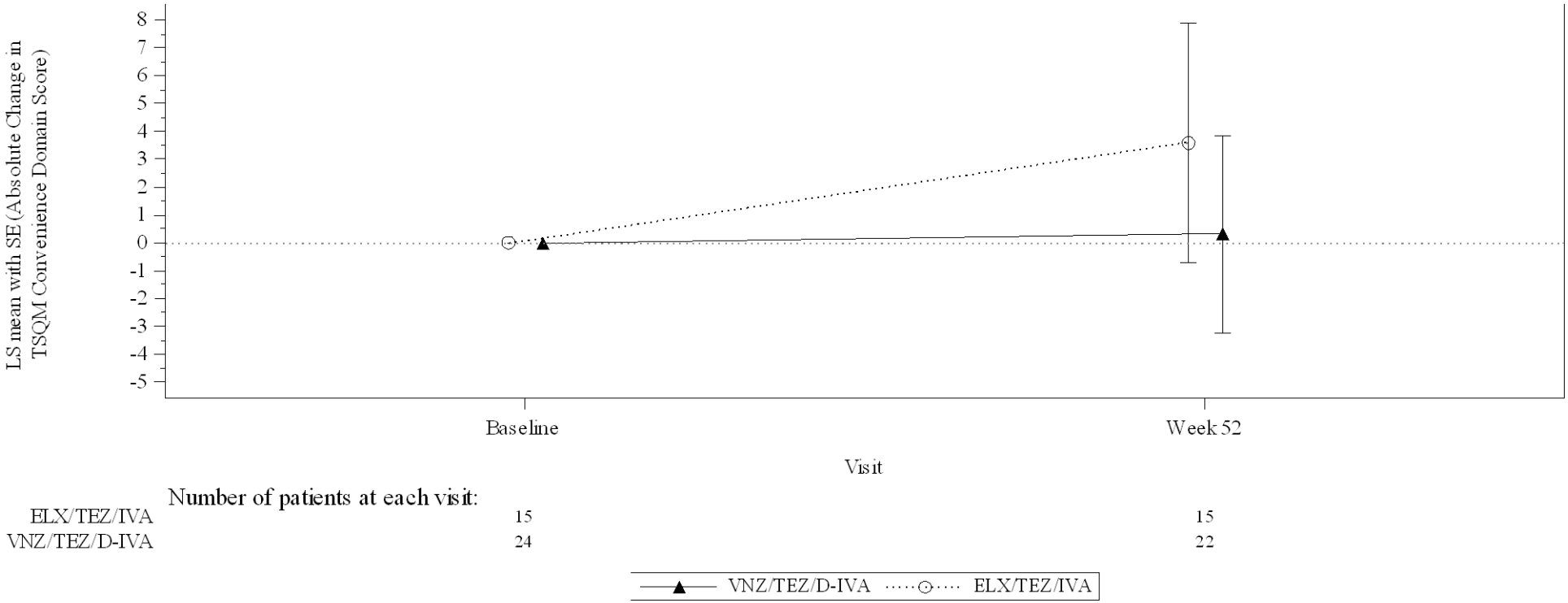
Domain: Convenience
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

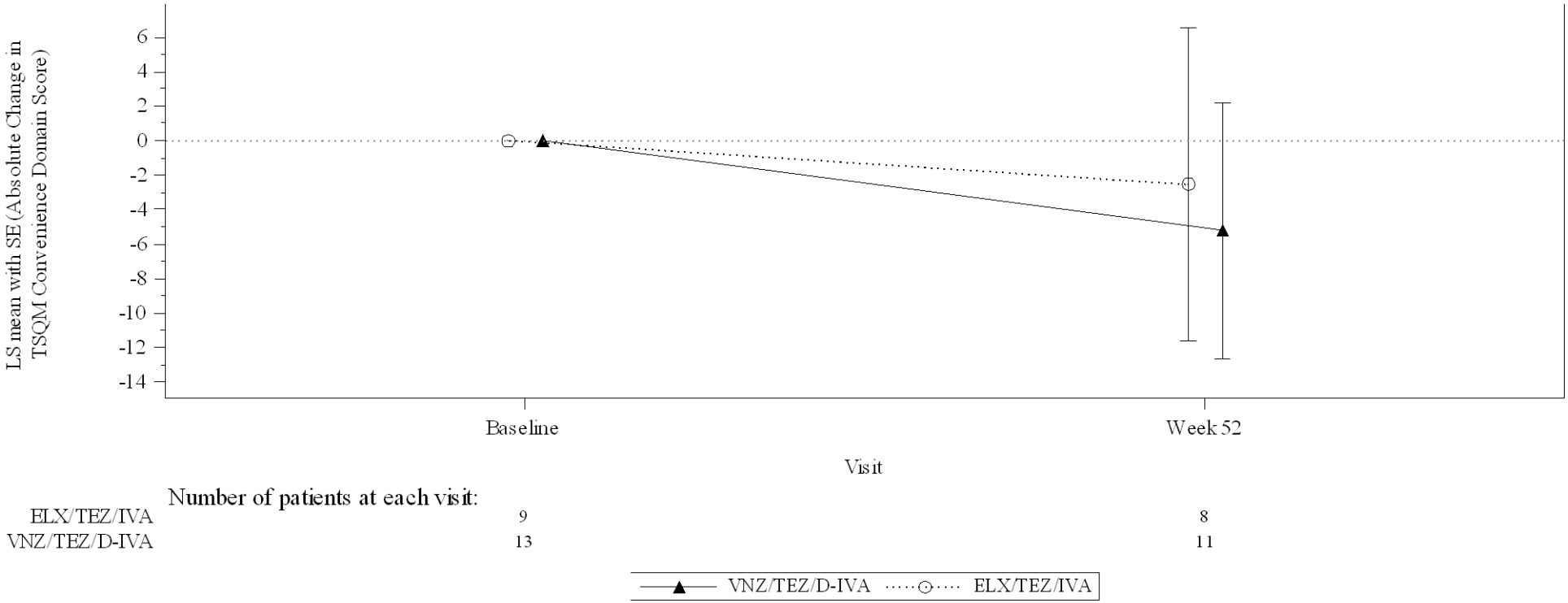
Domain: Convenience
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

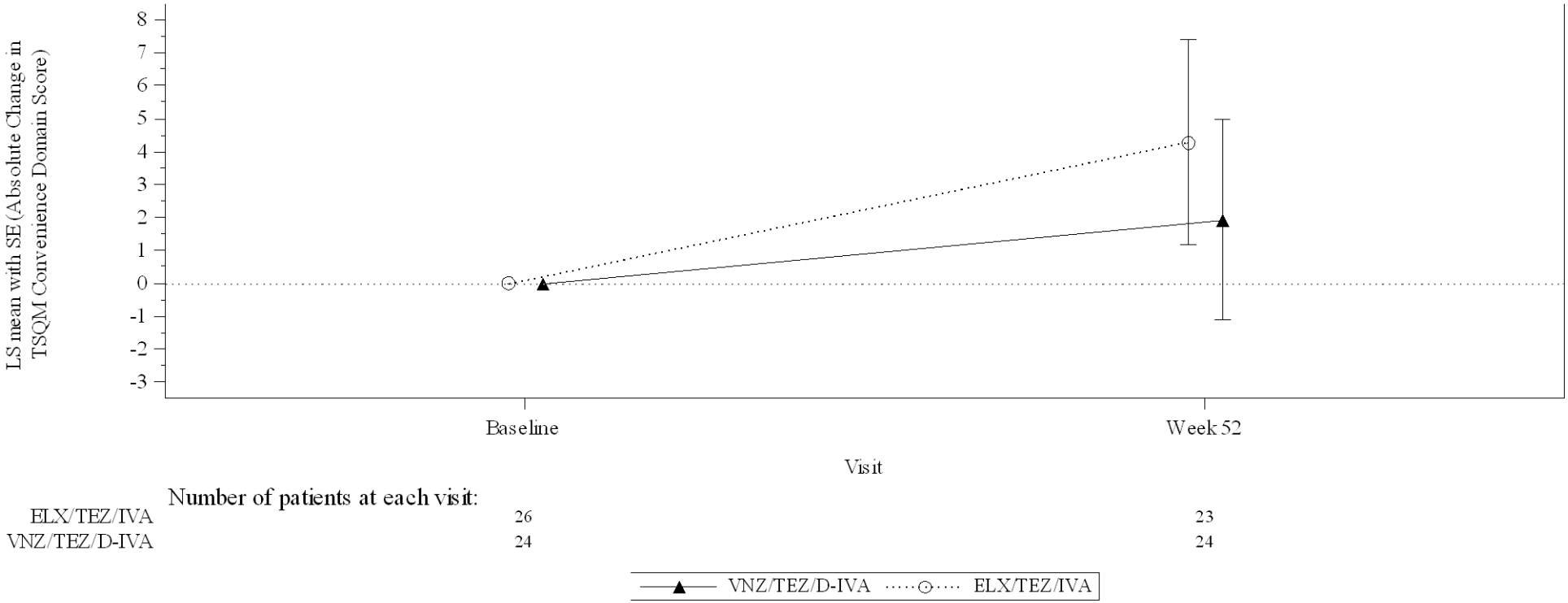
Domain: Convenience
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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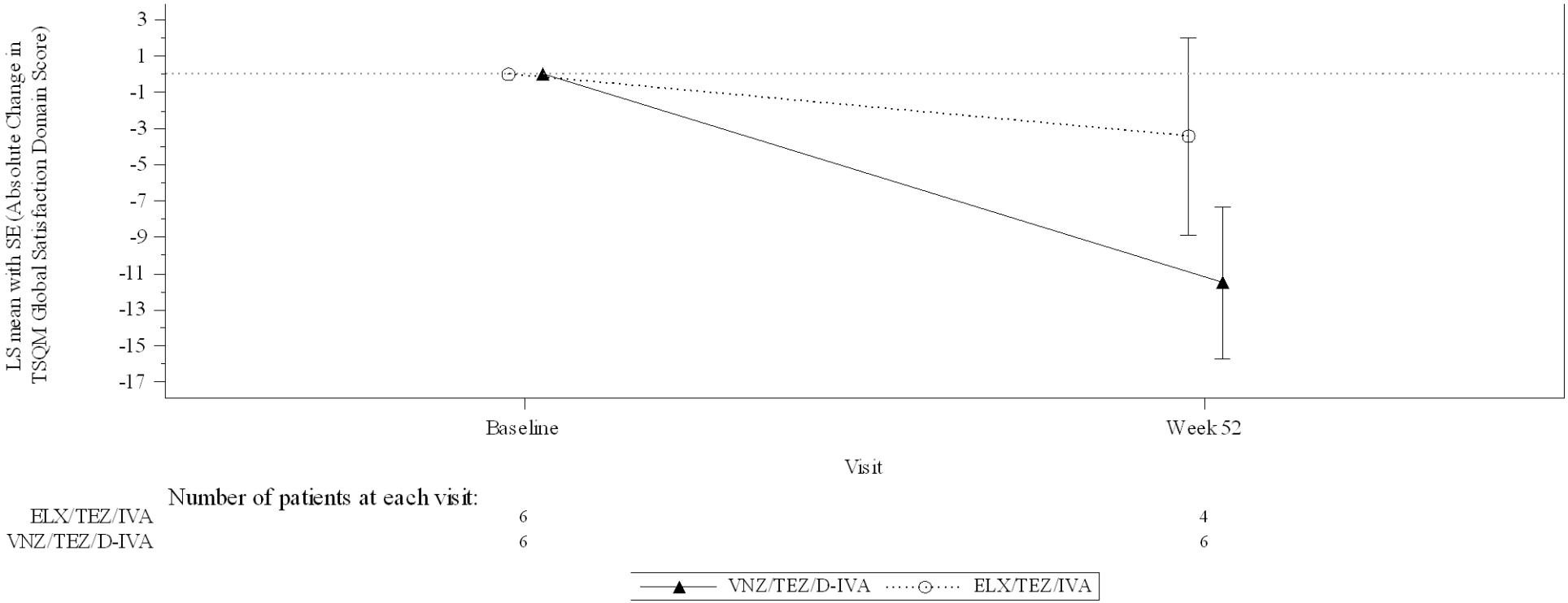
Domain: Convenience
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Full Analysis Set

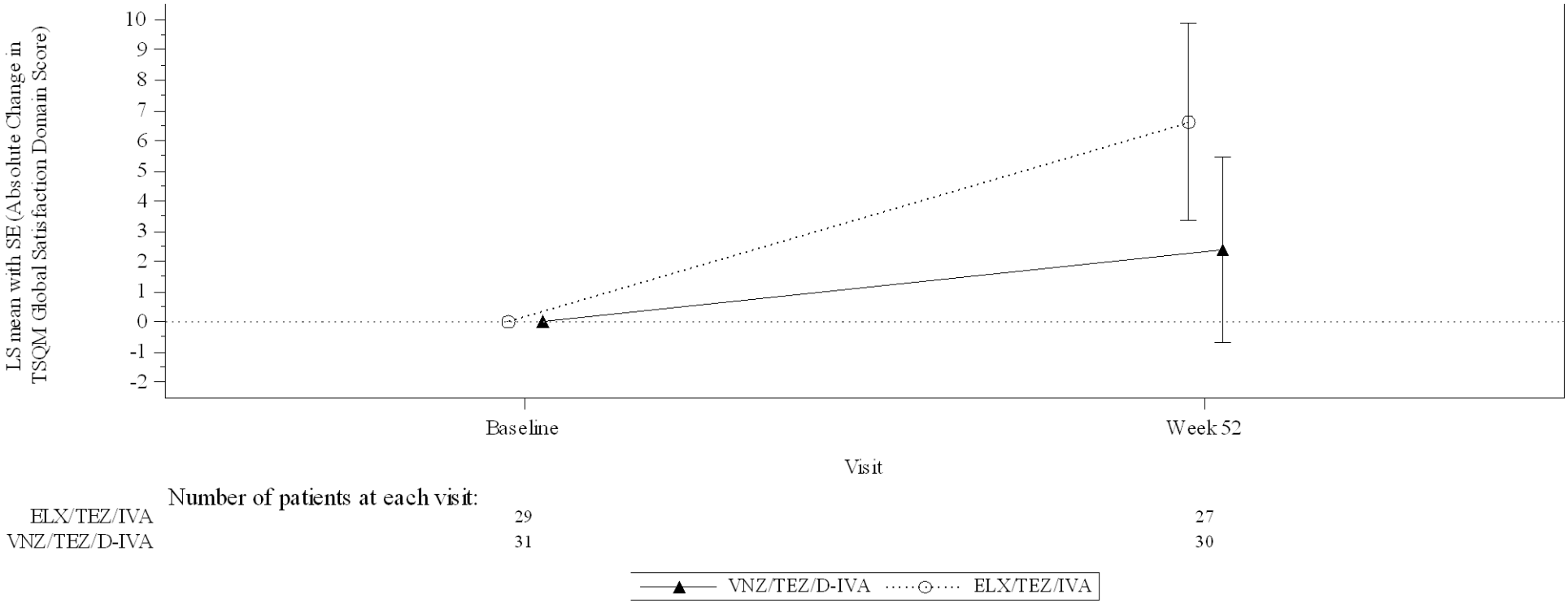
Domain: Global Satisfaction
$ppFEV_1$ at baseline <70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
$ppFEV_1$ at baseline ≥70 %



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.12.2
Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Age at screening <18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Full Analysis Set

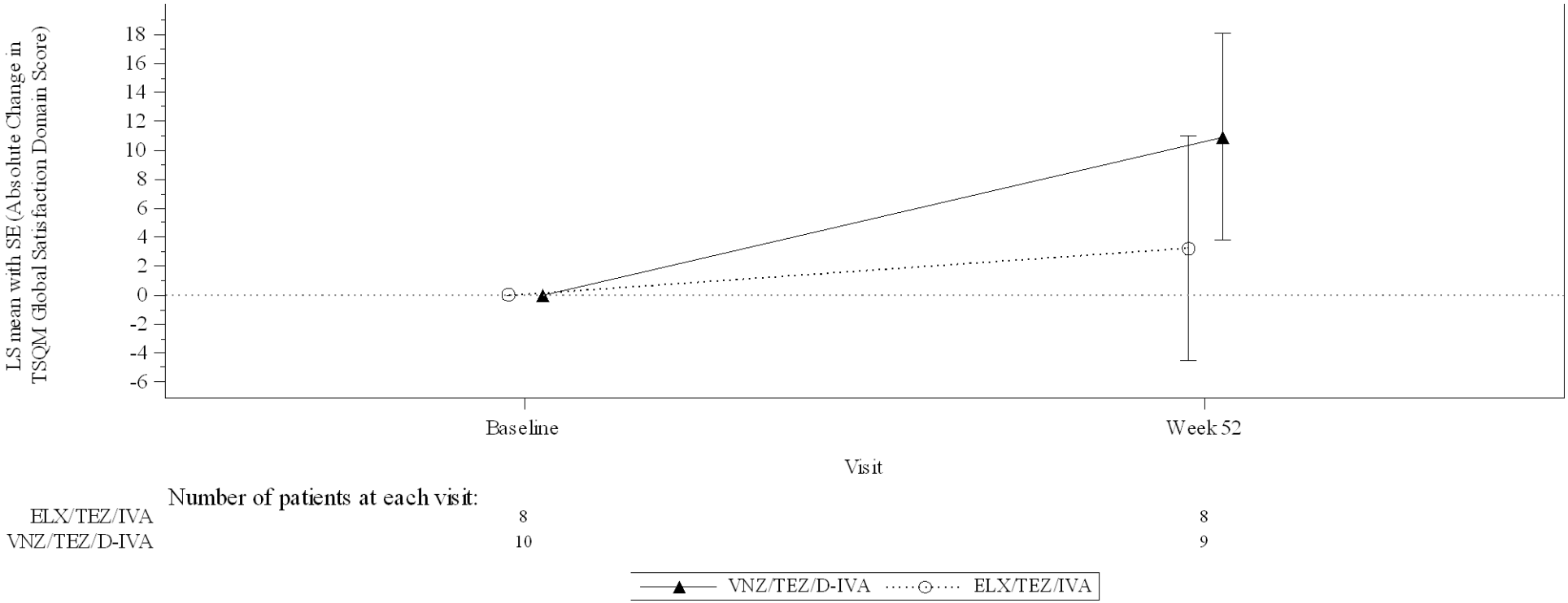
Domain: Global Satisfaction
Age at screening ≥18 years

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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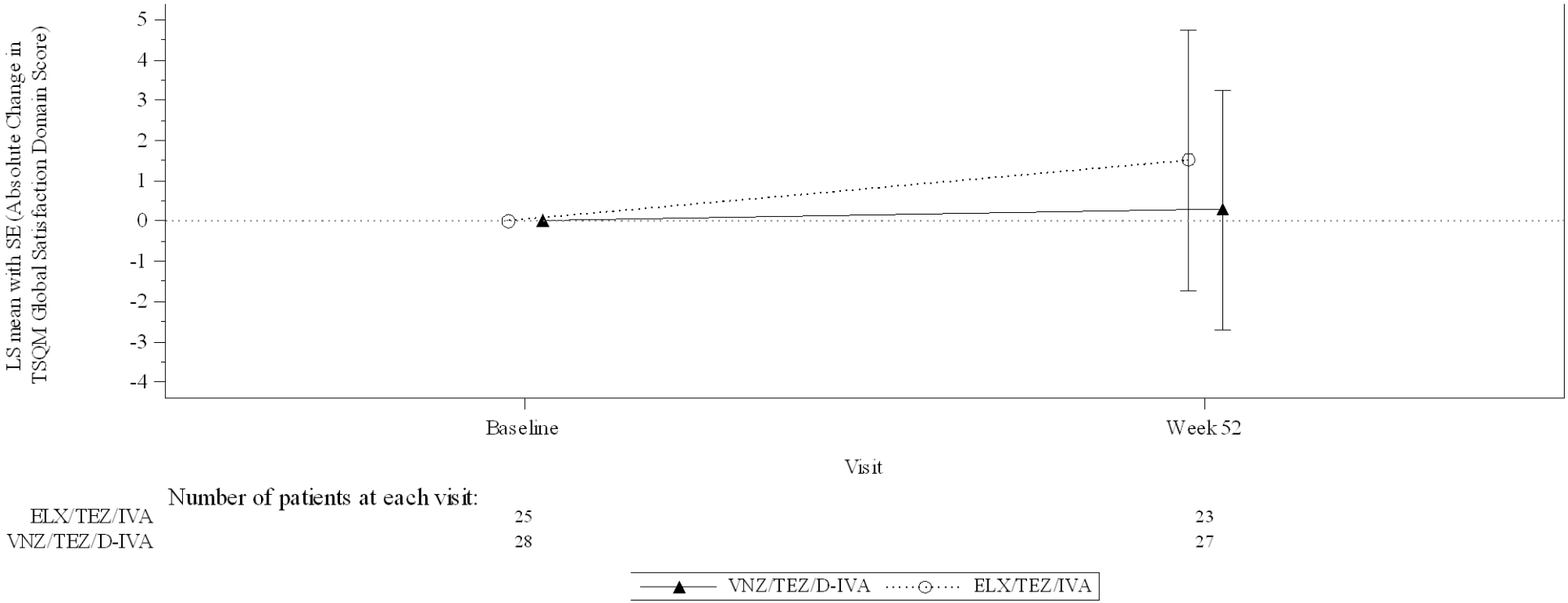
Domain: Global Satisfaction
SwCl at baseline <30 mmol/L



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Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
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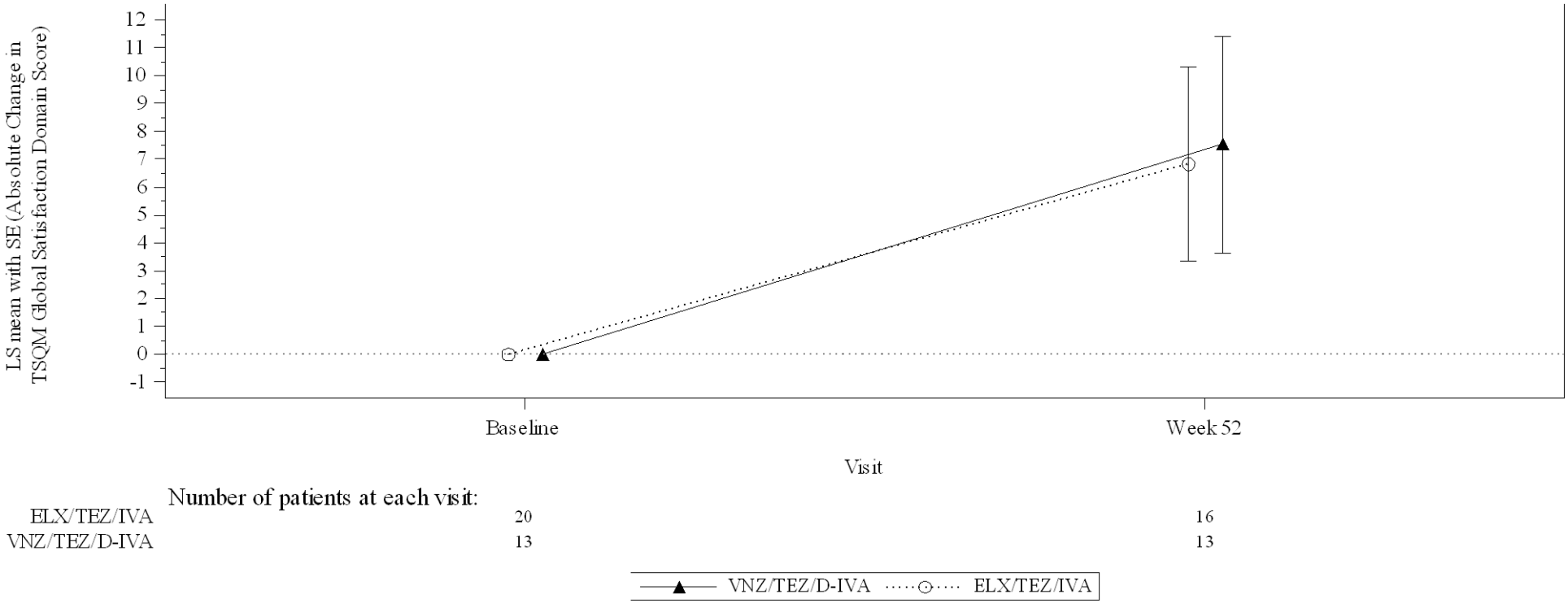
Domain: Global Satisfaction
SwCl at baseline ≥30 mmol/L



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Full Analysis Set

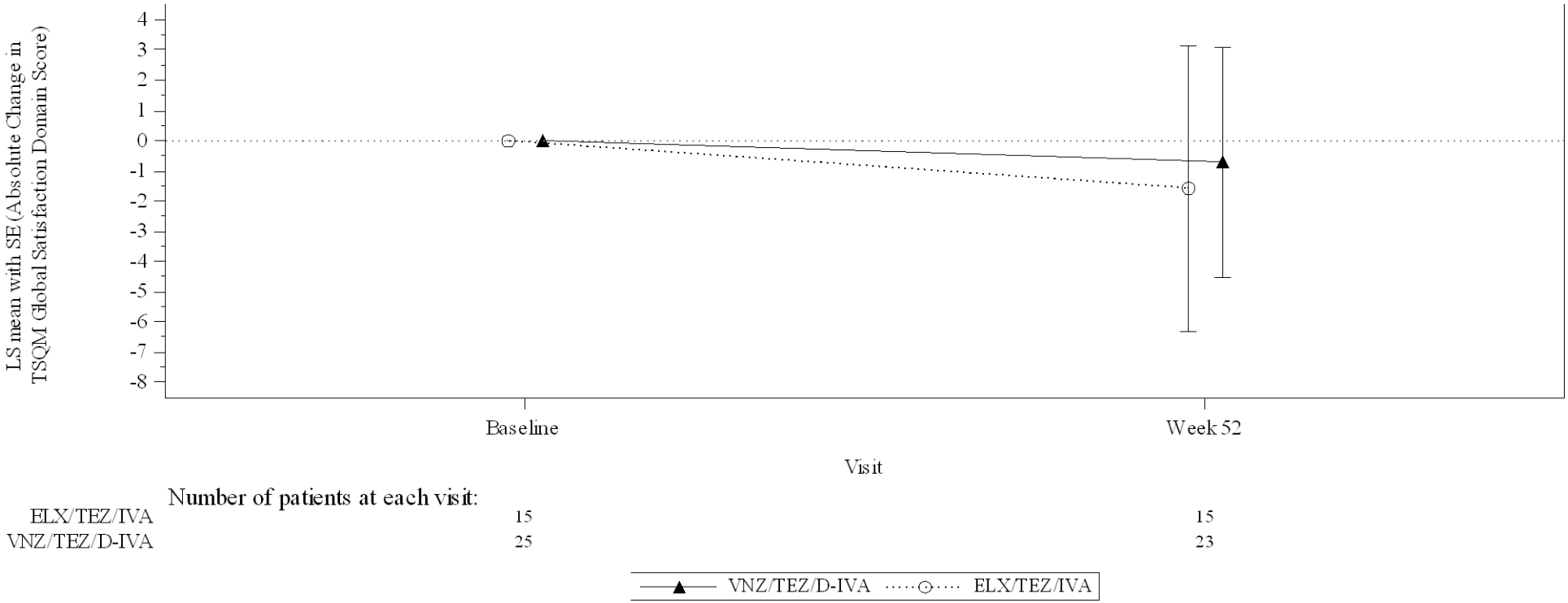
Domain: Global Satisfaction
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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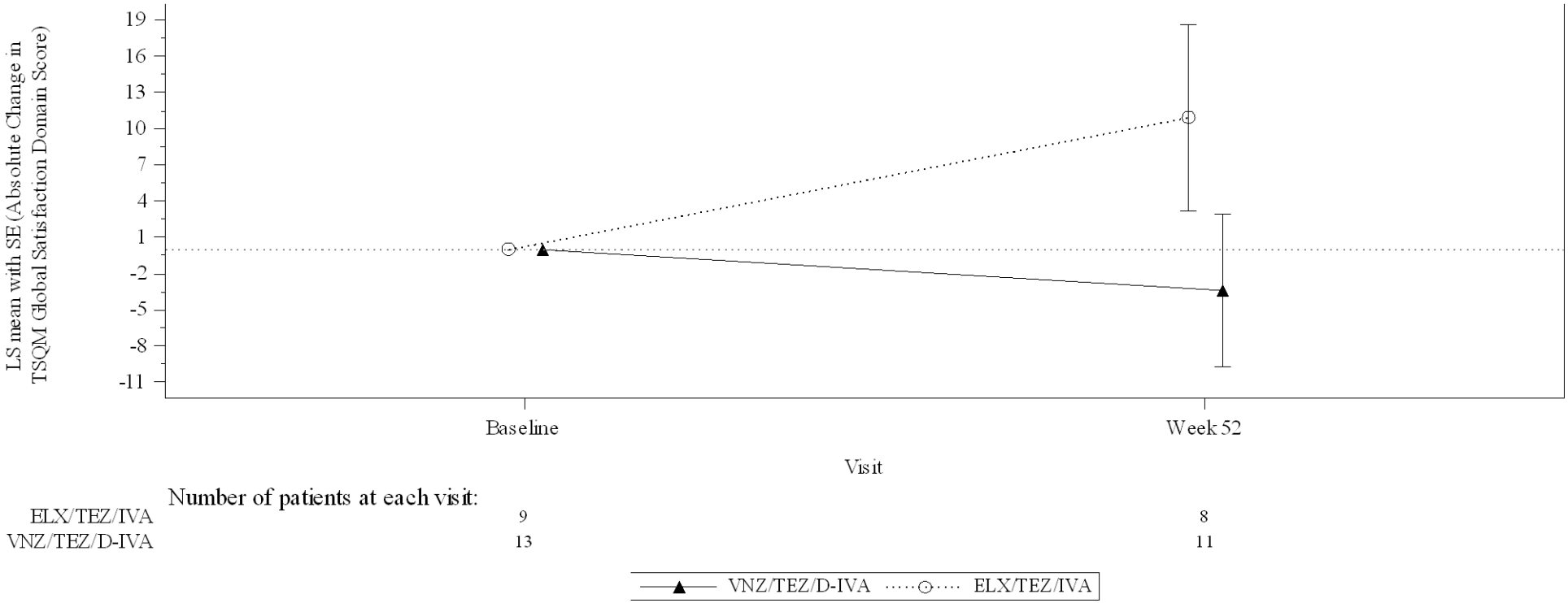
Domain: Global Satisfaction
Sex = Female



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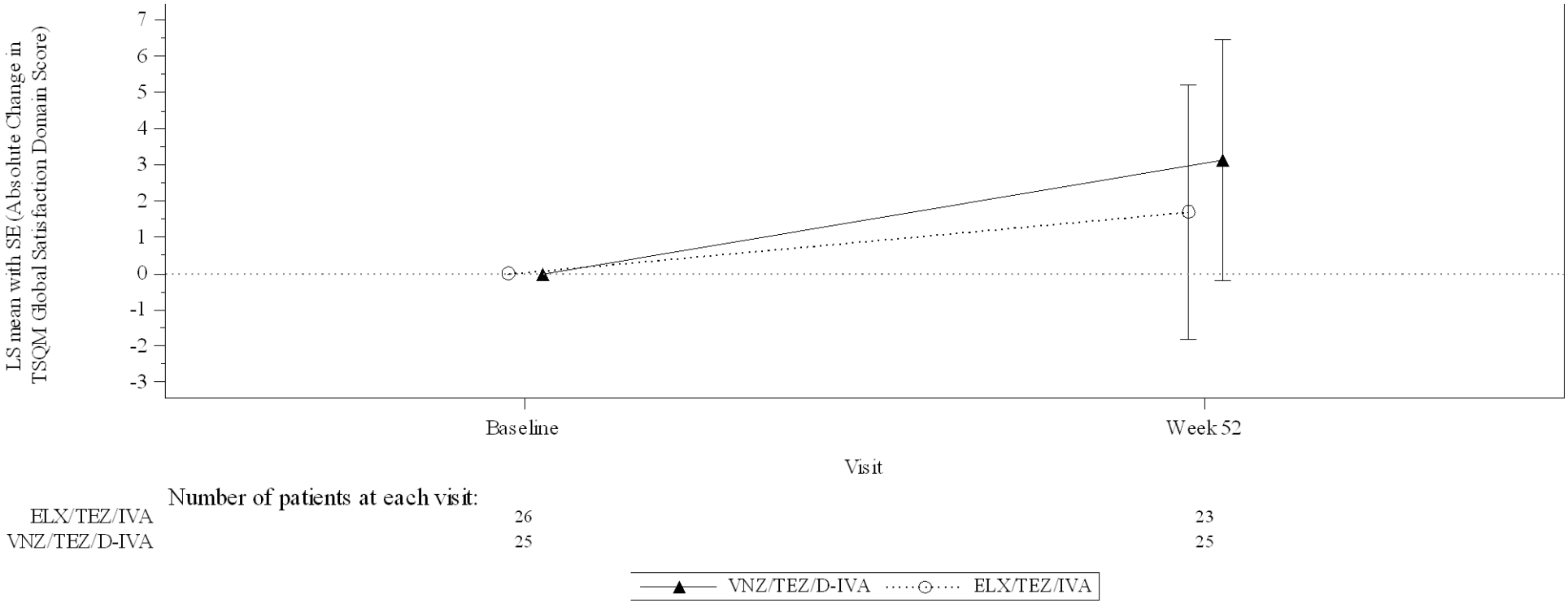
Domain: Global Satisfaction
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX20-121-103: Plot of Absolute Change from Baseline in TSQM Domain Score at Each Visit up to Week 52 by Subgroups for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent
Full Analysis Set

Domain: Global Satisfaction
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Physical

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	197	192
Mean (SD)	82.5 (18.6)	83.2 (19.8)
Absolute change at Week 8		
n	193	186
LS mean (SE)	-2.1 (1.1)	0.0 (1.1)
95% CI of LS mean	(-4.2, 0.0)	(-2.1, 2.2)
Absolute change at Week 16		
n	192	186
LS mean (SE)	-1.9 (1.1)	0.4 (1.1)
95% CI of LS mean	(-4.1, 0.2)	(-1.7, 2.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Physical

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	192	185
LS mean (SE)	-0.1 (1.0)	0.7 (1.0)
95% CI of LS mean	(-2.1, 1.8)	(-1.3, 2.6)
Absolute change at Week 52		
n	187	177
LS mean (SE)	1.1 (0.9)	2.1 (0.9)
95% CI of LS mean	(-0.7, 2.9)	(0.3, 3.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Physical

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
OL Efficacy Period for Part A		
N	170	166
Parent study baseline		
n	166	164
Mean (SD)	82.3 (18.8)	82.9 (19.7)
Absolute change at OL Part A Week 8		
n	164	162
LS mean (SE)	2.4 (1.1)	2.1 (1.1)
95% CI of LS mean	(0.2, 4.6)	(-0.1, 4.3)
Absolute change at OL Part A Week 16		
n	163	160
LS mean (SE)	0.5 (1.1)	1.7 (1.1)
95% CI of LS mean	(-1.7, 2.8)	(-0.5, 4.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Physical

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 24		
n	160	158
LS mean (SE)	2.1 (1.1)	1.4 (1.1)
95% CI of LS mean	(-0.1, 4.4)	(-0.8, 3.7)
Absolute change at OL Part A Week 48		
n	153	157
LS mean (SE)	2.1 (1.2)	2.8 (1.2)
95% CI of LS mean	(-0.2, 4.5)	(0.5, 5.1)
Absolute change at OL Part A Week 96		
n	145	149
LS mean (SE)	0.2 (1.4)	2.4 (1.3)
95% CI of LS mean	(-2.5, 2.9)	(-0.2, 5.1)
Average change through OL Part A Week 96		
n	164	162
LS mean (SE)	1.5 (0.9)	2.1 (0.9)
95% CI of LS mean	(-0.3, 3.3)	(0.3, 3.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Vitality

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	189	187
Mean (SD)	66.8 (17.7)	69.7 (20.1)
Absolute change at Week 8		
n	186	181
LS mean (SE)	-2.0 (1.3)	-1.6 (1.3)
95% CI of LS mean	(-4.5, 0.5)	(-4.1, 1.0)
Absolute change at Week 16		
n	184	182
LS mean (SE)	-2.2 (1.2)	-1.4 (1.2)
95% CI of LS mean	(-4.6, 0.2)	(-3.8, 1.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Vitality

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	184	181
LS mean (SE)	-2.7 (1.2)	-2.0 (1.2)
95% CI of LS mean	(-5.1, -0.2)	(-4.4, 0.5)
Absolute change at Week 52		
n	179	173
LS mean (SE)	-0.3 (1.2)	-0.6 (1.3)
95% CI of LS mean	(-2.7, 2.1)	(-3.0, 1.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Vitality

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
OL Efficacy Period for Part A		
N	170	166
Parent study baseline		
n	159	160
Mean (SD)	66.8 (17.8)	69.6 (20.8)
Absolute change at OL Part A Week 8		
n	156	158
LS mean (SE)	-1.4 (1.3)	-1.0 (1.3)
95% CI of LS mean	(-4.1, 1.2)	(-3.6, 1.7)
Absolute change at OL Part A Week 16		
n	156	156
LS mean (SE)	-1.8 (1.4)	-2.4 (1.4)
95% CI of LS mean	(-4.7, 1.0)	(-5.2, 0.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Vitality

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 24		
n	153	154
LS mean (SE)	-1.7 (1.5)	-2.8 (1.5)
95% CI of LS mean	(-4.5, 1.2)	(-5.6, 0.1)
Absolute change at OL Part A Week 48		
n	147	153
LS mean (SE)	-2.0 (1.4)	-2.4 (1.4)
95% CI of LS mean	(-4.7, 0.7)	(-5.0, 0.3)
Absolute change at OL Part A Week 96		
n	138	145
LS mean (SE)	-2.9 (1.5)	-1.1 (1.5)
95% CI of LS mean	(-5.9, 0.1)	(-4.0, 1.9)
Average change through OL Part A Week 96		
n	157	158
LS mean (SE)	-2.0 (1.1)	-1.9 (1.1)
95% CI of LS mean	(-4.1, 0.2)	(-4.1, 0.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Emotion

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	197	192
Mean (SD)	80.8 (18.3)	82.2 (17.5)
Absolute change at Week 8		
n	193	186
LS mean (SE)	0.2 (0.8)	1.2 (0.8)
95% CI of LS mean	(-1.3, 1.8)	(-0.4, 2.9)
Absolute change at Week 16		
n	192	186
LS mean (SE)	0.6 (0.9)	0.8 (0.9)
95% CI of LS mean	(-1.1, 2.4)	(-1.0, 2.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Emotion

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	192	185
LS mean (SE)	0.5 (1.0)	0.7 (1.0)
95% CI of LS mean	(-1.4, 2.4)	(-1.2, 2.6)
Absolute change at Week 52		
n	187	177
LS mean (SE)	0.1 (1.0)	1.2 (1.0)
95% CI of LS mean	(-1.8, 2.0)	(-0.7, 3.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Emotion

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
OL Efficacy Period for Part A		
N	170	166
Parent study baseline		
n	166	164
Mean (SD)	80.8 (18.6)	81.6 (18.0)
Absolute change at OL Part A Week 8		
n	164	162
LS mean (SE)	-0.3 (1.1)	2.2 (1.1)
95% CI of LS mean	(-2.5, 1.8)	(0.0, 4.3)
Absolute change at OL Part A Week 16		
n	163	160
LS mean (SE)	-1.3 (1.1)	1.3 (1.1)
95% CI of LS mean	(-3.3, 0.8)	(-0.8, 3.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Emotion

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 24		
n	160	158
LS mean (SE)	0.0 (1.1)	2.1 (1.2)
95% CI of LS mean	(-2.2, 2.3)	(-0.1, 4.4)
Absolute change at OL Part A Week 48		
n	153	157
LS mean (SE)	-1.4 (1.2)	1.8 (1.2)
95% CI of LS mean	(-3.7, 1.0)	(-0.5, 4.1)
Absolute change at OL Part A Week 96		
n	145	149
LS mean (SE)	0.0 (1.2)	1.0 (1.2)
95% CI of LS mean	(-2.3, 2.3)	(-1.3, 3.2)
Average change through OL Part A Week 96		
n	164	162
LS mean (SE)	-0.6 (0.9)	1.7 (0.9)
95% CI of LS mean	(-2.4, 1.3)	(-0.2, 3.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Body

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	197	192
Mean (SD)	76.6 (21.9)	77.8 (23.0)
Absolute change at Week 8		
n	193	186
LS mean (SE)	1.6 (0.9)	1.3 (1.0)
95% CI of LS mean	(-0.2, 3.5)	(-0.5, 3.2)
Absolute change at Week 16		
n	192	186
LS mean (SE)	1.0 (1.0)	2.7 (1.0)
95% CI of LS mean	(-1.0, 2.9)	(0.7, 4.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Body

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	192	185
LS mean (SE)	-0.3 (1.1)	2.0 (1.1)
95% CI of LS mean	(-2.6, 1.9)	(-0.3, 4.2)
Absolute change at Week 52		
n	187	177
LS mean (SE)	1.7 (1.1)	2.3 (1.1)
95% CI of LS mean	(-0.4, 3.8)	(0.2, 4.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Body

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
OL Efficacy Period for Part A		
N	170	166
Parent study baseline		
n	166	164
Mean (SD)	76.4 (22.0)	78.3 (22.4)
Absolute change at OL Part A Week 8		
n	164	162
LS mean (SE)	2.7 (1.2)	3.1 (1.2)
95% CI of LS mean	(0.3, 5.0)	(0.7, 5.5)
Absolute change at OL Part A Week 16		
n	163	160
LS mean (SE)	2.1 (1.3)	2.1 (1.3)
95% CI of LS mean	(-0.4, 4.5)	(-0.4, 4.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Body

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 24		
n	160	158
LS mean (SE)	3.5 (1.3)	3.0 (1.3)
95% CI of LS mean	(0.9, 6.1)	(0.4, 5.6)
Absolute change at OL Part A Week 48		
n	153	157
LS mean (SE)	4.2 (1.3)	2.0 (1.3)
95% CI of LS mean	(1.6, 6.9)	(-0.7, 4.6)
Absolute change at OL Part A Week 96		
n	145	149
LS mean (SE)	4.4 (1.4)	3.2 (1.4)
95% CI of LS mean	(1.7, 7.2)	(0.4, 5.9)
Average change through OL Part A Week 96		
n	164	162
LS mean (SE)	3.4 (1.1)	2.7 (1.1)
95% CI of LS mean	(1.2, 5.6)	(0.5, 4.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Eat

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	197	192
Mean (SD)	92.8 (14.4)	91.1 (16.5)
Absolute change at Week 8		
n	193	186
LS mean (SE)	-0.9 (0.8)	0.0 (0.8)
95% CI of LS mean	(-2.5, 0.7)	(-1.6, 1.6)
Absolute change at Week 16		
n	192	186
LS mean (SE)	-1.6 (0.8)	-0.1 (0.9)
95% CI of LS mean	(-3.2, 0.1)	(-1.8, 1.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Eat

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	192	185
LS mean (SE)	-0.3 (0.8)	-0.4 (0.8)
95% CI of LS mean	(-1.9, 1.3)	(-2.1, 1.2)
Absolute change at Week 52		
n	187	177
LS mean (SE)	0.2 (0.8)	0.3 (0.8)
95% CI of LS mean	(-1.4, 1.7)	(-1.3, 1.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Eat

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
OL Efficacy Period for Part A		
N	170	166
Parent study baseline		
n	166	164
Mean (SD)	92.6 (14.9)	91.5 (16.3)
Absolute change at OL Part A Week 8		
n	164	162
LS mean (SE)	-0.1 (0.9)	0.4 (0.9)
95% CI of LS mean	(-1.9, 1.8)	(-1.5, 2.2)
Absolute change at OL Part A Week 16		
n	163	160
LS mean (SE)	0.2 (1.0)	-0.1 (1.0)
95% CI of LS mean	(-1.8, 2.2)	(-2.1, 1.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Eat

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 24		
n	160	158
LS mean (SE)	0.0 (1.1)	0.0 (1.1)
95% CI of LS mean	(-2.1, 2.0)	(-2.1, 2.1)
Absolute change at OL Part A Week 48		
n	153	157
LS mean (SE)	0.6 (1.0)	0.3 (1.0)
95% CI of LS mean	(-1.3, 2.5)	(-1.7, 2.2)
Absolute change at OL Part A Week 96		
n	145	149
LS mean (SE)	0.6 (1.0)	-0.4 (1.0)
95% CI of LS mean	(-1.4, 2.6)	(-2.4, 1.6)
Average change through OL Part A Week 96		
n	164	162
LS mean (SE)	0.3 (0.8)	0.0 (0.8)
95% CI of LS mean	(-1.3, 1.8)	(-1.6, 1.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Treatment Burden

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	197	192
Mean (SD)	70.4 (20.1)	72.3 (19.8)
Absolute change at Week 8		
n	192	186
LS mean (SE)	0.6 (1.0)	1.2 (1.0)
95% CI of LS mean	(-1.4, 2.5)	(-0.8, 3.2)
Absolute change at Week 16		
n	192	186
LS mean (SE)	0.1 (1.1)	1.3 (1.1)
95% CI of LS mean	(-2.0, 2.2)	(-0.8, 3.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Treatment Burden

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	192	185
LS mean (SE)	1.9 (1.0)	1.1 (1.1)
95% CI of LS mean	(-0.1, 4.0)	(-1.0, 3.2)
Absolute change at Week 52		
n	187	177
LS mean (SE)	2.9 (1.1)	4.2 (1.2)
95% CI of LS mean	(0.7, 5.2)	(1.9, 6.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Treatment Burden

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
OL Efficacy Period for Part A		
N	170	166
Parent study baseline		
n	166	164
Mean (SD)	70.5 (20.6)	72.6 (19.5)
Absolute change at OL Part A Week 8		
n	164	162
LS mean (SE)	5.3 (1.2)	4.2 (1.2)
95% CI of LS mean	(2.8, 7.7)	(1.7, 6.6)
Absolute change at OL Part A Week 16		
n	163	160
LS mean (SE)	3.5 (1.3)	3.8 (1.3)
95% CI of LS mean	(1.0, 6.1)	(1.3, 6.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Treatment Burden

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 24		
n	160	158
LS mean (SE)	4.3 (1.3)	3.6 (1.3)
95% CI of LS mean	(1.8, 6.9)	(1.1, 6.2)
Absolute change at OL Part A Week 48		
n	153	157
LS mean (SE)	6.6 (1.3)	4.3 (1.3)
95% CI of LS mean	(3.9, 9.2)	(1.7, 6.9)
Absolute change at OL Part A Week 96		
n	145	149
LS mean (SE)	6.5 (1.5)	5.4 (1.5)
95% CI of LS mean	(3.7, 9.4)	(2.6, 8.3)
Average change through OL Part A Week 96		
n	164	162
LS mean (SE)	5.3 (1.1)	4.3 (1.1)
95% CI of LS mean	(3.0, 7.5)	(2.0, 6.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Health Perceptions

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	189	187
Mean (SD)	71.1 (19.2)	73.9 (19.5)
Absolute change at Week 8		
n	186	181
LS mean (SE)	-1.1 (1.0)	-0.8 (1.0)
95% CI of LS mean	(-3.1, 1.0)	(-2.8, 1.3)
Absolute change at Week 16		
n	184	182
LS mean (SE)	-0.3 (1.1)	-0.8 (1.1)
95% CI of LS mean	(-2.4, 1.7)	(-2.9, 1.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Health Perceptions

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	184	181
LS mean (SE)	-1.3 (1.0)	0.2 (1.0)
95% CI of LS mean	(-3.4, 0.7)	(-1.9, 2.2)
Absolute change at Week 52		
n	179	173
LS mean (SE)	1.4 (1.0)	1.2 (1.1)
95% CI of LS mean	(-0.7, 3.4)	(-0.8, 3.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Health Perceptions

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
OL Efficacy Period for Part A		
N	170	166
Parent study baseline		
n	159	160
Mean (SD)	71.6 (19.2)	73.5 (19.7)
Absolute change at OL Part A Week 8		
n	156	158
LS mean (SE)	1.8 (1.2)	1.0 (1.2)
95% CI of LS mean	(-0.5, 4.1)	(-1.3, 3.3)
Absolute change at OL Part A Week 16		
n	156	156
LS mean (SE)	-1.0 (1.2)	-0.7 (1.2)
95% CI of LS mean	(-3.4, 1.4)	(-3.1, 1.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Health Perceptions

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 24		
n	153	154
LS mean (SE)	0.2 (1.3)	0.6 (1.3)
95% CI of LS mean	(-2.3, 2.7)	(-1.9, 3.1)
Absolute change at OL Part A Week 48		
n	147	153
LS mean (SE)	0.6 (1.4)	0.6 (1.3)
95% CI of LS mean	(-2.1, 3.3)	(-2.0, 3.2)
Absolute change at OL Part A Week 96		
n	138	145
LS mean (SE)	-2.0 (1.5)	0.8 (1.5)
95% CI of LS mean	(-5.0, 1.0)	(-2.1, 3.8)
Average change through OL Part A Week 96		
n	157	158
LS mean (SE)	-0.1 (1.1)	0.5 (1.0)
95% CI of LS mean	(-2.2, 2.0)	(-1.6, 2.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Weight

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	189	187
Mean (SD)	84.8 (26.9)	82.4 (29.0)
Absolute change at Week 8		
n	185	181
LS mean (SE)	0.7 (1.6)	1.3 (1.6)
95% CI of LS mean	(-2.3, 3.8)	(-1.8, 4.4)
Absolute change at Week 16		
n	184	182
LS mean (SE)	-2.5 (1.8)	1.0 (1.8)
95% CI of LS mean	(-6.0, 1.0)	(-2.6, 4.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Weight

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	184	180
LS mean (SE)	0.2 (1.8)	0.8 (1.8)
95% CI of LS mean	(-3.3, 3.8)	(-2.8, 4.4)
Absolute change at Week 52		
n	178	173
LS mean (SE)	0.8 (1.8)	-0.3 (1.8)
95% CI of LS mean	(-2.6, 4.3)	(-3.8, 3.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Weight

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
OL Efficacy Period for Part A		
N	170	166
Parent study baseline		
n	159	160
Mean (SD)	84.5 (27.2)	82.7 (28.2)
Absolute change at OL Part A Week 8		
n	156	158
LS mean (SE)	3.5 (1.9)	2.6 (1.9)
95% CI of LS mean	(-0.3, 7.3)	(-1.1, 6.4)
Absolute change at OL Part A Week 16		
n	156	156
LS mean (SE)	3.3 (2.0)	2.2 (2.0)
95% CI of LS mean	(-0.7, 7.3)	(-1.8, 6.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Weight

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 24		
n	153	154
LS mean (SE)	3.3 (2.1)	-0.9 (2.0)
95% CI of LS mean	(-0.8, 7.3)	(-5.0, 3.1)
Absolute change at OL Part A Week 48		
n	147	153
LS mean (SE)	4.2 (2.1)	-2.4 (2.1)
95% CI of LS mean	(0.0, 8.4)	(-6.5, 1.8)
Absolute change at OL Part A Week 96		
n	138	144
LS mean (SE)	2.8 (2.1)	4.4 (2.0)
95% CI of LS mean	(-1.3, 6.9)	(0.4, 8.4)
Average change through OL Part A Week 96		
n	157	158
LS mean (SE)	3.4 (1.7)	1.2 (1.7)
95% CI of LS mean	(0.0, 6.8)	(-2.2, 4.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Digestion

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	197	191
Mean (SD)	82.7 (18.3)	85.0 (15.7)
Absolute change at Week 8		
n	192	185
LS mean (SE)	-1.2 (1.1)	1.8 (1.1)
95% CI of LS mean	(-3.3, 0.9)	(-0.4, 4.0)
Absolute change at Week 16		
n	192	185
LS mean (SE)	-1.5 (1.1)	-1.1 (1.1)
95% CI of LS mean	(-3.7, 0.7)	(-3.3, 1.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Digestion

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	192	183
LS mean (SE)	-0.6 (1.0)	1.2 (1.0)
95% CI of LS mean	(-2.6, 1.4)	(-0.8, 3.3)
Absolute change at Week 52		
n	186	176
LS mean (SE)	0.0 (1.1)	-2.1 (1.1)
95% CI of LS mean	(-2.1, 2.1)	(-4.3, 0.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Digestion

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
OL Efficacy Period for Part A		
N	170	166
Parent study baseline		
n	166	163
Mean (SD)	81.4 (19.0)	85.0 (15.7)
Absolute change at OL Part A Week 8		
n	163	161
LS mean (SE)	-1.3 (1.2)	-0.7 (1.2)
95% CI of LS mean	(-3.7, 1.0)	(-3.1, 1.7)
Absolute change at OL Part A Week 16		
n	162	159
LS mean (SE)	-1.7 (1.3)	0.2 (1.3)
95% CI of LS mean	(-4.1, 0.8)	(-2.3, 2.7)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Digestion

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 24		
n	160	157
LS mean (SE)	0.2 (1.3)	-0.6 (1.3)
95% CI of LS mean	(-2.3, 2.7)	(-3.1, 2.0)
Absolute change at OL Part A Week 48		
n	153	155
LS mean (SE)	-1.1 (1.2)	0.6 (1.2)
95% CI of LS mean	(-3.5, 1.4)	(-1.8, 3.1)
Absolute change at OL Part A Week 96		
n	145	147
LS mean (SE)	-1.5 (1.4)	-0.3 (1.4)
95% CI of LS mean	(-4.2, 1.3)	(-3.0, 2.4)
Average change through OL Part A Week 96		
n	164	161
LS mean (SE)	-1.1 (1.0)	-0.1 (1.1)
95% CI of LS mean	(-3.1, 1.0)	(-2.2, 1.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Role

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	189	186
Mean (SD)	87.7 (16.9)	87.4 (15.8)
Absolute change at Week 8		
n	185	180
LS mean (SE)	-0.7 (0.9)	0.5 (1.0)
95% CI of LS mean	(-2.5, 1.2)	(-1.4, 2.4)
Absolute change at Week 16		
n	184	181
LS mean (SE)	-1.7 (1.1)	2.0 (1.1)
95% CI of LS mean	(-3.7, 0.4)	(-0.1, 4.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Role

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	184	179
LS mean (SE)	-0.9 (1.0)	1.1 (1.0)
95% CI of LS mean	(-2.9, 1.1)	(-0.9, 3.2)
Absolute change at Week 52		
n	178	172
LS mean (SE)	1.0 (1.0)	1.6 (1.0)
95% CI of LS mean	(-1.0, 3.0)	(-0.5, 3.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Role

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
OL Efficacy Period for Part A		
N	170	166
Parent study baseline		
n	159	159
Mean (SD)	87.5 (17.2)	87.2 (15.3)
Absolute change at OL Part A Week 8		
n	156	157
LS mean (SE)	1.4 (1.1)	2.3 (1.1)
95% CI of LS mean	(-0.7, 3.6)	(0.2, 4.5)
Absolute change at OL Part A Week 16		
n	156	155
LS mean (SE)	0.2 (1.1)	1.8 (1.1)
95% CI of LS mean	(-2.0, 2.3)	(-0.4, 4.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Role

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 24		
n	153	153
LS mean (SE)	1.0 (1.2)	0.7 (1.2)
95% CI of LS mean	(-1.3, 3.3)	(-1.6, 3.0)
Absolute change at OL Part A Week 48		
n	147	152
LS mean (SE)	1.6 (1.1)	1.9 (1.0)
95% CI of LS mean	(-0.5, 3.7)	(-0.2, 3.9)
Absolute change at OL Part A Week 96		
n	138	143
LS mean (SE)	0.2 (1.3)	1.5 (1.2)
95% CI of LS mean	(-2.3, 2.7)	(-0.9, 3.9)
Average change through OL Part A Week 96		
n	157	157
LS mean (SE)	0.9 (0.9)	1.6 (0.9)
95% CI of LS mean	(-1.0, 2.7)	(-0.2, 3.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	197	192
Mean (SD)	74.3 (17.2)	75.1 (18.4)
Absolute change at Week 8		
n	193	186
LS mean (SE)	1.1 (1.0)	1.1 (1.0)
95% CI of LS mean	(-0.8, 3.1)	(-0.9, 3.1)
Absolute change at Week 16		
n	192	186
LS mean (SE)	0.2 (1.1)	-0.2 (1.1)
95% CI of LS mean	(-1.8, 2.3)	(-2.3, 1.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	192	185
LS mean (SE)	2.0 (1.0)	2.1 (1.0)
95% CI of LS mean	(0.1, 3.8)	(0.2, 4.0)
Absolute change at Week 52		
n	187	177
LS mean (SE)	3.2 (1.0)	2.8 (1.0)
95% CI of LS mean	(1.2, 5.2)	(0.8, 4.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
OL Efficacy Period for Part A		
N	170	166
Parent study baseline		
n	166	164
Mean (SD)	74.2 (17.3)	74.7 (18.1)
Absolute change at OL Part A Week 8		
n	164	162
LS mean (SE)	3.3 (1.1)	3.1 (1.1)
95% CI of LS mean	(1.2, 5.3)	(1.1, 5.2)
Absolute change at OL Part A Week 16		
n	163	160
LS mean (SE)	2.2 (1.1)	3.3 (1.1)
95% CI of LS mean	(0.0, 4.4)	(1.2, 5.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 24		
n	160	158
LS mean (SE)	4.3 (1.0)	3.8 (1.0)
95% CI of LS mean	(2.3, 6.3)	(1.8, 5.8)
Absolute change at OL Part A Week 48		
n	153	157
LS mean (SE)	5.4 (1.1)	3.8 (1.1)
95% CI of LS mean	(3.2, 7.6)	(1.6, 5.9)
Absolute change at OL Part A Week 96		
n	145	149
LS mean (SE)	3.6 (1.2)	2.0 (1.2)
95% CI of LS mean	(1.3, 5.9)	(-0.3, 4.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 102 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Average change through OL Part A Week 96		
n	164	162
LS mean (SE)	3.8 (0.9)	3.2 (0.9)
95% CI of LS mean	(2.0, 5.5)	(1.4, 5.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Physical

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	282	280
Mean (SD)	80.7 (20.3)	82.8 (18.6)
Absolute change at Week 8		
n	270	271
LS mean (SE)	-0.6 (1.0)	-0.8 (1.0)
95% CI of LS mean	(-2.5, 1.3)	(-2.7, 1.0)
Absolute change at Week 16		
n	266	265
LS mean (SE)	0.8 (0.9)	-0.3 (0.9)
95% CI of LS mean	(-1.0, 2.6)	(-2.1, 1.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Physical

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	266	262
LS mean (SE)	-0.3 (0.9)	-0.7 (0.9)
95% CI of LS mean	(-2.1, 1.5)	(-2.5, 1.1)
Absolute change at Week 52		
n	262	255
LS mean (SE)	1.0 (0.9)	1.1 (0.9)
95% CI of LS mean	(-0.8, 2.8)	(-0.7, 2.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Physical

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
OL Efficacy Period for Part A		
N	248	238
Parent study baseline		
n	243	235
Mean (SD)	80.6 (21.1)	82.7 (18.9)
Absolute change at OL Part A Week 8		
n	233	229
LS mean (SE)	-0.2 (1.0)	0.6 (1.0)
95% CI of LS mean	(-2.1, 1.7)	(-1.4, 2.5)
Absolute change at OL Part A Week 16		
n	228	223
LS mean (SE)	1.3 (1.0)	-1.1 (1.0)
95% CI of LS mean	(-0.7, 3.3)	(-3.1, 0.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
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- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Physical

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 24		
n	228	222
LS mean (SE)	1.5 (1.0)	0.7 (1.0)
95% CI of LS mean	(-0.4, 3.5)	(-1.3, 2.6)
Absolute change at OL Part A Week 48		
n	219	213
LS mean (SE)	0.4 (1.1)	-0.1 (1.1)
95% CI of LS mean	(-1.8, 2.6)	(-2.3, 2.1)
Absolute change at OL Part A Week 96		
n	213	205
LS mean (SE)	2.3 (1.1)	0.7 (1.2)
95% CI of LS mean	(0.1, 4.5)	(-1.5, 3.0)
Average change through OL Part A Week 96		
n	234	229
LS mean (SE)	1.1 (0.9)	0.2 (0.9)
95% CI of LS mean	(-0.6, 2.7)	(-1.5, 1.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Vitality

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	269	266
Mean (SD)	66.8 (19.0)	66.8 (18.9)
Absolute change at Week 8		
n	261	258
LS mean (SE)	-2.2 (1.0)	-0.3 (1.0)
95% CI of LS mean	(-4.2, -0.3)	(-2.3, 1.6)
Absolute change at Week 16		
n	257	252
LS mean (SE)	-2.2 (1.0)	-1.1 (1.0)
95% CI of LS mean	(-4.1, -0.3)	(-3.0, 0.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
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- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Vitality

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	255	249
LS mean (SE)	-3.6 (1.1)	-2.0 (1.1)
95% CI of LS mean	(-5.7, -1.5)	(-4.1, 0.1)
Absolute change at Week 52		
n	253	242
LS mean (SE)	-1.7 (1.0)	0.2 (1.0)
95% CI of LS mean	(-3.6, 0.3)	(-1.8, 2.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Vitality

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
OL Efficacy Period for Part A		
N	248	238
Parent study baseline		
n	231	223
Mean (SD)	66.5 (19.5)	67.9 (18.8)
Absolute change at OL Part A Week 8		
n	223	217
LS mean (SE)	-1.7 (1.1)	-0.5 (1.1)
95% CI of LS mean	(-3.9, 0.5)	(-2.7, 1.7)
Absolute change at OL Part A Week 16		
n	218	212
LS mean (SE)	-2.3 (1.2)	-2.0 (1.2)
95% CI of LS mean	(-4.7, 0.1)	(-4.4, 0.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Vitality

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 24		
n	218	211
LS mean (SE)	-2.0 (1.2)	-2.2 (1.2)
95% CI of LS mean	(-4.4, 0.4)	(-4.6, 0.2)
Absolute change at OL Part A Week 48		
n	209	202
LS mean (SE)	-1.4 (1.1)	-2.7 (1.2)
95% CI of LS mean	(-3.6, 0.9)	(-5.0, -0.4)
Absolute change at OL Part A Week 96		
n	203	194
LS mean (SE)	-0.7 (1.2)	-1.2 (1.3)
95% CI of LS mean	(-3.1, 1.8)	(-3.6, 1.3)
Average change through OL Part A Week 96		
n	224	217
LS mean (SE)	-1.6 (0.9)	-1.7 (1.0)
95% CI of LS mean	(-3.5, 0.2)	(-3.6, 0.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Emotion

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	282	280
Mean (SD)	81.8 (16.3)	81.8 (17.8)
Absolute change at Week 8		
n	270	271
LS mean (SE)	0.6 (0.7)	1.1 (0.7)
95% CI of LS mean	(-0.7, 2.0)	(-0.2, 2.4)
Absolute change at Week 16		
n	266	265
LS mean (SE)	1.0 (0.7)	-0.5 (0.7)
95% CI of LS mean	(-0.4, 2.4)	(-2.0, 0.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Emotion

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	266	262
LS mean (SE)	0.1 (0.8)	-0.6 (0.8)
95% CI of LS mean	(-1.4, 1.6)	(-2.1, 0.9)
Absolute change at Week 52		
n	262	255
LS mean (SE)	-0.3 (0.9)	0.1 (0.9)
95% CI of LS mean	(-2.1, 1.4)	(-1.7, 1.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
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- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Emotion

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
OL Efficacy Period for Part A		
N	248	238
Parent study baseline		
n	243	235
Mean (SD)	82.1 (16.9)	82.2 (17.3)
Absolute change at OL Part A Week 8		
n	233	229
LS mean (SE)	0.2 (0.9)	0.4 (1.0)
95% CI of LS mean	(-1.6, 2.1)	(-1.4, 2.3)
Absolute change at OL Part A Week 16		
n	228	223
LS mean (SE)	0.0 (1.0)	0.6 (1.0)
95% CI of LS mean	(-1.9, 1.8)	(-1.3, 2.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Emotion

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 24		
n	228	222
LS mean (SE)	0.7 (0.9)	1.0 (0.9)
95% CI of LS mean	(-1.1, 2.4)	(-0.9, 2.8)
Absolute change at OL Part A Week 48		
n	219	213
LS mean (SE)	1.3 (1.0)	0.1 (1.0)
95% CI of LS mean	(-0.7, 3.2)	(-1.8, 2.1)
Absolute change at OL Part A Week 96		
n	213	205
LS mean (SE)	2.4 (1.0)	1.2 (1.0)
95% CI of LS mean	(0.5, 4.3)	(-0.8, 3.1)
Average change through OL Part A Week 96		
n	234	229
LS mean (SE)	0.9 (0.8)	0.6 (0.8)
95% CI of LS mean	(-0.6, 2.5)	(-0.9, 2.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Body

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	282	280
Mean (SD)	75.8 (23.7)	78.6 (21.4)
Absolute change at Week 8		
n	270	270
LS mean (SE)	2.4 (0.9)	0.5 (0.9)
95% CI of LS mean	(0.7, 4.2)	(-1.2, 2.3)
Absolute change at Week 16		
n	266	264
LS mean (SE)	2.1 (0.9)	0.7 (0.9)
95% CI of LS mean	(0.4, 3.8)	(-1.0, 2.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Body

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	267	262
LS mean (SE)	3.1 (0.9)	1.0 (0.9)
95% CI of LS mean	(1.3, 5.0)	(-0.9, 2.8)
Absolute change at Week 52		
n	262	255
LS mean (SE)	2.2 (1.0)	1.4 (1.0)
95% CI of LS mean	(0.2, 4.3)	(-0.7, 3.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Body

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
OL Efficacy Period for Part A		
N	248	238
Parent study baseline		
n	243	235
Mean (SD)	76.0 (23.8)	78.5 (21.4)
Absolute change at OL Part A Week 8		
n	233	228
LS mean (SE)	3.7 (1.1)	2.1 (1.1)
95% CI of LS mean	(1.5, 5.8)	(-0.1, 4.2)
Absolute change at OL Part A Week 16		
n	228	223
LS mean (SE)	3.0 (1.1)	1.1 (1.1)
95% CI of LS mean	(0.8, 5.1)	(-1.1, 3.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Body

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 24		
n	228	221
LS mean (SE)	2.6 (1.2)	3.4 (1.2)
95% CI of LS mean	(0.3, 4.9)	(1.1, 5.7)
Absolute change at OL Part A Week 48		
n	219	213
LS mean (SE)	3.7 (1.1)	1.4 (1.1)
95% CI of LS mean	(1.5, 5.9)	(-0.8, 3.6)
Absolute change at OL Part A Week 96		
n	213	205
LS mean (SE)	5.1 (1.2)	3.4 (1.2)
95% CI of LS mean	(2.7, 7.5)	(1.0, 5.9)
Average change through OL Part A Week 96		
n	234	229
LS mean (SE)	3.6 (0.9)	2.3 (1.0)
95% CI of LS mean	(1.8, 5.4)	(0.4, 4.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
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- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Eat

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	282	280
Mean (SD)	92.8 (14.5)	94.2 (11.9)
Absolute change at Week 8		
n	270	271
LS mean (SE)	0.2 (0.7)	-0.1 (0.7)
95% CI of LS mean	(-1.1, 1.5)	(-1.4, 1.2)
Absolute change at Week 16		
n	266	265
LS mean (SE)	0.3 (0.7)	-1.0 (0.7)
95% CI of LS mean	(-1.1, 1.7)	(-2.5, 0.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Eat

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	267	262
LS mean (SE)	0.1 (0.7)	-1.6 (0.8)
95% CI of LS mean	(-1.4, 1.5)	(-3.1, -0.2)
Absolute change at Week 52		
n	262	255
LS mean (SE)	0.4 (0.8)	-0.8 (0.8)
95% CI of LS mean	(-1.1, 1.9)	(-2.3, 0.7)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Eat

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
OL Efficacy Period for Part A		
N	248	238
Parent study baseline		
n	243	235
Mean (SD)	92.1 (15.1)	94.4 (12.0)
Absolute change at OL Part A Week 8		
n	233	229
LS mean (SE)	-0.2 (0.9)	-1.0 (0.9)
95% CI of LS mean	(-1.9, 1.6)	(-2.7, 0.8)
Absolute change at OL Part A Week 16		
n	228	223
LS mean (SE)	1.1 (0.8)	-1.0 (0.8)
95% CI of LS mean	(-0.5, 2.7)	(-2.6, 0.7)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
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Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Eat

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 24		
n	228	221
LS mean (SE)	1.6 (0.8)	-0.1 (0.8)
95% CI of LS mean	(0.1, 3.2)	(-1.6, 1.4)
Absolute change at OL Part A Week 48		
n	219	213
LS mean (SE)	0.5 (0.8)	-0.2 (0.8)
95% CI of LS mean	(-1.1, 2.1)	(-1.8, 1.4)
Absolute change at OL Part A Week 96		
n	213	205
LS mean (SE)	0.2 (0.9)	-0.2 (0.9)
95% CI of LS mean	(-1.5, 2.0)	(-2.0, 1.6)
Average change through OL Part A Week 96		
n	234	229
LS mean (SE)	0.7 (0.7)	-0.5 (0.7)
95% CI of LS mean	(-0.6, 2.0)	(-1.8, 0.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Treatment Burden

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	282	280
Mean (SD)	70.3 (19.7)	71.7 (19.1)
Absolute change at Week 8		
n	270	270
LS mean (SE)	0.8 (0.8)	1.8 (0.8)
95% CI of LS mean	(-0.8, 2.5)	(0.1, 3.4)
Absolute change at Week 16		
n	266	265
LS mean (SE)	2.0 (0.9)	1.7 (0.9)
95% CI of LS mean	(0.2, 3.7)	(0.0, 3.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Treatment Burden

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	267	262
LS mean (SE)	0.9 (0.9)	2.0 (0.9)
95% CI of LS mean	(-0.8, 2.7)	(0.2, 3.8)
Absolute change at Week 52		
n	262	255
LS mean (SE)	3.5 (1.0)	4.1 (1.0)
95% CI of LS mean	(1.6, 5.4)	(2.1, 6.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Treatment Burden

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
OL Efficacy Period for Part A		
N	248	238
Parent study baseline		
n	243	235
Mean (SD)	70.8 (20.1)	70.8 (19.5)
Absolute change at OL Part A Week 8		
n	233	229
LS mean (SE)	4.7 (1.0)	4.9 (1.1)
95% CI of LS mean	(2.7, 6.8)	(2.9, 7.0)
Absolute change at OL Part A Week 16		
n	228	223
LS mean (SE)	3.9 (1.1)	4.2 (1.1)
95% CI of LS mean	(1.7, 6.1)	(2.0, 6.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Treatment Burden

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 24		
n	228	221
LS mean (SE)	4.8 (1.1)	5.8 (1.1)
95% CI of LS mean	(2.6, 7.0)	(3.6, 8.0)
Absolute change at OL Part A Week 48		
n	219	213
LS mean (SE)	6.2 (1.1)	5.5 (1.1)
95% CI of LS mean	(4.0, 8.4)	(3.3, 7.7)
Absolute change at OL Part A Week 96		
n	213	205
LS mean (SE)	7.0 (1.2)	6.8 (1.2)
95% CI of LS mean	(4.7, 9.4)	(4.4, 9.1)
Average change through OL Part A Week 96		
n	234	229
LS mean (SE)	5.3 (1.0)	5.4 (1.0)
95% CI of LS mean	(3.5, 7.2)	(3.5, 7.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Health Perceptions

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	269	266
Mean (SD)	71.5 (19.6)	72.8 (20.1)
Absolute change at Week 8		
n	261	257
LS mean (SE)	0.0 (0.9)	-1.1 (0.9)
95% CI of LS mean	(-1.8, 1.8)	(-2.9, 0.7)
Absolute change at Week 16		
n	257	251
LS mean (SE)	0.0 (0.9)	-1.1 (1.0)
95% CI of LS mean	(-1.9, 1.9)	(-2.9, 0.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Health Perceptions

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	256	249
LS mean (SE)	-1.5 (1.0)	-0.9 (1.0)
95% CI of LS mean	(-3.5, 0.5)	(-2.9, 1.1)
Absolute change at Week 52		
n	253	242
LS mean (SE)	2.3 (1.0)	0.2 (1.0)
95% CI of LS mean	(0.4, 4.2)	(-1.8, 2.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Health Perceptions

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
OL Efficacy Period for Part A		
N	248	238
Parent study baseline		
n	231	223
Mean (SD)	71.8 (20.3)	73.0 (19.8)
Absolute change at OL Part A Week 8		
n	223	216
LS mean (SE)	1.2 (1.1)	0.8 (1.1)
95% CI of LS mean	(-1.0, 3.3)	(-1.4, 3.0)
Absolute change at OL Part A Week 16		
n	218	212
LS mean (SE)	0.4 (1.1)	-0.8 (1.1)
95% CI of LS mean	(-1.7, 2.6)	(-3.0, 1.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Health Perceptions

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 24		
n	218	210
LS mean (SE)	0.1 (1.1)	-0.6 (1.1)
95% CI of LS mean	(-2.0, 2.3)	(-2.7, 1.6)
Absolute change at OL Part A Week 48		
n	208	202
LS mean (SE)	0.9 (1.1)	1.0 (1.1)
95% CI of LS mean	(-1.2, 3.1)	(-1.1, 3.2)
Absolute change at OL Part A Week 96		
n	203	194
LS mean (SE)	3.1 (1.2)	2.0 (1.3)
95% CI of LS mean	(0.7, 5.5)	(-0.4, 4.5)
Average change through OL Part A Week 96		
n	224	217
LS mean (SE)	1.2 (0.9)	0.5 (0.9)
95% CI of LS mean	(-0.6, 2.9)	(-1.3, 2.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Weight

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	266	266
Mean (SD)	88.5 (24.1)	84.3 (27.0)
Absolute change at Week 8		
n	258	257
LS mean (SE)	-1.3 (1.3)	0.7 (1.3)
95% CI of LS mean	(-3.9, 1.2)	(-1.8, 3.2)
Absolute change at Week 16		
n	253	252
LS mean (SE)	-2.3 (1.4)	1.6 (1.4)
95% CI of LS mean	(-5.1, 0.5)	(-1.2, 4.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Weight

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	253	249
LS mean (SE)	-2.3 (1.3)	1.2 (1.3)
95% CI of LS mean	(-4.9, 0.3)	(-1.4, 3.8)
Absolute change at Week 52		
n	250	241
LS mean (SE)	-1.9 (1.4)	0.2 (1.4)
95% CI of LS mean	(-4.7, 0.9)	(-2.7, 3.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Weight

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
OL Efficacy Period for Part A		
N	248	238
Parent study baseline		
n	228	223
Mean (SD)	88.6 (24.2)	83.6 (27.7)
Absolute change at OL Part A Week 8		
n	220	217
LS mean (SE)	-2.4 (1.5)	2.2 (1.5)
95% CI of LS mean	(-5.3, 0.5)	(-0.7, 5.1)
Absolute change at OL Part A Week 16		
n	216	212
LS mean (SE)	-1.3 (1.5)	-0.2 (1.5)
95% CI of LS mean	(-4.2, 1.6)	(-3.1, 2.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Weight

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 24		
n	216	210
LS mean (SE)	-1.4 (1.5)	2.7 (1.5)
95% CI of LS mean	(-4.5, 1.6)	(-0.3, 5.8)
Absolute change at OL Part A Week 48		
n	207	202
LS mean (SE)	-3.4 (1.7)	2.5 (1.7)
95% CI of LS mean	(-6.6, -0.1)	(-0.8, 5.8)
Absolute change at OL Part A Week 96		
n	202	193
LS mean (SE)	-2.4 (1.7)	2.1 (1.7)
95% CI of LS mean	(-5.7, 0.8)	(-1.2, 5.4)
Average change through OL Part A Week 96		
n	221	217
LS mean (SE)	-2.2 (1.3)	1.9 (1.3)
95% CI of LS mean	(-4.7, 0.3)	(-0.6, 4.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Digestion

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	282	280
Mean (SD)	81.1 (17.1)	82.1 (18.4)
Absolute change at Week 8		
n	270	270
LS mean (SE)	0.2 (0.9)	-0.7 (0.9)
95% CI of LS mean	(-1.6, 1.9)	(-2.4, 1.1)
Absolute change at Week 16		
n	265	265
LS mean (SE)	-0.2 (0.9)	-0.8 (0.9)
95% CI of LS mean	(-2.0, 1.6)	(-2.6, 1.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Digestion

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	266	262
LS mean (SE)	0.1 (0.9)	-2.0 (0.9)
95% CI of LS mean	(-1.7, 1.9)	(-3.8, -0.1)
Absolute change at Week 52		
n	262	254
LS mean (SE)	-1.9 (1.0)	-2.1 (1.0)
95% CI of LS mean	(-3.8, 0.1)	(-4.0, -0.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Digestion

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
OL Efficacy Period for Part A		
N	248	238
Parent study baseline		
n	243	235
Mean (SD)	80.9 (17.2)	81.8 (18.4)
Absolute change at OL Part A Week 8		
n	233	229
LS mean (SE)	-1.8 (1.1)	-1.3 (1.1)
95% CI of LS mean	(-4.0, 0.4)	(-3.5, 1.0)
Absolute change at OL Part A Week 16		
n	228	223
LS mean (SE)	-2.0 (1.1)	-0.9 (1.1)
95% CI of LS mean	(-4.1, 0.2)	(-3.2, 1.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Digestion

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 24		
n	228	221
LS mean (SE)	-2.5 (1.1)	-1.6 (1.1)
95% CI of LS mean	(-4.7, -0.3)	(-3.8, 0.6)
Absolute change at OL Part A Week 48		
n	219	213
LS mean (SE)	-2.1 (1.2)	-1.0 (1.2)
95% CI of LS mean	(-4.4, 0.2)	(-3.3, 1.4)
Absolute change at OL Part A Week 96		
n	212	204
LS mean (SE)	-1.6 (1.2)	-1.4 (1.2)
95% CI of LS mean	(-3.9, 0.8)	(-3.8, 0.9)
Average change through OL Part A Week 96		
n	234	229
LS mean (SE)	-2.0 (1.0)	-1.2 (1.0)
95% CI of LS mean	(-3.9, -0.1)	(-3.1, 0.7)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Role

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	269	266
Mean (SD)	86.6 (15.6)	86.7 (16.4)
Absolute change at Week 8		
n	261	256
LS mean (SE)	-0.1 (0.8)	0.7 (0.8)
95% CI of LS mean	(-1.7, 1.5)	(-0.9, 2.3)
Absolute change at Week 16		
n	255	252
LS mean (SE)	0.1 (0.9)	0.1 (0.9)
95% CI of LS mean	(-1.6, 1.8)	(-1.6, 1.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Role

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	256	248
LS mean (SE)	-0.5 (1.0)	-0.3 (1.0)
95% CI of LS mean	(-2.4, 1.4)	(-2.2, 1.7)
Absolute change at Week 52		
n	253	241
LS mean (SE)	0.5 (0.9)	2.1 (0.9)
95% CI of LS mean	(-1.2, 2.3)	(0.3, 3.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Role

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
OL Efficacy Period for Part A		
N	248	238
Parent study baseline		
n	231	223
Mean (SD)	86.1 (16.3)	87.0 (15.7)
Absolute change at OL Part A Week 8		
n	222	217
LS mean (SE)	1.9 (1.0)	2.2 (1.0)
95% CI of LS mean	(0.0, 3.9)	(0.2, 4.1)
Absolute change at OL Part A Week 16		
n	218	211
LS mean (SE)	2.0 (0.9)	1.7 (0.9)
95% CI of LS mean	(0.2, 3.8)	(-0.1, 3.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Role

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 24		
n	218	210
LS mean (SE)	1.7 (1.0)	1.3 (1.0)
95% CI of LS mean	(-0.2, 3.6)	(-0.7, 3.2)
Absolute change at OL Part A Week 48		
n	209	202
LS mean (SE)	1.9 (1.0)	1.6 (1.0)
95% CI of LS mean	(-0.1, 3.9)	(-0.4, 3.6)
Absolute change at OL Part A Week 96		
n	202	193
LS mean (SE)	3.0 (1.0)	1.8 (1.0)
95% CI of LS mean	(1.1, 5.0)	(-0.2, 3.8)
Average change through OL Part A Week 96		
n	224	217
LS mean (SE)	2.1 (0.8)	1.7 (0.8)
95% CI of LS mean	(0.5, 3.7)	(0.1, 3.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	282	280
Mean (SD)	72.5 (17.8)	75.0 (17.8)
Absolute change at Week 8		
n	270	270
LS mean (SE)	0.9 (0.8)	0.5 (0.8)
95% CI of LS mean	(-0.8, 2.5)	(-1.1, 2.1)
Absolute change at Week 16		
n	266	264
LS mean (SE)	2.0 (0.9)	1.0 (0.9)
95% CI of LS mean	(0.3, 3.7)	(-0.7, 2.7)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	267	262
LS mean (SE)	0.7 (0.9)	2.1 (0.9)
95% CI of LS mean	(-1.0, 2.4)	(0.4, 3.8)
Absolute change at Week 52		
n	262	255
LS mean (SE)	3.6 (0.9)	4.2 (0.9)
95% CI of LS mean	(1.9, 5.4)	(2.5, 5.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
OL Efficacy Period for Part A		
N	248	238
Parent study baseline		
n	243	235
Mean (SD)	72.5 (18.0)	76.0 (18.0)
Absolute change at OL Part A Week 8		
n	233	228
LS mean (SE)	3.1 (0.9)	3.7 (0.9)
95% CI of LS mean	(1.3, 4.9)	(1.9, 5.6)
Absolute change at OL Part A Week 16		
n	228	223
LS mean (SE)	3.2 (1.0)	3.1 (1.0)
95% CI of LS mean	(1.3, 5.1)	(1.1, 5.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 24		
n	228	221
LS mean (SE)	4.2 (1.0)	3.6 (1.0)
95% CI of LS mean	(2.3, 6.1)	(1.6, 5.6)
Absolute change at OL Part A Week 48		
n	219	213
LS mean (SE)	5.1 (1.0)	4.4 (1.0)
95% CI of LS mean	(3.1, 7.1)	(2.4, 6.4)
Absolute change at OL Part A Week 96		
n	213	205
LS mean (SE)	6.3 (1.0)	5.1 (1.0)
95% CI of LS mean	(4.5, 8.2)	(3.2, 7.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 1.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study 103 Full Analysis Set and OL Full Analysis Set
Subjects from Parent Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Domain: Social

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Average change through OL Part A Week 96		
n	234	229
LS mean (SE)	4.4 (0.8)	4.0 (0.8)
95% CI of LS mean	(2.8, 6.0)	(2.4, 5.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the Day -14 visit, including unscheduled visits, is used as baseline.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for treatment, visit, age at screening (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with baseline ppFEV$_1$ and baseline sweat chloride as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging across all available visit in OL Part A.

Table 14.1.1a
Disposition - Part A
OL All Subjects Set

Disposition Reason	ELX/TEZ/IVA in 121-102 n (%)	VNZ/TEZ/D-IVA in 121-102 n (%)	ELX/TEZ/IVA in 121-103 n (%)	VNZ/TEZ/D-IVA in 121-103 n (%)	Any VNZ/TEZ/D-IVA n (%)
OL All Subjects Set	170	166	248	238	822
OL Safety Set	170	166	248	238	822
OL Full Analysis Set	170	166	248	238	822
Enrolled but not dosed in Part A	0	0	0	0	0
Completed treatment in Part A	151 (88.8)	144 (86.7)	222 (89.5)	211 (88.7)	728 (88.6)
Discontinued treatment in Part A	19 (11.2)	22 (13.3)	26 (10.5)	27 (11.3)	94 (11.4)
Reason for discontinuation of treatment in Part A					
Adverse event	10 (5.9)	3 (1.8)	14 (5.6)	7 (2.9)	34 (4.1)
Subject refused further dosing (not due to AE)	4 (2.4)	8 (4.8)	3 (1.2)	6 (2.5)	21 (2.6)
Lost to follow-up	2 (1.2)	1 (0.6)	0	0	3 (0.4)
Commercial drug is available for subject	0	0	0	0	0
Death	0	0	0	0	0
Did not meet eligibility criteria	0	0	0	0	0
Non-compliance with study drug	0	0	0	3 (1.3)	3 (0.4)
Other non-compliance	0	1 (0.6)	0	0	1 (0.1)
Physician decision	1 (0.6)	2 (1.2)	2 (0.8)	1 (0.4)	6 (0.7)
Pregnancy	1 (0.6)	1 (0.6)	3 (1.2)	4 (1.7)	9 (1.1)
Requires prohibited medication	0	2 (1.2)	0	0	2 (0.2)
Sponsor decision	0	0	1 (0.4)	0	1 (0.1)
Study terminated by sponsor	0	0	0	0	0
Other	1 (0.6)	4 (2.4)	3 (1.2)	6 (2.5)	14 (1.7)

- OL All Subjects Set: all subjects who were enrolled in the OL study
- OL Safety Set: all subjects who received at least 1 dose of study drug in the OL study
- OL Full Analysis Set: all enrolled subjects who received at least 1 dose of study drug in the OL study
- Percentages are based on the number of subjects in the OL Full Analysis Set.

Table 14.1.1a
Disposition - Part A
OL All Subjects Set

Disposition Reason	ELX/TEZ/IVA in 121-102 n (%)	VNZ/TEZ/D-IVA in 121-102 n (%)	ELX/TEZ/IVA in 121-103 n (%)	VNZ/TEZ/D-IVA in 121-103 n (%)	Any VNZ/TEZ/D-IVA n (%)
Completed study in Part A	151 (88.8)	144 (86.7)	222 (89.5)	211 (88.7)	728 (88.6)
Discontinued study in Part A	19 (11.2)	22 (13.3)	26 (10.5)	27 (11.3)	94 (11.4)
Reason for discontinuation from study in Part A					
Adverse event	9 (5.3)	3 (1.8)	14 (5.6)	7 (2.9)	33 (4.0)
Withdrawal of consent (not due to AE)	5 (2.9)	9 (5.4)	4 (1.6)	5 (2.1)	23 (2.8)
Lost to follow-up	2 (1.2)	1 (0.6)	0	0	3 (0.4)
Commercial drug is available for subject	0	0	0	0	0
Death	0	0	0	0	0
Other non-compliance	0	1 (0.6)	0	5 (2.1)	6 (0.7)
Physician decision	1 (0.6)	2 (1.2)	2 (0.8)	1 (0.4)	6 (0.7)
Sponsor decision	0	0	1 (0.4)	0	1 (0.1)
Study terminated by sponsor	0	0	0	0	0
Other	2 (1.2)	6 (3.6)	5 (2.0)	9 (3.8)	22 (2.7)
Rolled over to Part B	145 (85.3)	141 (84.9)	214 (86.3)	203 (85.3)	703 (85.5)

- OL All Subjects Set: all subjects who were enrolled in the OL study
- OL Safety Set: all subjects who received at least 1 dose of study drug in the OL study
- OL Full Analysis Set: all enrolled subjects who received at least 1 dose of study drug in the OL study
- Percentages are based on the number of subjects in the OL Full Analysis Set.

Zusatzanalysen zur Studie VX20-121-104

Table 14.1.3a
Demographics - Part A
OL Full Analysis Set

- [1]: Female n is the denominator
- [2]: Female n with no childbearing potential is the denominator
- Sex and childbearing potential are based on data collected in the OL study. Race and Ethnicity are based on data collected in the parent study.
- For reporting purposes, North America includes subjects from the United States and Canada, and Rest of the World includes subjects from Europe, Israel, Australia, and New Zealand.

Zusatzanalysen zur Studie VX20-121-104

	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238	Any VNZ/TEZ/D-IVA N = 822
Sex, n (%)					
Male	101 (59.4)	105 (63.3)	129 (52.0)	132 (55.5)	467 (56.8)
Female	69 (40.6)	61 (36.7)	119 (48.0)	106 (44.5)	355 (43.2)
Childbearing potential[1], n (%)					
Yes	67 (97.1)	55 (90.2)	102 (85.7)	90 (84.9)	314 (88.5)
No	2 (2.9)	6 (9.8)	17 (14.3)	16 (15.1)	41 (11.5)
Reason not of childbearing potential[2], n (%)					
Surgical Procedure	0	3 (50.0)	5 (29.4)	6 (37.5)	14 (34.1)
Postmenopausal	2 (100.0)	3 (50.0)	12 (70.6)	10 (62.5)	27 (65.9)
Premenarchal	0	0	0	0	0
Other	0	0	0	0	0
Age at Day 1 in the parent study (years)					
n	170	166	248	238	822
Mean (SD)	31.4 (11.3)	31.1 (10.9)	34.7 (12.6)	33.8 (12.7)	33.0 (12.1)
Median	32.6	30.3	34.2	33.1	32.7
Min, max	12.2, 71.6	12.4, 61.7	12.7, 63.4	12.2, 71.2	12.2, 71.6
Race, n (%)					
White	165 (97.1)	162 (97.6)	224 (90.3)	224 (94.1)	775 (94.3)
Black or African American	1 (0.6)	3 (1.8)	0	0	4 (0.5)
Asian	0	1 (0.6)	1 (0.4)	1 (0.4)	3 (0.4)
Northeast Asian	0	0	0	0	0
Southeast Asian	0	0	0	1 (0.4)	1 (0.1)
Other Asian	0	1 (0.6)	1 (0.4)	0	2 (0.2)
Asian, Region Not Reported	0	0	0	0	0
American Indian or Alaska Native	0	0	1 (0.4)	0	1 (0.1)
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Other	1 (0.6)	0	1 (0.4)	1 (0.4)	3 (0.4)

- [1]: Female n is the denominator
- [2]: Female n with no childbearing potential is the denominator
- Sex and childbearing potential are based on data collected in the OL study. Race and Ethnicity are based on data collected in the parent study.
- For reporting purposes, North America includes subjects from the United States and Canada, and Rest of the World includes subjects from Europe, Israel, Australia, and New Zealand.

Table 14.1.3a
Demographics - Part A
OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238	Any VNZ/TEZ/D-IVA N = 822
Not Collected per Local Regulations	0	0	20 (8.1)	10 (4.2)	30 (3.6)
More than one race	3 (1.8)	0	1 (0.4)	2 (0.8)	6 (0.7)
Ethnicity, n (%)					
Hispanic or Latino	10 (5.9)	8 (4.8)	5 (2.0)	4 (1.7)	27 (3.3)
Not Hispanic or Latino	160 (94.1)	158 (95.2)	223 (89.9)	220 (92.4)	761 (92.6)
Not Collected per Local Regulations	0	0	20 (8.1)	14 (5.9)	34 (4.1)
Geographic Region, n (%)					
North America	81 (47.6)	71 (42.8)	92 (37.1)	96 (40.3)	340 (41.4)
Rest of the World	89 (52.4)	95 (57.2)	156 (62.9)	142 (59.7)	482 (58.6)

- [1]: Female n is the denominator
- [2]: Female n with no childbearing potential is the denominator
- Sex and childbearing potential are based on data collected in the OL study. Race and Ethnicity are based on data collected in the parent study.
- For reporting purposes, North America includes subjects from the United States and Canada, and Rest of the World includes subjects from Europe, Israel, Australia, and New Zealand.

Table 14.1.4a
Parent Study Baseline Characteristics - Part A
OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238	Any VNZ/TEZ/D-IVA N = 822
Weight (kg)					
n	170	165	248	236	819
Mean (SD)	64.64 (13.94)	66.24 (13.64)	65.32 (13.68)	66.66 (13.63)	65.75 (13.71)
Median	63.00	65.00	63.00	65.00	64.00
Min, max	33.00, 116.57	33.00, 130.18	32.00, 106.00	34.00, 110.00	32.00, 130.18
Height (cm)					
n	169	166	248	237	820
Mean (SD)	167.1 (9.8)	169.7 (9.6)	168.3 (10.3)	168.9 (9.3)	168.5 (9.8)
Median	167.0	170.0	167.0	169.0	168.0
Min, max	137.2, 192.0	147.0, 195.0	140.0, 200.0	139.7, 191.0	137.2, 200.0
BMI (kg/m^2)					
n	170	165	248	236	819
Mean (SD)	23.01 (3.88)	22.86 (3.46)	22.90 (3.35)	23.24 (3.80)	23.01 (3.62)
Median	22.40	22.39	22.77	22.48	22.50
Min, max	15.81, 44.72	14.28, 35.31	15.43, 35.42	15.56, 39.84	14.28, 44.72
BMI z-score (subjects ≤20 years old at parent study baseline)					
n	29	28	36	42	135
Mean (SD)	-0.13 (0.77)	-0.43 (1.13)	-0.33 (1.03)	-0.08 (0.98)	-0.23 (0.99)
Median	-0.31	-0.35	-0.26	-0.03	-0.22
Min, max	-1.31, 1.56	-4.15, 1.92	-3.07, 1.21	-2.62, 2.12	-4.15, 2.12
Age category at the Screening Visit of the parent study, n (%)					
12 to <18 years	22 (12.9)	23 (13.9)	33 (13.3)	31 (13.0)	109 (13.3)
≥18 years	148 (87.1)	143 (86.1)	215 (86.7)	207 (87.0)	713 (86.7)

- Prior CFTR modulator use includes the most recent CFTRm prior to parent study informed consent for each subject.
- **: If the parent study Day -14 value is not valid or is not available, the most recent available clinic-assessed value is used.
- *: Includes medications administered during the 56 days prior to the first dose of study drug in the parent study Treatment Period, excluding the ones that started in the Run-in Period

Table 14.1.4a
Parent Study Baseline Characteristics - Part A
OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238	Any VNZ/TEZ/D-IVA N = 822
$ppFEV_1$ category at Day -14 of the parent study**, n (%)					
<70 percentage points	95 (55.9)	94 (56.6)	144 (58.1)	137 (57.6)	470 (57.2)
≥70 percentage points	75 (44.1)	72 (43.4)	104 (41.9)	101 (42.4)	352 (42.8)
SwCl category at Day -14 of the parent study**, n (%)					
<30 mmol/L	19 (11.2)	15 (9.0)	70 (28.2)	65 (27.3)	169 (20.6)
≥30 mmol/L	151 (88.8)	150 (90.4)	175 (70.6)	173 (72.7)	649 (79.0)
Missing	0	1 (0.6)	3 (1.2)	0	4 (0.5)
Prior CFTR modulator use, n (%)					
Yes	153 (90.0)	144 (86.7)	221 (89.1)	206 (86.6)	724 (88.1)
Kalydeco	0	0	5 (2.0)	7 (2.9)	12 (1.5)
Orkambi	0	0	13 (5.2)	14 (5.9)	27 (3.3)
Symdeko/Symkevi	0	0	19 (7.7)	25 (10.5)	44 (5.4)
Trikafta/Kaftrio	153 (90.0)	144 (86.7)	184 (74.2)	160 (67.2)	641 (78.0)
No	17 (10.0)	22 (13.3)	27 (10.9)	32 (13.4)	98 (11.9)
Genotype Group, n (%)					
F/MF	170 (100.0)	166 (100.0)	0	0	336 (40.9)
F/F	0	0	189 (76.2)	187 (78.6)	376 (45.7)
F/G	0	0	19 (7.7)	16 (6.7)	35 (4.3)
F/RF	0	0	20 (8.1)	20 (8.4)	40 (4.9)
TCR/non-F	0	0	20 (8.1)	15 (6.3)	35 (4.3)
$ppFEV_1$ (percentage points)					
n	169	165	245	234	813
Mean (SD)	66.8 (14.7)	66.2 (15.7)	66.3 (15.1)	66.8 (14.5)	66.5 (14.9)
Median	67.7	66.3	67.5	66.8	66.9
Min, max	37.2, 100.1	28.0, 108.6	36.4, 104.6	38.3, 112.5	28.0, 112.5

- Prior CFTR modulator use includes the most recent CFTRm prior to parent study informed consent for each subject.
- **: If the parent study Day -14 value is not valid or is not available, the most recent available clinic-assessed value is used.
- *: Includes medications administered during the 56 days prior to the first dose of study drug in the parent study Treatment Period, excluding the ones that started in the Run-in Period

Table 14.1.4a
Parent Study Baseline Characteristics - Part A
OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238	Any VNZ/TEZ/D-IVA N = 822
$ppFEV_1$ category, n (%)					
<40 percentage points	2 (1.2)	6 (3.6)	7 (2.8)	4 (1.7)	19 (2.3)
≥40 to <70 percentage points	99 (58.2)	84 (50.6)	135 (54.4)	126 (52.9)	444 (54.0)
≥70 to ≤90 percentage points	60 (35.3)	68 (41.0)	93 (37.5)	96 (40.3)	317 (38.6)
>90 percentage points	8 (4.7)	7 (4.2)	10 (4.0)	8 (3.4)	33 (4.0)
Missing	1 (0.6)	1 (0.6)	3 (1.2)	4 (1.7)	9 (1.1)
SwCl (mmol/L)					
n	169	165	242	237	813
Mean (SD)	54.7 (18.6)	53.5 (16.4)	41.6 (17.3)	43.2 (18.4)	47.2 (18.6)
Median	54.5	52.3	41.5	42.5	46.8
Min, max	10.0, 113.5	20.5, 104.8	10.8, 109.3	10.0, 113.3	10.0, 113.5
SwCl category, n (%)					
<30 mmol/L	16 (9.4)	13 (7.8)	67 (27.0)	60 (25.2)	156 (19.0)
≥30 to <60 mmol/L	86 (50.6)	98 (59.0)	141 (56.9)	135 (56.7)	460 (56.0)
≥60 mmol/L	67 (39.4)	54 (32.5)	34 (13.7)	42 (17.6)	197 (24.0)
Missing	1 (0.6)	1 (0.6)	6 (2.4)	1 (0.4)	9 (1.1)
CFQ-R respiratory domain score					
n	166	164	243	235	808
Mean (SD)	82.8 (15.3)	85.7 (14.9)	85.5 (13.5)	85.8 (13.6)	85.1 (14.2)
Median	83.3	88.9	88.9	88.9	88.9
Min, max	22.2, 100.0	27.8, 100.0	27.8, 100.0	33.3, 100.0	22.2, 100.0
Prior use of dornase alfa*, n (%)					
Yes	117 (68.8)	105 (63.3)	153 (61.7)	149 (62.6)	524 (63.7)
No	53 (31.2)	61 (36.7)	95 (38.3)	89 (37.4)	298 (36.3)

- Prior CFTR modulator use includes the most recent CFTRm prior to parent study informed consent for each subject.
- **: If the parent study Day -14 value is not valid or is not available, the most recent available clinic-assessed value is used.
- *: Includes medications administered during the 56 days prior to the first dose of study drug in the parent study Treatment Period, excluding the ones that started in the Run-in Period

Table 14.1.4a
Parent Study Baseline Characteristics - Part A
OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238	Any VNZ/TEZ/D-IVA N = 822
Prior use of azithromycin*, n (%)					
Yes	70 (41.2)	75 (45.2)	91 (36.7)	95 (39.9)	331 (40.3)
No	100 (58.8)	91 (54.8)	157 (63.3)	143 (60.1)	491 (59.7)
Prior use of inhaled antibiotic*, n (%)					
Yes	79 (46.5)	71 (42.8)	94 (37.9)	84 (35.3)	328 (39.9)
No	91 (53.5)	95 (57.2)	154 (62.1)	154 (64.7)	494 (60.1)
Prior use of any bronchodilator*, n (%)					
Yes	146 (85.9)	147 (88.6)	206 (83.1)	214 (89.9)	713 (86.7)
No	24 (14.1)	19 (11.4)	42 (16.9)	24 (10.1)	109 (13.3)
Prior use of any inhaled hypertonic saline*, n (%)					
Yes	113 (66.5)	108 (65.1)	135 (54.4)	121 (50.8)	477 (58.0)
No	57 (33.5)	58 (34.9)	113 (45.6)	117 (49.2)	345 (42.0)
Infection with *Pseudomonas aeruginosa* within 2 years prior to screening in the parent study, n (%)					
Positive	94 (55.3)	93 (56.0)	134 (54.0)	133 (55.9)	454 (55.2)
Negative	76 (44.7)	73 (44.0)	114 (46.0)	105 (44.1)	368 (44.8)

- Prior CFTR modulator use includes the most recent CFTRm prior to parent study informed consent for each subject.
- **: If the parent study Day -14 value is not valid or is not available, the most recent available clinic-assessed value is used.
- *: Includes medications administered during the 56 days prior to the first dose of study drug in the parent study Treatment Period, excluding the ones that started in the Run-in Period

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Forced Expiratory Volume in 1 Second (L)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	169	165
	Mean (SD)	2.42 (0.72)	2.50 (0.75)
	Median	2.38	2.47
	Min, max	1.01, 4.49	1.08, 4.57
OL Part A Day 15	n	163	160
	Mean (SD)	2.45 (0.75)	2.55 (0.75)
	Median	2.41	2.57
	Min, max	1.19, 4.69	1.02, 4.44
Absolute change at OL Part A Day 15	n	162	159
	Mean (SD)	0.03 (0.20)	0.03 (0.22)
	Median	0.01	0.02
	Min, max	-0.39, 0.95	-0.50, 0.77
OL Part A Week 4	n	163	156
	Mean (SD)	2.47 (0.76)	2.56 (0.75)
	Median	2.44	2.53
	Min, max	1.21, 4.67	0.98, 4.70
Absolute change at OL Part A Week 4	n	163	155
	Mean (SD)	0.04 (0.20)	0.04 (0.23)
	Median	0.01	0.02
	Min, max	-0.41, 0.74	-0.51, 0.85

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Forced Expiratory Volume in 1 Second (L)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 8	n	164	155
	Mean (SD)	2.44 (0.76)	2.53 (0.75)
	Median	2.41	2.46
	Min, max	0.96, 4.56	0.99, 4.79
Absolute change at OL Part A Week 8	n	164	154
	Mean (SD)	0.04 (0.25)	0.04 (0.23)
	Median	0.00	0.03
	Min, max	-0.95, 0.98	-0.90, 0.71
OL Part A Week 16	n	161	158
	Mean (SD)	2.45 (0.76)	2.54 (0.77)
	Median	2.37	2.50
	Min, max	1.18, 4.74	0.75, 4.61
Absolute change at OL Part A Week 16	n	161	157
	Mean (SD)	0.06 (0.22)	0.03 (0.24)
	Median	0.04	0.03
	Min, max	-0.48, 1.08	-0.77, 0.90
OL Part A Week 24	n	158	154
	Mean (SD)	2.47 (0.75)	2.53 (0.76)
	Median	2.42	2.56
	Min, max	1.20, 4.93	0.88, 4.61
Absolute change at OL Part A Week 24	n	158	154
	Mean (SD)	0.05 (0.23)	0.04 (0.25)
	Median	0.02	0.02
	Min, max	-0.68, 1.13	-0.61, 0.88

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Forced Expiratory Volume in 1 Second (L)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 36	n	154	152
	Mean (SD)	2.46 (0.77)	2.58 (0.77)
	Median	2.45	2.54
	Min, max	1.15, 5.18	0.96, 4.56
Absolute change at OL Part A Week 36	n	154	152
	Mean (SD)	0.04 (0.28)	0.07 (0.27)
	Median	0.02	0.04
	Min, max	-0.87, 1.19	-0.71, 0.84
OL Part A Week 48	n	155	153
	Mean (SD)	2.48 (0.79)	2.58 (0.77)
	Median	2.47	2.53
	Min, max	1.01, 4.94	0.93, 4.57
Absolute change at OL Part A Week 48	n	155	152
	Mean (SD)	0.04 (0.28)	0.05 (0.27)
	Median	0.01	0.03
	Min, max	-1.03, 1.22	-0.52, 0.98
OL Part A Week 60	n	151	151
	Mean (SD)	2.52 (0.79)	2.60 (0.77)
	Median	2.52	2.57
	Min, max	1.14, 4.75	0.91, 4.37
Absolute change at OL Part A Week 60	n	150	150
	Mean (SD)	0.07 (0.29)	0.07 (0.28)
	Median	0.04	0.05
	Min, max	-0.78, 1.13	-0.64, 1.13

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Forced Expiratory Volume in 1 Second (L)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 72	n	153	147
	Mean (SD)	2.49 (0.78)	2.57 (0.76)
	Median	2.44	2.49
	Min, max	1.10, 4.71	0.89, 4.10
Absolute change at OL Part A Week 72	n	152	146
	Mean (SD)	0.06 (0.29)	0.06 (0.28)
	Median	0.03	0.01
	Min, max	-0.59, 1.21	-0.80, 1.02
OL Part A Week 84	n	148	143
	Mean (SD)	2.53 (0.82)	2.61 (0.79)
	Median	2.43	2.56
	Min, max	1.11, 4.91	0.96, 4.40
Absolute change at OL Part A Week 84	n	147	142
	Mean (SD)	0.07 (0.33)	0.07 (0.31)
	Median	0.03	0.06
	Min, max	-0.81, 1.33	-1.16, 1.12
OL Part A Week 96	n	143	141
	Mean (SD)	2.48 (0.77)	2.55 (0.78)
	Median	2.47	2.45
	Min, max	1.06, 4.59	0.90, 4.55
Absolute change at OL Part A Week 96	n	142	141
	Mean (SD)	0.05 (0.28)	0.02 (0.33)
	Median	0.03	0.00
	Min, max	-1.03, 1.19	-0.95, 1.36

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Ratio of FEV1/FVC (RATIO)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	169	163
	Mean (SD)	0.64 (0.12)	0.63 (0.13)
	Median	0.63	0.62
	Min, max	0.38, 0.94	0.33, 0.97
OL Part A Day 15	n	154	155
	Mean (SD)	0.64 (0.12)	0.63 (0.13)
	Median	0.64	0.62
	Min, max	0.38, 0.96	0.31, 0.98
Absolute change at OL Part A Day 15	n	153	153
	Mean (SD)	0.00 (0.03)	0.00 (0.03)
	Median	-0.01	0.00
	Min, max	-0.14, 0.15	-0.12, 0.10
OL Part A Week 4	n	159	152
	Mean (SD)	0.64 (0.12)	0.63 (0.12)
	Median	0.64	0.63
	Min, max	0.38, 0.96	0.31, 0.98
Absolute change at OL Part A Week 4	n	159	150
	Mean (SD)	0.00 (0.03)	0.00 (0.03)
	Median	0.00	0.00
	Min, max	-0.09, 0.11	-0.12, 0.10

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Ratio of FEV1/FVC (RATIO)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 8	n	162	147
	Mean (SD)	0.64 (0.12)	0.63 (0.13)
	Median	0.64	0.63
	Min, max	0.36, 0.97	0.31, 0.96
Absolute change at OL Part A Week 8	n	162	144
	Mean (SD)	0.00 (0.04)	0.00 (0.04)
	Median	0.00	0.00
	Min, max	-0.19, 0.12	-0.16, 0.11
OL Part A Week 16	n	154	150
	Mean (SD)	0.63 (0.11)	0.63 (0.13)
	Median	0.62	0.62
	Min, max	0.38, 0.95	0.31, 0.95
Absolute change at OL Part A Week 16	n	154	147
	Mean (SD)	0.00 (0.03)	0.00 (0.03)
	Median	0.00	0.00
	Min, max	-0.11, 0.12	-0.17, 0.10
OL Part A Week 24	n	153	148
	Mean (SD)	0.64 (0.11)	0.62 (0.13)
	Median	0.63	0.62
	Min, max	0.36, 0.95	0.32, 0.96
Absolute change at OL Part A Week 24	n	153	147
	Mean (SD)	-0.01 (0.04)	0.00 (0.03)
	Median	-0.01	0.00
	Min, max	-0.19, 0.11	-0.15, 0.08

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Ratio of FEV1/FVC (RATIO)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 36	n	150	145
	Mean (SD)	0.63 (0.12)	0.62 (0.12)
	Median	0.62	0.63
	Min, max	0.36, 0.94	0.30, 0.98
Absolute change at OL Part A Week 36	n	150	144
	Mean (SD)	-0.01 (0.04)	0.00 (0.03)
	Median	-0.01	0.00
	Min, max	-0.21, 0.17	-0.15, 0.08
OL Part A Week 48	n	148	147
	Mean (SD)	0.63 (0.12)	0.63 (0.12)
	Median	0.63	0.63
	Min, max	0.36, 0.93	0.28, 0.96
Absolute change at OL Part A Week 48	n	148	146
	Mean (SD)	-0.01 (0.04)	-0.01 (0.04)
	Median	-0.01	-0.01
	Min, max	-0.18, 0.14	-0.13, 0.10
OL Part A Week 60	n	148	147
	Mean (SD)	0.64 (0.12)	0.62 (0.11)
	Median	0.63	0.64
	Min, max	0.38, 0.94	0.29, 0.88
Absolute change at OL Part A Week 60	n	147	145
	Mean (SD)	-0.01 (0.04)	0.00 (0.04)
	Median	-0.01	0.00
	Min, max	-0.19, 0.16	-0.11, 0.15

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Ratio of FEV1/FVC (RATIO)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 72	n	144	146
	Mean (SD)	0.63 (0.12)	0.62 (0.12)
	Median	0.63	0.63
	Min, max	0.35, 0.94	0.29, 0.97
Absolute change at OL Part A Week 72	n	143	144
	Mean (SD)	-0.01 (0.04)	-0.01 (0.04)
	Median	-0.01	0.00
	Min, max	-0.13, 0.15	-0.12, 0.09
OL Part A Week 84	n	140	136
	Mean (SD)	0.63 (0.12)	0.63 (0.12)
	Median	0.62	0.64
	Min, max	0.32, 0.93	0.29, 0.95
Absolute change at OL Part A Week 84	n	139	134
	Mean (SD)	-0.01 (0.04)	0.00 (0.04)
	Median	-0.01	0.00
	Min, max	-0.15, 0.18	-0.17, 0.12
OL Part A Week 96	n	140	133
	Mean (SD)	0.63 (0.11)	0.61 (0.12)
	Median	0.63	0.61
	Min, max	0.35, 0.90	0.29, 0.97
Absolute change at OL Part A Week 96	n	139	133
	Mean (SD)	-0.01 (0.04)	-0.01 (0.05)
	Median	-0.01	-0.01
	Min, max	-0.25, 0.11	-0.21, 0.14

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Forced Vital Capacity (L)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	170	165
	Mean (SD)	3.79 (0.95)	3.98 (0.94)
	Median	3.72	3.88
	Min, max	2.01, 6.02	1.87, 6.24
OL Part A Day 15	n	156	158
	Mean (SD)	3.86 (0.98)	4.06 (0.92)
	Median	3.81	3.98
	Min, max	2.16, 6.05	2.22, 6.07
Absolute change at OL Part A Day 15	n	156	157
	Mean (SD)	0.06 (0.23)	0.07 (0.26)
	Median	0.04	0.05
	Min, max	-0.56, 0.87	-0.49, 1.05
OL Part A Week 4	n	161	156
	Mean (SD)	3.88 (0.97)	4.03 (0.92)
	Median	3.87	3.90
	Min, max	2.14, 5.95	2.12, 6.51
Absolute change at OL Part A Week 4	n	161	156
	Mean (SD)	0.07 (0.24)	0.07 (0.28)
	Median	0.03	0.03
	Min, max	-0.46, 0.80	-0.73, 1.19

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Forced Vital Capacity (L)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 8	n	163	151
	Mean (SD)	3.84 (0.96)	4.00 (0.91)
	Median	3.82	3.86
	Min, max	2.10, 5.98	2.16, 6.15
Absolute change at OL Part A Week 8	n	163	150
	Mean (SD)	0.06 (0.27)	0.06 (0.25)
	Median	0.04	0.05
	Min, max	-0.80, 1.01	-0.72, 0.94
OL Part A Week 16	n	157	154
	Mean (SD)	3.91 (0.96)	4.03 (0.96)
	Median	3.94	3.91
	Min, max	2.19, 6.04	2.16, 6.42
Absolute change at OL Part A Week 16	n	157	153
	Mean (SD)	0.12 (0.26)	0.06 (0.32)
	Median	0.09	0.06
	Min, max	-0.36, 1.15	-1.49, 1.29
OL Part A Week 24	n	159	154
	Mean (SD)	3.88 (0.93)	4.03 (0.93)
	Median	3.84	3.88
	Min, max	2.10, 6.05	2.20, 6.20
Absolute change at OL Part A Week 24	n	159	154
	Mean (SD)	0.11 (0.28)	0.08 (0.30)
	Median	0.09	0.04
	Min, max	-0.91, 1.17	-0.94, 1.43

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Forced Vital Capacity (L)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 36	n	155	149
	Mean (SD)	3.92 (0.96)	4.11 (0.92)
	Median	3.95	4.07
	Min, max	1.99, 6.43	2.19, 6.33
Absolute change at OL Part A Week 36	n	155	149
	Mean (SD)	0.10 (0.31)	0.11 (0.30)
	Median	0.08	0.06
	Min, max	-0.72, 1.25	-0.77, 1.16
OL Part A Week 48	n	150	148
	Mean (SD)	3.89 (0.99)	4.10 (0.93)
	Median	3.90	3.93
	Min, max	1.91, 6.28	2.02, 6.53
Absolute change at OL Part A Week 48	n	150	148
	Mean (SD)	0.09 (0.34)	0.11 (0.31)
	Median	0.07	0.06
	Min, max	-1.58, 1.31	-0.68, 1.29
OL Part A Week 60	n	150	148
	Mean (SD)	3.96 (1.00)	4.14 (0.95)
	Median	3.95	4.09
	Min, max	2.16, 6.36	2.02, 6.77
Absolute change at OL Part A Week 60	n	150	148
	Mean (SD)	0.13 (0.33)	0.12 (0.34)
	Median	0.09	0.05
	Min, max	-0.61, 1.41	-0.93, 1.65

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Forced Vital Capacity (L)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 72	n	144	148
	Mean (SD)	3.95 (0.95)	4.10 (0.94)
	Median	3.96	3.96
	Min, max	2.11, 6.02	2.05, 6.96
Absolute change at OL Part A Week 72	n	144	148
	Mean (SD)	0.13 (0.35)	0.11 (0.34)
	Median	0.08	0.07
	Min, max	-0.72, 1.63	-0.73, 1.40
OL Part A Week 84	n	142	137
	Mean (SD)	3.96 (1.00)	4.11 (0.96)
	Median	3.88	4.02
	Min, max	2.13, 5.98	1.96, 6.69
Absolute change at OL Part A Week 84	n	142	136
	Mean (SD)	0.11 (0.39)	0.12 (0.37)
	Median	0.06	0.07
	Min, max	-1.42, 1.59	-1.00, 1.62
OL Part A Week 96	n	144	136
	Mean (SD)	3.93 (0.99)	4.06 (0.97)
	Median	3.91	3.99
	Min, max	1.97, 5.96	2.05, 6.87
Absolute change at OL Part A Week 96	n	144	136
	Mean (SD)	0.12 (0.37)	0.08 (0.38)
	Median	0.06	0.04
	Min, max	-0.78, 1.67	-1.33, 1.47

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Percent Predicted Forced Expiratory Volume in 1 Second (%)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	169	165
	Mean (SD)	66.8 (14.7)	66.2 (15.7)
	Median	67.7	66.3
	Min, max	37.2, 100.1	28.0, 108.6
OL Part A Day 15	n	163	160
	Mean (SD)	67.2 (15.0)	67.2 (15.6)
	Median	67.4	68.3
	Min, max	35.7, 103.0	32.0, 99.4
Absolute change at OL Part A Day 15	n	162	159
	Mean (SD)	0.2 (4.9)	0.6 (5.0)
	Median	0.4	0.4
	Min, max	-12.8, 23.7	-12.7, 20.4
OL Part A Week 4	n	163	156
	Mean (SD)	67.5 (15.0)	67.3 (15.6)
	Median	67.5	66.9
	Min, max	36.4, 103.8	34.0, 104.2
Absolute change at OL Part A Week 4	n	163	155
	Mean (SD)	0.6 (4.4)	0.7 (5.5)
	Median	0.5	0.6
	Min, max	-11.4, 20.9	-14.0, 22.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Percent Predicted Forced Expiratory Volume in 1 Second (%)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 8	n	164	155
	Mean (SD)	66.9 (15.3)	67.1 (15.7)
	Median	67.6	67.8
	Min, max	26.7, 104.4	29.9, 102.8
Absolute change at OL Part A Week 8	n	164	154
	Mean (SD)	0.4 (6.0)	1.0 (5.3)
	Median	0.2	1.1
	Min, max	-29.0, 24.8	-18.3, 18.9
OL Part A Week 16	n	161	158
	Mean (SD)	66.9 (14.7)	66.7 (15.9)
	Median	67.6	66.2
	Min, max	34.9, 104.4	20.7, 102.9
Absolute change at OL Part A Week 16	n	161	157
	Mean (SD)	0.9 (5.0)	0.5 (5.6)
	Median	0.8	0.9
	Min, max	-11.9, 23.5	-26.0, 23.7
OL Part A Week 24	n	158	154
	Mean (SD)	67.6 (14.8)	66.8 (16.0)
	Median	67.6	67.3
	Min, max	37.4, 105.1	24.4, 100.9
Absolute change at OL Part A Week 24	n	158	154
	Mean (SD)	0.7 (5.1)	0.7 (5.5)
	Median	0.7	0.9
	Min, max	-16.8, 19.8	-14.6, 19.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Percent Predicted Forced Expiratory Volume in 1 Second (%)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 36	n	154	152
	Mean (SD)	67.4 (15.2)	67.7 (15.5)
	Median	68.1	67.7
	Min, max	36.9, 104.7	30.2, 101.5
Absolute change at OL Part A Week 36	n	154	152
	Mean (SD)	0.3 (6.2)	1.3 (5.5)
	Median	0.5	1.5
	Min, max	-26.4, 25.6	-18.0, 20.2
OL Part A Week 48	n	155	153
	Mean (SD)	67.4 (15.4)	67.8 (15.4)
	Median	68.3	68.7
	Min, max	34.4, 104.0	24.0, 101.7
Absolute change at OL Part A Week 48	n	155	152
	Mean (SD)	0.2 (6.1)	0.9 (5.6)
	Median	0.6	1.2
	Min, max	-34.7, 23.6	-20.9, 24.3
OL Part A Week 60	n	151	151
	Mean (SD)	68.0 (15.1)	68.2 (15.3)
	Median	68.3	69.7
	Min, max	36.6, 102.9	31.9, 101.2
Absolute change at OL Part A Week 60	n	150	150
	Mean (SD)	0.8 (6.2)	1.3 (5.7)
	Median	1.2	1.6
	Min, max	-23.5, 26.7	-16.1, 30.1

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Percent Predicted Forced Expiratory Volume in 1 Second (%)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 72	n	153	147
	Mean (SD)	67.7 (15.4)	67.7 (15.5)
	Median	68.6	69.0
	Min, max	38.4, 108.0	27.6, 98.5
Absolute change at OL Part A Week 72	n	152	146
	Mean (SD)	0.7 (5.8)	1.1 (5.3)
	Median	1.1	1.0
	Min, max	-19.1, 23.3	-19.0, 24.0
OL Part A Week 84	n	148	143
	Mean (SD)	67.8 (15.9)	68.6 (15.5)
	Median	68.5	70.3
	Min, max	31.9, 104.2	33.6, 101.6
Absolute change at OL Part A Week 84	n	147	142
	Mean (SD)	0.9 (6.9)	1.4 (6.4)
	Median	1.0	1.9
	Min, max	-26.1, 29.4	-27.7, 30.1
OL Part A Week 96	n	143	141
	Mean (SD)	67.4 (15.3)	67.3 (15.4)
	Median	68.0	67.9
	Min, max	33.0, 98.1	31.6, 101.1
Absolute change at OL Part A Week 96	n	142	141
	Mean (SD)	0.9 (5.8)	0.3 (6.8)
	Median	1.0	0.4
	Min, max	-31.0, 13.2	-22.6, 19.8

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Percent Predicted Ratio of FEV1/FVC (%)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	169	163
	Mean (SD)	76.1 (12.7)	74.8 (13.7)
	Median	76.2	75.2
	Min, max	47.2, 106.5	40.2, 109.2
OL Part A Day 15	n	154	155
	Mean (SD)	76.2 (12.7)	74.7 (14.0)
	Median	75.8	75.6
	Min, max	45.6, 111.8	37.1, 113.6
Absolute change at OL Part A Day 15	n	153	153
	Mean (SD)	-0.3 (3.9)	-0.2 (3.8)
	Median	-0.4	-0.2
	Min, max	-16.3, 17.5	-13.6, 12.2
OL Part A Week 4	n	159	152
	Mean (SD)	76.2 (12.8)	75.0 (13.5)
	Median	76.0	76.0
	Min, max	45.0, 111.2	36.7, 113.2
Absolute change at OL Part A Week 4	n	159	150
	Mean (SD)	0.0 (3.8)	0.0 (4.1)
	Median	0.1	0.2
	Min, max	-10.3, 13.1	-13.2, 12.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Percent Predicted Ratio of FEV1/FVC (%)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 8	n	162	147
	Mean (SD)	76.2 (13.0)	75.3 (13.9)
	Median	75.2	76.9
	Min, max	43.4, 108.8	36.5, 107.1
Absolute change at OL Part A Week 8	n	162	144
	Mean (SD)	0.0 (5.0)	0.1 (4.4)
	Median	0.3	0.1
	Min, max	-22.5, 14.2	-17.3, 13.6
OL Part A Week 16	n	154	150
	Mean (SD)	75.2 (12.4)	75.1 (13.8)
	Median	73.9	75.5
	Min, max	45.2, 105.1	37.6, 107.8
Absolute change at OL Part A Week 16	n	154	147
	Mean (SD)	-0.3 (4.0)	-0.1 (3.9)
	Median	-0.1	0.0
	Min, max	-12.5, 14.4	-18.4, 12.7
OL Part A Week 24	n	153	148
	Mean (SD)	75.7 (12.2)	74.6 (13.7)
	Median	74.9	75.2
	Min, max	44.4, 107.3	37.5, 107.1
Absolute change at OL Part A Week 24	n	153	147
	Mean (SD)	-0.6 (4.4)	-0.2 (4.1)
	Median	-0.5	-0.1
	Min, max	-21.1, 13.5	-16.7, 10.2

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Percent Predicted Ratio of FEV1/FVC (%)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 36	n	150	145
	Mean (SD)	75.6 (12.7)	74.7 (13.5)
	Median	74.1	75.9
	Min, max	44.9, 108.2	36.4, 113.9
Absolute change at OL Part A Week 36	n	150	144
	Mean (SD)	-0.7 (4.7)	-0.1 (4.1)
	Median	-0.2	0.2
	Min, max	-24.4, 20.6	-16.0, 10.4
OL Part A Week 48	n	148	147
	Mean (SD)	75.7 (12.8)	75.0 (13.3)
	Median	74.7	76.1
	Min, max	44.7, 104.7	35.0, 111.1
Absolute change at OL Part A Week 48	n	148	146
	Mean (SD)	-0.5 (4.7)	-0.2 (4.3)
	Median	-0.1	-0.3
	Min, max	-19.4, 17.1	-14.6, 13.1
OL Part A Week 60	n	148	147
	Mean (SD)	75.9 (13.0)	74.6 (12.5)
	Median	74.8	76.7
	Min, max	45.2, 106.1	34.2, 99.0
Absolute change at OL Part A Week 60	n	147	145
	Mean (SD)	-0.6 (4.9)	-0.1 (4.6)
	Median	-0.5	0.2
	Min, max	-21.9, 19.3	-13.2, 18.8

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Percent Predicted Ratio of FEV1/FVC (%)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 72	n	144	146
	Mean (SD)	75.5 (12.7)	74.6 (13.2)
	Median	74.9	76.1
	Min, max	44.0, 104.2	33.8, 111.1
Absolute change at OL Part A Week 72	n	143	144
	Mean (SD)	-0.5 (4.5)	-0.2 (4.2)
	Median	-0.3	-0.1
	Min, max	-15.3, 17.5	-13.3, 11.5
OL Part A Week 84	n	140	136
	Mean (SD)	75.1 (12.8)	75.6 (13.3)
	Median	74.0	77.1
	Min, max	39.8, 104.7	34.9, 108.9
Absolute change at OL Part A Week 84	n	139	134
	Mean (SD)	-0.3 (5.0)	0.0 (4.6)
	Median	-0.4	0.4
	Min, max	-16.7, 21.3	-20.1, 14.8
OL Part A Week 96	n	140	133
	Mean (SD)	75.6 (12.3)	73.7 (13.1)
	Median	75.6	75.2
	Min, max	43.9, 100.6	34.1, 107.8
Absolute change at OL Part A Week 96	n	139	133
	Mean (SD)	-0.4 (4.8)	-0.5 (5.4)
	Median	-0.3	-0.3
	Min, max	-28.1, 13.6	-22.5, 18.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Percent Predicted Forced Vital Capacity (%)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	170	165
	Mean (SD)	87.0 (11.4)	87.6 (12.6)
	Median	86.9	89.2
	Min, max	58.4, 122.7	50.8, 116.0
OL Part A Day 15	n	156	158
	Mean (SD)	87.9 (11.8)	89.1 (12.0)
	Median	88.7	90.3
	Min, max	57.9, 120.2	59.2, 113.9
Absolute change at OL Part A Day 15	n	156	157
	Mean (SD)	0.7 (4.5)	1.2 (4.9)
	Median	0.7	1.1
	Min, max	-14.3, 15.8	-11.6, 22.5
OL Part A Week 4	n	161	156
	Mean (SD)	87.8 (11.8)	88.6 (12.7)
	Median	87.9	89.8
	Min, max	57.3, 119.3	49.7, 119.7
Absolute change at OL Part A Week 4	n	161	156
	Mean (SD)	0.9 (4.6)	1.2 (5.5)
	Median	0.2	0.6
	Min, max	-11.6, 18.0	-19.3, 25.5

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Percent Predicted Forced Vital Capacity (%)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 8	n	163	151
	Mean (SD)	87.6 (11.9)	88.8 (12.4)
	Median	89.0	90.5
	Min, max	57.2, 116.8	53.5, 118.6
Absolute change at OL Part A Week 8	n	163	150
	Mean (SD)	0.6 (5.1)	1.1 (4.9)
	Median	0.9	1.1
	Min, max	-18.8, 18.7	-19.1, 20.3
OL Part A Week 16	n	157	154
	Mean (SD)	88.9 (11.5)	88.3 (13.7)
	Median	89.6	90.1
	Min, max	62.1, 120.9	46.6, 118.5
Absolute change at OL Part A Week 16	n	157	153
	Mean (SD)	1.7 (4.7)	0.9 (6.3)
	Median	1.6	1.6
	Min, max	-6.8, 20.0	-31.4, 27.7
OL Part A Week 24	n	159	154
	Mean (SD)	88.2 (11.3)	89.0 (12.9)
	Median	88.7	91.0
	Min, max	58.9, 116.5	51.4, 117.0
Absolute change at OL Part A Week 24	n	159	154
	Mean (SD)	1.5 (4.7)	1.1 (5.4)
	Median	1.6	0.9
	Min, max	-18.2, 20.5	-19.5, 25.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Percent Predicted Forced Vital Capacity (%)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 36	n	155	149
	Mean (SD)	88.6 (11.9)	89.9 (12.4)
	Median	89.2	89.9
	Min, max	54.5, 120.0	49.1, 117.7
Absolute change at OL Part A Week 36	n	155	149
	Mean (SD)	1.2 (5.2)	1.8 (5.2)
	Median	1.4	1.4
	Min, max	-14.5, 16.0	-16.4, 25.1
OL Part A Week 48	n	150	148
	Mean (SD)	88.0 (12.3)	89.7 (12.2)
	Median	88.9	91.2
	Min, max	54.4, 119.3	55.1, 117.4
Absolute change at OL Part A Week 48	n	150	148
	Mean (SD)	0.7 (6.0)	1.6 (5.2)
	Median	0.9	1.7
	Min, max	-43.1, 14.4	-14.4, 28.1
OL Part A Week 60	n	150	148
	Mean (SD)	89.0 (12.0)	90.3 (12.5)
	Median	90.4	91.2
	Min, max	59.2, 122.0	53.9, 120.7
Absolute change at OL Part A Week 60	n	150	148
	Mean (SD)	1.6 (5.2)	2.0 (5.7)
	Median	1.6	1.4
	Min, max	-11.8, 22.2	-16.5, 35.9

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.1a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Percent Predicted Forced Vital Capacity (%)

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 72	n	144	148
	Mean (SD)	89.3 (12.1)	89.8 (12.9)
	Median	90.7	91.7
	Min, max	59.9, 122.8	52.8, 119.7
Absolute change at OL Part A Week 72	n	144	148
	Mean (SD)	1.5 (5.4)	1.8 (5.5)
	Median	1.6	1.7
	Min, max	-20.3, 18.8	-15.2, 30.2
OL Part A Week 84	n	142	137
	Mean (SD)	88.8 (12.8)	90.1 (13.0)
	Median	90.4	91.7
	Min, max	57.9, 122.5	54.2, 115.2
Absolute change at OL Part A Week 84	n	142	136
	Mean (SD)	1.3 (6.5)	1.8 (6.2)
	Median	1.6	1.8
	Min, max	-40.2, 19.9	-19.3, 35.3
OL Part A Week 96	n	144	136
	Mean (SD)	89.0 (12.7)	89.4 (13.1)
	Median	90.3	91.8
	Min, max	53.5, 117.8	55.8, 125.1
Absolute change at OL Part A Week 96	n	144	136
	Mean (SD)	1.5 (5.3)	1.0 (6.2)
	Median	1.4	0.7
	Min, max	-12.6, 16.3	-23.9, 17.2

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Forced Expiratory Volume in 1 Second (L)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	245	234
	Mean (SD)	2.36 (0.75)	2.42 (0.70)
	Median	2.30	2.38
	Min, max	0.99, 4.90	1.17, 4.50
OL Part A Day 15	n	229	229
	Mean (SD)	2.41 (0.78)	2.47 (0.74)
	Median	2.33	2.42
	Min, max	0.98, 4.80	1.26, 4.64
Absolute change at OL Part A Day 15	n	227	227
	Mean (SD)	0.03 (0.20)	0.05 (0.18)
	Median	0.01	0.03
	Min, max	-0.45, 0.86	-0.50, 0.71
OL Part A Week 4	n	237	225
	Mean (SD)	2.39 (0.80)	2.45 (0.72)
	Median	2.29	2.42
	Min, max	1.00, 4.97	1.19, 4.50
Absolute change at OL Part A Week 4	n	235	221
	Mean (SD)	0.02 (0.20)	0.04 (0.20)
	Median	-0.01	0.04
	Min, max	-0.61, 0.97	-0.64, 0.74

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Forced Expiratory Volume in 1 Second (L)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 8	n	234	226
	Mean (SD)	2.37 (0.79)	2.46 (0.72)
	Median	2.31	2.39
	Min, max	0.92, 5.13	1.10, 4.63
Absolute change at OL Part A Week 8	n	231	223
	Mean (SD)	0.02 (0.20)	0.03 (0.20)
	Median	-0.01	0.02
	Min, max	-0.57, 0.90	-0.46, 0.81
OL Part A Week 16	n	232	222
	Mean (SD)	2.39 (0.80)	2.46 (0.73)
	Median	2.30	2.43
	Min, max	0.70, 4.91	1.19, 4.83
Absolute change at OL Part A Week 16	n	229	219
	Mean (SD)	0.03 (0.23)	0.04 (0.23)
	Median	0.01	0.02
	Min, max	-0.88, 0.86	-0.72, 1.00
OL Part A Week 24	n	230	223
	Mean (SD)	2.41 (0.81)	2.46 (0.74)
	Median	2.34	2.41
	Min, max	0.98, 4.85	1.11, 4.72
Absolute change at OL Part A Week 24	n	228	220
	Mean (SD)	0.05 (0.22)	0.04 (0.23)
	Median	0.02	0.02
	Min, max	-0.50, 0.91	-0.64, 0.88

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Forced Expiratory Volume in 1 Second (L)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 36	n	223	217
	Mean (SD)	2.40 (0.82)	2.47 (0.76)
	Median	2.29	2.39
	Min, max	0.77, 4.83	1.14, 4.83
Absolute change at OL Part A Week 36	n	221	214
	Mean (SD)	0.03 (0.26)	0.06 (0.25)
	Median	0.01	0.02
	Min, max	-0.84, 0.96	-0.59, 1.01
OL Part A Week 48	n	227	218
	Mean (SD)	2.40 (0.82)	2.44 (0.75)
	Median	2.31	2.38
	Min, max	1.10, 4.93	1.22, 4.74
Absolute change at OL Part A Week 48	n	224	214
	Mean (SD)	0.03 (0.26)	0.04 (0.24)
	Median	0.00	0.01
	Min, max	-0.74, 1.13	-0.59, 1.25
OL Part A Week 60	n	216	209
	Mean (SD)	2.39 (0.81)	2.48 (0.75)
	Median	2.30	2.44
	Min, max	0.95, 5.03	1.17, 4.65
Absolute change at OL Part A Week 60	n	213	206
	Mean (SD)	0.04 (0.28)	0.07 (0.27)
	Median	0.01	0.03
	Min, max	-0.62, 1.23	-0.37, 1.27

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Forced Expiratory Volume in 1 Second (L)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 72	n	216	209
	Mean (SD)	2.41 (0.84)	2.46 (0.75)
	Median	2.28	2.40
	Min, max	1.03, 5.07	1.20, 4.63
Absolute change at OL Part A Week 72	n	213	206
	Mean (SD)	0.05 (0.28)	0.06 (0.26)
	Median	0.01	0.03
	Min, max	-0.77, 1.31	-0.45, 1.43
OL Part A Week 84	n	217	207
	Mean (SD)	2.43 (0.85)	2.49 (0.78)
	Median	2.33	2.40
	Min, max	1.05, 4.90	1.17, 4.73
Absolute change at OL Part A Week 84	n	214	203
	Mean (SD)	0.06 (0.30)	0.08 (0.30)
	Median	0.02	0.03
	Min, max	-0.53, 1.29	-0.50, 1.70
OL Part A Week 96	n	216	205
	Mean (SD)	2.42 (0.83)	2.46 (0.76)
	Median	2.32	2.40
	Min, max	1.06, 4.96	1.16, 4.77
Absolute change at OL Part A Week 96	n	213	202
	Mean (SD)	0.04 (0.31)	0.04 (0.27)
	Median	0.01	0.01
	Min, max	-1.63, 1.34	-0.51, 1.29

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Ratio of FEV1/FVC (RATIO)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	243	228
	Mean (SD)	0.63 (0.12)	0.63 (0.11)
	Median	0.63	0.62
	Min, max	0.34, 0.90	0.36, 0.96
OL Part A Day 15	n	227	225
	Mean (SD)	0.63 (0.12)	0.63 (0.12)
	Median	0.63	0.63
	Min, max	0.39, 0.93	0.35, 0.96
Absolute change at OL Part A Day 15	n	224	218
	Mean (SD)	0.00 (0.03)	0.00 (0.03)
	Median	0.00	0.00
	Min, max	-0.10, 0.27	-0.08, 0.12
OL Part A Week 4	n	231	216
	Mean (SD)	0.63 (0.12)	0.63 (0.11)
	Median	0.63	0.62
	Min, max	0.37, 1.00	0.33, 0.94
Absolute change at OL Part A Week 4	n	227	209
	Mean (SD)	0.00 (0.04)	0.00 (0.03)
	Median	0.00	0.00
	Min, max	-0.11, 0.29	-0.09, 0.12

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Ratio of FEV1/FVC (RATIO)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 8	n	227	223
	Mean (SD)	0.63 (0.12)	0.63 (0.12)
	Median	0.62	0.63
	Min, max	0.37, 0.92	0.36, 0.98
Absolute change at OL Part A Week 8	n	224	214
	Mean (SD)	0.00 (0.03)	0.00 (0.03)
	Median	0.00	0.00
	Min, max	-0.12, 0.28	-0.09, 0.14
OL Part A Week 16	n	227	214
	Mean (SD)	0.63 (0.12)	0.63 (0.12)
	Median	0.62	0.62
	Min, max	0.36, 1.00	0.37, 0.98
Absolute change at OL Part A Week 16	n	222	206
	Mean (SD)	0.00 (0.04)	0.00 (0.03)
	Median	-0.01	0.00
	Min, max	-0.23, 0.27	-0.09, 0.13
OL Part A Week 24	n	219	214
	Mean (SD)	0.63 (0.12)	0.63 (0.11)
	Median	0.63	0.63
	Min, max	0.38, 0.94	0.30, 0.96
Absolute change at OL Part A Week 24	n	216	207
	Mean (SD)	0.00 (0.04)	0.00 (0.03)
	Median	0.00	0.00
	Min, max	-0.11, 0.26	-0.09, 0.10

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Ratio of FEV1/FVC (RATIO)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 36	n	217	208
	Mean (SD)	0.63 (0.12)	0.63 (0.12)
	Median	0.62	0.63
	Min, max	0.35, 0.95	0.35, 0.94
Absolute change at OL Part A Week 36	n	214	201
	Mean (SD)	0.00 (0.04)	0.00 (0.03)
	Median	0.00	0.00
	Min, max	-0.11, 0.26	-0.11, 0.12
OL Part A Week 48	n	219	212
	Mean (SD)	0.63 (0.12)	0.63 (0.11)
	Median	0.62	0.62
	Min, max	0.36, 0.93	0.32, 0.91
Absolute change at OL Part A Week 48	n	216	204
	Mean (SD)	-0.01 (0.04)	0.00 (0.03)
	Median	-0.01	0.00
	Min, max	-0.12, 0.26	-0.07, 0.14
OL Part A Week 60	n	211	202
	Mean (SD)	0.62 (0.12)	0.63 (0.11)
	Median	0.62	0.62
	Min, max	0.37, 0.91	0.33, 0.95
Absolute change at OL Part A Week 60	n	207	195
	Mean (SD)	-0.01 (0.04)	0.00 (0.03)
	Median	-0.01	0.00
	Min, max	-0.11, 0.19	-0.10, 0.13

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Ratio of FEV1/FVC (RATIO)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 72	n	207	198
	Mean (SD)	0.63 (0.12)	0.62 (0.11)
	Median	0.62	0.62
	Min, max	0.35, 0.91	0.37, 0.91
Absolute change at OL Part A Week 72	n	203	190
	Mean (SD)	-0.01 (0.04)	0.00 (0.03)
	Median	-0.01	0.00
	Min, max	-0.14, 0.27	-0.08, 0.11
OL Part A Week 84	n	204	199
	Mean (SD)	0.63 (0.11)	0.63 (0.12)
	Median	0.62	0.62
	Min, max	0.37, 0.90	0.36, 0.95
Absolute change at OL Part A Week 84	n	200	191
	Mean (SD)	-0.01 (0.04)	0.00 (0.03)
	Median	0.00	0.00
	Min, max	-0.11, 0.26	-0.10, 0.11
OL Part A Week 96	n	204	198
	Mean (SD)	0.63 (0.12)	0.62 (0.11)
	Median	0.63	0.61
	Min, max	0.37, 0.93	0.37, 0.93
Absolute change at OL Part A Week 96	n	201	192
	Mean (SD)	-0.01 (0.05)	0.00 (0.04)
	Median	-0.01	0.00
	Min, max	-0.25, 0.23	-0.15, 0.13

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Forced Vital Capacity (L)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	246	233
	Mean (SD)	3.74 (1.00)	3.86 (0.95)
	Median	3.58	3.91
	Min, max	1.89, 7.31	1.82, 6.94
OL Part A Day 15	n	236	230
	Mean (SD)	3.80 (1.01)	3.90 (0.96)
	Median	3.60	3.87
	Min, max	2.01, 7.04	2.07, 7.12
Absolute change at OL Part A Day 15	n	235	226
	Mean (SD)	0.05 (0.23)	0.05 (0.25)
	Median	0.05	0.04
	Min, max	-0.62, 0.73	-0.65, 1.17
OL Part A Week 4	n	234	217
	Mean (SD)	3.76 (1.02)	3.92 (0.96)
	Median	3.56	3.86
	Min, max	1.82, 7.12	2.01, 7.02
Absolute change at OL Part A Week 4	n	232	214
	Mean (SD)	0.03 (0.23)	0.05 (0.24)
	Median	0.02	0.04
	Min, max	-0.91, 0.69	-0.87, 1.18

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Forced Vital Capacity (L)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 8	n	230	226
	Mean (SD)	3.78 (1.03)	3.92 (0.93)
	Median	3.55	3.84
	Min, max	1.72, 7.22	2.24, 6.96
Absolute change at OL Part A Week 8	n	229	221
	Mean (SD)	0.03 (0.23)	0.04 (0.26)
	Median	0.01	0.00
	Min, max	-0.68, 0.85	-0.60, 1.22
OL Part A Week 16	n	230	216
	Mean (SD)	3.76 (1.01)	3.92 (0.92)
	Median	3.56	3.84
	Min, max	1.48, 6.99	2.12, 6.82
Absolute change at OL Part A Week 16	n	228	211
	Mean (SD)	0.04 (0.27)	0.05 (0.28)
	Median	0.01	0.02
	Min, max	-1.06, 1.25	-0.66, 1.25
OL Part A Week 24	n	223	218
	Mean (SD)	3.79 (1.03)	3.91 (0.96)
	Median	3.62	3.83
	Min, max	1.72, 7.22	2.04, 7.10
Absolute change at OL Part A Week 24	n	222	213
	Mean (SD)	0.08 (0.27)	0.05 (0.29)
	Median	0.04	0.02
	Min, max	-0.59, 1.33	-0.69, 1.36

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Forced Vital Capacity (L)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 36	n	222	213
	Mean (SD)	3.78 (1.02)	3.95 (0.97)
	Median	3.61	3.86
	Min, max	1.39, 6.85	2.07, 7.04
Absolute change at OL Part A Week 36	n	221	209
	Mean (SD)	0.05 (0.34)	0.08 (0.33)
	Median	0.04	0.05
	Min, max	-2.14, 1.48	-0.58, 1.76
OL Part A Week 48	n	221	216
	Mean (SD)	3.77 (1.01)	3.91 (0.96)
	Median	3.58	3.85
	Min, max	1.88, 7.06	1.94, 7.04
Absolute change at OL Part A Week 48	n	220	212
	Mean (SD)	0.05 (0.33)	0.06 (0.30)
	Median	0.00	0.01
	Min, max	-1.27, 1.65	-0.68, 1.52
OL Part A Week 60	n	220	207
	Mean (SD)	3.81 (1.02)	3.93 (0.96)
	Median	3.65	3.81
	Min, max	1.91, 7.02	1.98, 6.93
Absolute change at OL Part A Week 60	n	219	203
	Mean (SD)	0.09 (0.33)	0.09 (0.34)
	Median	0.04	0.05
	Min, max	-0.71, 1.72	-0.54, 1.74

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Forced Vital Capacity (L)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 72	n	210	199
	Mean (SD)	3.80 (1.03)	3.94 (0.97)
	Median	3.67	3.79
	Min, max	1.84, 6.99	2.27, 7.06
Absolute change at OL Part A Week 72	n	209	195
	Mean (SD)	0.08 (0.35)	0.08 (0.30)
	Median	0.02	0.05
	Min, max	-0.65, 1.82	-0.52, 1.31
OL Part A Week 84	n	208	200
	Mean (SD)	3.84 (1.05)	3.95 (0.99)
	Median	3.67	3.80
	Min, max	1.83, 7.00	2.07, 6.94
Absolute change at OL Part A Week 84	n	207	196
	Mean (SD)	0.09 (0.37)	0.11 (0.37)
	Median	0.04	0.04
	Min, max	-0.86, 1.78	-0.76, 2.18
OL Part A Week 96	n	206	198
	Mean (SD)	3.81 (1.03)	3.94 (0.98)
	Median	3.61	3.88
	Min, max	1.74, 6.97	1.98, 7.19
Absolute change at OL Part A Week 96	n	205	195
	Mean (SD)	0.07 (0.38)	0.07 (0.33)
	Median	0.03	0.01
	Min, max	-0.83, 2.08	-0.64, 1.66

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Percent Predicted Forced Expiratory Volume in 1 Second (%)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	245	234
	Mean (SD)	66.3 (15.1)	66.8 (14.5)
	Median	67.5	66.8
	Min, max	36.4, 104.6	38.3, 112.5
OL Part A Day 15	n	229	229
	Mean (SD)	66.8 (15.1)	67.7 (15.1)
	Median	67.7	68.1
	Min, max	36.5, 101.3	35.1, 117.7
Absolute change at OL Part A Day 15	n	227	227
	Mean (SD)	0.4 (5.0)	0.9 (4.4)
	Median	0.0	1.1
	Min, max	-19.8, 27.4	-15.3, 13.7
OL Part A Week 4	n	237	225
	Mean (SD)	66.4 (15.5)	67.4 (14.8)
	Median	66.9	67.8
	Min, max	34.7, 102.5	32.3, 116.8
Absolute change at OL Part A Week 4	n	235	221
	Mean (SD)	0.1 (5.1)	0.9 (4.9)
	Median	-0.2	0.8
	Min, max	-19.1, 30.7	-19.6, 18.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Percent Predicted Forced Expiratory Volume in 1 Second (%)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 8	n	234	226
	Mean (SD)	66.1 (15.1)	67.5 (15.0)
	Median	66.3	68.3
	Min, max	34.5, 100.7	36.2, 117.2
Absolute change at OL Part A Week 8	n	231	223
	Mean (SD)	0.0 (4.9)	0.6 (4.6)
	Median	0.0	0.5
	Min, max	-23.7, 28.5	-9.9, 14.6
OL Part A Week 16	n	232	222
	Mean (SD)	66.6 (15.6)	67.3 (15.0)
	Median	67.7	67.2
	Min, max	25.9, 105.2	36.5, 117.6
Absolute change at OL Part A Week 16	n	229	219
	Mean (SD)	0.1 (5.6)	0.6 (5.1)
	Median	-0.1	0.6
	Min, max	-30.3, 27.6	-17.1, 21.2
OL Part A Week 24	n	230	223
	Mean (SD)	67.0 (15.3)	67.2 (15.0)
	Median	67.2	67.5
	Min, max	36.8, 101.8	28.2, 115.9
Absolute change at OL Part A Week 24	n	228	220
	Mean (SD)	0.8 (5.1)	0.7 (5.2)
	Median	0.2	0.6
	Min, max	-16.0, 24.5	-14.5, 19.3

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Percent Predicted Forced Expiratory Volume in 1 Second (%)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 36	n	223	217
	Mean (SD)	66.7 (16.0)	67.7 (15.2)
	Median	67.7	67.3
	Min, max	19.8, 102.7	35.6, 115.3
Absolute change at OL Part A Week 36	n	221	214
	Mean (SD)	0.3 (5.8)	1.2 (5.3)
	Median	0.8	0.8
	Min, max	-21.6, 22.9	-15.7, 24.9
OL Part A Week 48	n	227	218
	Mean (SD)	66.4 (15.8)	67.2 (15.2)
	Median	67.5	67.1
	Min, max	34.7, 101.8	31.1, 115.2
Absolute change at OL Part A Week 48	n	224	214
	Mean (SD)	0.1 (5.9)	0.7 (4.8)
	Median	0.2	0.5
	Min, max	-25.2, 24.3	-15.0, 13.8
OL Part A Week 60	n	216	209
	Mean (SD)	66.7 (15.5)	68.0 (15.2)
	Median	67.6	68.1
	Min, max	33.8, 104.6	32.5, 114.8
Absolute change at OL Part A Week 60	n	213	206
	Mean (SD)	0.6 (6.0)	1.5 (5.5)
	Median	0.8	1.3
	Min, max	-25.1, 19.9	-22.3, 24.9

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Percent Predicted Forced Expiratory Volume in 1 Second (%)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 72	n	216	209
	Mean (SD)	66.9 (15.9)	67.7 (15.1)
	Median	68.3	67.6
	Min, max	36.4, 105.2	33.5, 115.5
Absolute change at OL Part A Week 72	n	213	206
	Mean (SD)	0.5 (5.8)	1.2 (5.6)
	Median	0.5	1.5
	Min, max	-17.5, 23.7	-25.9, 18.6
OL Part A Week 84	n	217	207
	Mean (SD)	67.3 (15.9)	68.3 (15.4)
	Median	67.6	69.4
	Min, max	34.4, 107.0	31.9, 116.3
Absolute change at OL Part A Week 84	n	214	203
	Mean (SD)	0.8 (6.3)	1.7 (5.6)
	Median	0.7	1.6
	Min, max	-20.7, 26.9	-18.2, 20.9
OL Part A Week 96	n	216	205
	Mean (SD)	67.0 (15.6)	67.6 (14.9)
	Median	68.1	67.2
	Min, max	36.3, 102.8	34.3, 115.2
Absolute change at OL Part A Week 96	n	213	202
	Mean (SD)	0.2 (6.7)	0.8 (5.7)
	Median	0.3	0.9
	Min, max	-43.7, 20.4	-21.8, 21.5

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Percent Predicted Ratio of FEV1/FVC (%)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	243	228
	Mean (SD)	75.7 (12.8)	75.2 (12.0)
	Median	76.3	75.2
	Min, max	40.7, 103.9	44.0, 108.3
OL Part A Day 15	n	227	225
	Mean (SD)	75.6 (13.2)	75.8 (12.7)
	Median	75.6	76.2
	Min, max	47.0, 105.5	43.1, 114.1
Absolute change at OL Part A Day 15	n	224	218
	Mean (SD)	0.0 (4.1)	0.5 (3.5)
	Median	0.0	0.3
	Min, max	-12.3, 31.9	-9.3, 15.0
OL Part A Week 4	n	231	216
	Mean (SD)	75.8 (13.3)	75.4 (12.3)
	Median	75.8	75.6
	Min, max	44.4, 112.2	41.1, 109.7
Absolute change at OL Part A Week 4	n	227	209
	Mean (SD)	0.0 (4.2)	0.3 (3.6)
	Median	-0.1	0.1
	Min, max	-13.2, 34.2	-11.2, 14.3

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Percent Predicted Ratio of FEV1/FVC (%)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 8	n	227	223
	Mean (SD)	75.8 (13.0)	75.5 (12.8)
	Median	76.1	75.7
	Min, max	44.8, 104.1	45.2, 111.0
Absolute change at OL Part A Week 8	n	224	214
	Mean (SD)	0.1 (4.0)	0.3 (3.6)
	Median	-0.1	0.1
	Min, max	-13.7, 32.4	-10.4, 17.4
OL Part A Week 16	n	227	214
	Mean (SD)	75.9 (13.3)	75.5 (12.9)
	Median	75.3	75.5
	Min, max	45.3, 112.0	45.6, 112.3
Absolute change at OL Part A Week 16	n	222	206
	Mean (SD)	-0.1 (4.5)	0.0 (3.9)
	Median	-0.4	-0.1
	Min, max	-25.8, 31.0	-10.3, 15.6
OL Part A Week 24	n	219	214
	Mean (SD)	76.0 (12.9)	76.0 (12.3)
	Median	75.8	75.6
	Min, max	46.8, 105.6	37.2, 111.1
Absolute change at OL Part A Week 24	n	216	207
	Mean (SD)	0.2 (4.3)	0.5 (3.7)
	Median	-0.1	0.2
	Min, max	-12.6, 30.5	-10.7, 12.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Percent Predicted Ratio of FEV1/FVC (%)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 36	n	217	208
	Mean (SD)	75.8 (13.1)	75.5 (12.6)
	Median	75.1	75.9
	Min, max	42.7, 108.4	44.1, 110.0
Absolute change at OL Part A Week 36	n	214	201
	Mean (SD)	0.0 (4.5)	0.4 (3.7)
	Median	-0.2	0.2
	Min, max	-13.4, 30.3	-12.4, 14.9
OL Part A Week 48	n	219	212
	Mean (SD)	75.4 (13.1)	75.3 (12.3)
	Median	75.6	75.0
	Min, max	45.4, 106.2	39.9, 112.7
Absolute change at OL Part A Week 48	n	216	204
	Mean (SD)	-0.4 (4.3)	0.3 (3.6)
	Median	-0.5	0.3
	Min, max	-12.9, 30.2	-8.0, 17.2
OL Part A Week 60	n	211	202
	Mean (SD)	75.3 (13.0)	75.3 (12.5)
	Median	74.9	75.8
	Min, max	46.2, 103.3	41.2, 105.1
Absolute change at OL Part A Week 60	n	207	195
	Mean (SD)	-0.4 (4.4)	0.4 (4.0)
	Median	-0.4	0.2
	Min, max	-12.2, 22.2	-11.2, 16.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Percent Predicted Ratio of FEV1/FVC (%)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 72	n	207	198
	Mean (SD)	75.6 (13.0)	75.4 (12.6)
	Median	76.0	76.0
	Min, max	42.3, 103.4	46.0, 111.3
Absolute change at OL Part A Week 72	n	203	190
	Mean (SD)	-0.4 (4.5)	0.4 (3.6)
	Median	-0.6	0.2
	Min, max	-16.4, 31.7	-8.1, 14.1
OL Part A Week 84	n	204	199
	Mean (SD)	75.9 (12.6)	75.7 (12.7)
	Median	76.3	75.8
	Min, max	45.8, 102.5	44.6, 108.3
Absolute change at OL Part A Week 84	n	200	191
	Mean (SD)	-0.2 (4.5)	0.4 (3.9)
	Median	0.0	0.3
	Min, max	-11.0, 30.6	-11.5, 13.4
OL Part A Week 96	n	204	198
	Mean (SD)	76.1 (13.3)	75.2 (12.6)
	Median	77.1	75.7
	Min, max	44.6, 103.4	45.7, 109.3
Absolute change at OL Part A Week 96	n	201	192
	Mean (SD)	-0.5 (5.4)	0.1 (4.3)
	Median	-0.4	0.1
	Min, max	-28.8, 28.0	-16.5, 16.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Percent Predicted Forced Vital Capacity (%)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	246	233
	Mean (SD)	86.7 (11.9)	88.2 (12.4)
	Median	86.8	87.6
	Min, max	57.3, 119.7	44.4, 122.3
OL Part A Day 15	n	236	230
	Mean (SD)	87.2 (12.0)	88.8 (12.6)
	Median	87.5	88.6
	Min, max	55.2, 119.5	50.6, 122.0
Absolute change at OL Part A Day 15	n	235	226
	Mean (SD)	0.4 (4.7)	0.8 (4.7)
	Median	0.6	1.0
	Min, max	-17.8, 16.9	-15.2, 23.9
OL Part A Week 4	n	234	217
	Mean (SD)	86.8 (12.3)	89.0 (12.5)
	Median	87.4	88.9
	Min, max	57.6, 121.5	49.2, 118.7
Absolute change at OL Part A Week 4	n	232	214
	Mean (SD)	0.2 (4.8)	0.7 (5.2)
	Median	0.4	0.9
	Min, max	-16.7, 20.1	-23.2, 24.2

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Percent Predicted Forced Vital Capacity (%)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 8	n	230	226
	Mean (SD)	86.9 (12.3)	88.8 (12.5)
	Median	87.9	88.3
	Min, max	55.6, 121.6	54.9, 122.3
Absolute change at OL Part A Week 8	n	229	221
	Mean (SD)	0.0 (4.5)	0.4 (4.8)
	Median	0.2	0.3
	Min, max	-23.9, 17.3	-11.3, 22.9
OL Part A Week 16	n	230	216
	Mean (SD)	86.8 (12.6)	88.9 (12.2)
	Median	87.9	87.8
	Min, max	49.5, 118.4	57.4, 120.7
Absolute change at OL Part A Week 16	n	228	211
	Mean (SD)	0.2 (5.6)	0.6 (4.9)
	Median	0.3	0.3
	Min, max	-23.9, 17.5	-10.7, 25.1
OL Part A Week 24	n	223	218
	Mean (SD)	87.5 (12.4)	88.7 (12.7)
	Median	87.6	87.9
	Min, max	52.7, 121.2	52.7, 120.6
Absolute change at OL Part A Week 24	n	222	213
	Mean (SD)	1.0 (5.2)	0.5 (5.2)
	Median	0.6	0.3
	Min, max	-19.6, 19.9	-12.9, 23.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Percent Predicted Forced Vital Capacity (%)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 36	n	222	213
	Mean (SD)	87.1 (13.1)	89.3 (12.7)
	Median	87.5	89.0
	Min, max	27.8, 121.2	55.8, 127.5
Absolute change at OL Part A Week 36	n	221	209
	Mean (SD)	0.5 (6.4)	1.2 (5.5)
	Median	0.8	1.1
	Min, max	-41.9, 22.7	-12.2, 30.3
OL Part A Week 48	n	221	216
	Mean (SD)	86.9 (12.6)	88.7 (12.7)
	Median	86.9	88.4
	Min, max	57.1, 116.9	52.2, 120.1
Absolute change at OL Part A Week 48	n	220	212
	Mean (SD)	0.5 (6.2)	0.7 (4.5)
	Median	0.2	0.4
	Min, max	-36.7, 18.0	-12.5, 23.2
OL Part A Week 60	n	220	207
	Mean (SD)	87.4 (12.4)	89.2 (12.4)
	Median	87.8	88.9
	Min, max	56.2, 121.0	53.3, 121.8
Absolute change at OL Part A Week 60	n	219	203
	Mean (SD)	1.3 (5.9)	1.4 (5.5)
	Median	1.5	1.5
	Min, max	-23.3, 18.8	-14.4, 27.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.1.2a
Summary of Spirometry Assessments and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Percent Predicted Forced Vital Capacity (%)

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 72	n	210	199
	Mean (SD)	87.2 (12.4)	89.5 (12.4)
	Median	87.6	89.3
	Min, max	54.7, 118.0	52.4, 122.2
Absolute change at OL Part A Week 72	n	209	195
	Mean (SD)	1.1 (5.7)	1.6 (5.1)
	Median	1.0	1.1
	Min, max	-19.7, 16.9	-10.2, 24.3
OL Part A Week 84	n	208	200
	Mean (SD)	87.5 (12.8)	89.5 (12.8)
	Median	87.4	89.2
	Min, max	52.7, 120.7	55.9, 126.8
Absolute change at OL Part A Week 84	n	207	196
	Mean (SD)	1.2 (6.0)	1.7 (5.8)
	Median	1.2	1.1
	Min, max	-20.7, 18.2	-14.2, 30.6
OL Part A Week 96	n	206	198
	Mean (SD)	87.1 (12.2)	89.0 (12.5)
	Median	87.4	89.2
	Min, max	52.0, 117.7	55.4, 122.5
Absolute change at OL Part A Week 96	n	205	195
	Mean (SD)	0.7 (6.0)	0.9 (5.4)
	Median	1.2	0.7
	Min, max	-25.4, 14.8	-11.8, 23.9

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.1.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in $ppFEV_1$ (percentage points) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	201	193
Mean (SD)	67.2 (14.6)	67.0 (15.3)
Absolute change at Day 15		
n	189	185
LS mean (SE)	0.4 (0.3)	0.2 (0.3)
95% CI of LS mean	(-0.2, 1.0)	(-0.4, 0.8)
Absolute change at Week 4		
n	186	176
LS mean (SE)	0.4 (0.4)	-0.2 (0.4)
95% CI of LS mean	(-0.3, 1.1)	(-0.9, 0.5)
Absolute change at Week 8		
n	190	181
LS mean (SE)	0.5 (0.4)	-0.4 (0.4)
95% CI of LS mean	(-0.3, 1.2)	(-1.2, 0.3)
Absolute change at Week 16		
n	186	181
LS mean (SE)	0.0 (0.3)	0.6 (0.3)
95% CI of LS mean	(-0.6, 0.7)	(-0.1, 1.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.1.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in ppFEV$_1$ (percentage points) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	187	179
LS mean (SE)	0.6 (0.4)	0.2 (0.4)
95% CI of LS mean	(-0.1, 1.4)	(-0.5, 1.0)
Absolute change at Week 36		
n	188	172
LS mean (SE)	0.6 (0.4)	0.7 (0.4)
95% CI of LS mean	(-0.2, 1.4)	(-0.1, 1.5)
Absolute change at Week 52		
n	183	174
LS mean (SE)	0.3 (0.4)	0.4 (0.4)
95% CI of LS mean	(-0.5, 1.0)	(-0.4, 1.1)
OL Efficacy Period for Part A		
N	170	166
Absolute change at OL Part A Day 15		
n	161	158
LS mean (SE)	0.2 (0.4)	0.7 (0.4)
95% CI of LS mean	(-0.5, 1.0)	(0.0, 1.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.1.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in $ppFEV_1$ (percentage points) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 4		
n	162	154
LS mean (SE)	0.7 (0.4)	0.8 (0.4)
95% CI of LS mean	(-0.1, 1.5)	(0.0, 1.6)
Absolute change at OL Part A Week 8		
n	164	153
LS mean (SE)	0.4 (0.4)	0.8 (0.4)
95% CI of LS mean	(-0.4, 1.3)	(0.0, 1.7)
Absolute change at OL Part A Week 16		
n	160	156
LS mean (SE)	1.0 (0.4)	0.6 (0.4)
95% CI of LS mean	(0.2, 1.8)	(-0.3, 1.4)
Absolute change at OL Part A Week 24		
n	158	153
LS mean (SE)	0.8 (0.4)	0.8 (0.4)
95% CI of LS mean	(0.0, 1.6)	(0.0, 1.6)
Absolute change at OL Part A Week 36		
n	153	151
LS mean (SE)	0.4 (0.5)	1.2 (0.5)
95% CI of LS mean	(-0.5, 1.3)	(0.3, 2.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.1.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in $ppFEV_1$ (percentage points) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 48		
n	155	151
LS mean (SE)	0.2 (0.5)	0.8 (0.5)
95% CI of LS mean	(-0.7, 1.1)	(-0.1, 1.7)
Absolute change at OL Part A Week 60		
n	149	150
LS mean (SE)	0.7 (0.5)	1.2 (0.5)
95% CI of LS mean	(-0.2, 1.6)	(0.3, 2.1)
Absolute change at OL Part A Week 72		
n	151	146
LS mean (SE)	0.8 (0.4)	0.8 (0.4)
95% CI of LS mean	(0.0, 1.6)	(0.0, 1.7)
Absolute change at OL Part A Week 84		
n	146	142
LS mean (SE)	0.9 (0.5)	1.1 (0.5)
95% CI of LS mean	(-0.1, 1.9)	(0.1, 2.2)
Absolute change at OL Part A Week 96		
n	141	141
LS mean (SE)	0.8 (0.5)	0.2 (0.5)
95% CI of LS mean	(-0.3, 1.8)	(-0.9, 1.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.1.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in $ppFEV_1$ (percentage points) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	286	279
Mean (SD)	66.4 (14.9)	67.2 (14.6)
Absolute change at Day 15		
n	261	266
LS mean (SE)	-0.1 (0.2)	0.3 (0.2)
95% CI of LS mean	(-0.6, 0.3)	(-0.2, 0.7)
Absolute change at Week 4		
n	264	267
LS mean (SE)	0.0 (0.2)	0.1 (0.2)
95% CI of LS mean	(-0.5, 0.5)	(-0.4, 0.6)
Absolute change at Week 8		
n	263	263
LS mean (SE)	-0.2 (0.3)	0.1 (0.3)
95% CI of LS mean	(-0.7, 0.3)	(-0.4, 0.7)
Absolute change at Week 16		
n	267	252
LS mean (SE)	-0.1 (0.3)	0.1 (0.3)
95% CI of LS mean	(-0.7, 0.4)	(-0.5, 0.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.1.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in $ppFEV_1$ (percentage points) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	268	257
LS mean (SE)	0.1 (0.3)	0.4 (0.3)
95% CI of LS mean	(-0.4, 0.7)	(-0.2, 0.9)
Absolute change at Week 36		
n	260	254
LS mean (SE)	0.0 (0.3)	0.6 (0.3)
95% CI of LS mean	(-0.6, 0.6)	(0.0, 1.2)
Absolute change at Week 52		
n	263	252
LS mean (SE)	0.0 (0.3)	0.2 (0.3)
95% CI of LS mean	(-0.7, 0.6)	(-0.5, 0.8)
OL Efficacy Period for Part A		
N	248	238
Absolute change at OL Part A Day 15		
n	222	226
LS mean (SE)	0.3 (0.3)	1.0 (0.3)
95% CI of LS mean	(-0.3, 0.9)	(0.4, 1.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.1.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in $ppFEV_1$ (percentage points) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 4		
n	229	220
LS mean (SE)	0.2 (0.3)	0.8 (0.3)
95% CI of LS mean	(-0.5, 0.8)	(0.2, 1.5)
Absolute change at OL Part A Week 8		
n	227	222
LS mean (SE)	0.0 (0.3)	0.7 (0.3)
95% CI of LS mean	(-0.6, 0.6)	(0.1, 1.4)
Absolute change at OL Part A Week 16		
n	224	218
LS mean (SE)	0.2 (0.4)	0.6 (0.4)
95% CI of LS mean	(-0.5, 0.9)	(-0.1, 1.3)
Absolute change at OL Part A Week 24		
n	223	219
LS mean (SE)	0.9 (0.3)	0.6 (0.3)
95% CI of LS mean	(0.3, 1.6)	(-0.1, 1.2)
Absolute change at OL Part A Week 36		
n	216	213
LS mean (SE)	0.6 (0.4)	1.1 (0.4)
95% CI of LS mean	(-0.1, 1.3)	(0.4, 1.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.1.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in $ppFEV_1$ (percentage points) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 48		
n	219	213
LS mean (SE)	0.3 (0.3)	0.7 (0.4)
95% CI of LS mean	(-0.4, 0.9)	(0.0, 1.4)
Absolute change at OL Part A Week 60		
n	208	205
LS mean (SE)	0.8 (0.4)	1.3 (0.4)
95% CI of LS mean	(0.1, 1.5)	(0.6, 2.0)
Absolute change at OL Part A Week 72		
n	208	205
LS mean (SE)	0.7 (0.4)	1.0 (0.4)
95% CI of LS mean	(-0.1, 1.4)	(0.3, 1.8)
Absolute change at OL Part A Week 84		
n	209	202
LS mean (SE)	0.8 (0.4)	1.6 (0.4)
95% CI of LS mean	(0.1, 1.6)	(0.8, 2.3)
Absolute change at OL Part A Week 96		
n	208	201
LS mean (SE)	0.4 (0.4)	0.7 (0.4)
95% CI of LS mean	(-0.4, 1.2)	(0.0, 1.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.2.1.1a
Summary of Sweat Chloride (mmol/L) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	169	165
	Mean (SD)	54.7 (18.6)	53.5 (16.4)
	Median	54.5	52.3
	Min, max	10.0, 113.5	20.5, 104.8
OL Part A Day 15	n	153	154
	Mean (SD)	47.2 (18.4)	45.5 (18.0)
	Median	49.5	43.3
	Min, max	10.0, 103.0	12.0, 98.5
Change at OL Part A Day 15	n	153	153
	Mean (SD)	-8.1 (13.5)	-8.3 (10.3)
	Median	-8.0	-9.0
	Min, max	-63.5, 50.3	-33.5, 19.5
OL Part A Week 4	n	158	157
	Mean (SD)	47.7 (17.8)	47.5 (19.0)
	Median	50.0	47.0
	Min, max	10.0, 104.0	16.0, 107.0
Change at OL Part A Week 4	n	157	156
	Mean (SD)	-6.6 (13.8)	-5.7 (10.8)
	Median	-6.0	-5.4
	Min, max	-49.0, 65.3	-45.0, 20.3

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.

Table 14.2.2.1.1a
Summary of Sweat Chloride (mmol/L) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 16	n	159	155
	Mean (SD)	47.6 (18.9)	46.1 (19.5)
	Median	48.0	43.5
	Min, max	10.0, 116.0	12.0, 107.0
Change at OL Part A Week 16	n	158	154
	Mean (SD)	-7.5 (13.7)	-7.4 (12.3)
	Median	-7.6	-8.4
	Min, max	-49.0, 62.8	-55.0, 46.0
OL Part A Week 24	n	154	156
	Mean (SD)	47.9 (19.6)	46.1 (18.1)
	Median	47.0	44.3
	Min, max	10.0, 111.0	11.0, 98.0
Change at OL Part A Week 24	n	154	155
	Mean (SD)	-6.9 (13.5)	-7.7 (10.6)
	Median	-7.1	-7.5
	Min, max	-42.5, 69.3	-37.8, 31.5
OL Part A Week 48	n	154	151
	Mean (SD)	46.6 (19.6)	45.1 (19.2)
	Median	45.3	44.5
	Min, max	11.5, 106.0	11.0, 107.0
Change at OL Part A Week 48	n	153	150
	Mean (SD)	-7.9 (14.9)	-8.4 (11.6)
	Median	-8.5	-8.4
	Min, max	-44.5, 52.5	-47.0, 32.5

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.

Table 14.2.2.1.1a
Summary of Sweat Chloride (mmol/L) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 72	n	148	145
	Mean (SD)	48.3 (19.9)	44.7 (19.2)
	Median	45.5	43.5
	Min, max	10.0, 108.0	13.0, 112.0
Change at OL Part A Week 72	n	148	145
	Mean (SD)	-6.5 (15.1)	-9.0 (12.7)
	Median	-7.4	-10.0
	Min, max	-52.0, 69.0	-43.0, 46.3
OL Part A Week 96	n	147	140
	Mean (SD)	45.0 (18.9)	45.1 (18.8)
	Median	44.0	43.0
	Min, max	10.0, 111.0	10.0, 101.5
Change at OL Part A Week 96	n	146	140
	Mean (SD)	-9.7 (12.9)	-8.8 (12.4)
	Median	-9.3	-10.5
	Min, max	-54.0, 44.8	-46.5, 28.8

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.

Table 14.2.2.1.2a
Summary of Sweat Chloride (mmol/L) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	242	237
	Mean (SD)	41.6 (17.3)	43.2 (18.4)
	Median	41.5	42.5
	Min, max	10.8, 109.3	10.0, 113.3
OL Part A Day 15	n	224	221
	Mean (SD)	33.9 (16.0)	36.6 (17.9)
	Median	32.5	34.0
	Min, max	10.0, 108.5	10.0, 102.5
Change at OL Part A Day 15	n	221	221
	Mean (SD)	-8.3 (12.1)	-6.6 (11.7)
	Median	-7.3	-6.8
	Min, max	-50.5, 31.8	-40.3, 49.3
OL Part A Week 4	n	231	209
	Mean (SD)	36.6 (16.7)	39.4 (19.6)
	Median	35.0	36.5
	Min, max	10.0, 111.0	10.0, 105.5
Change at OL Part A Week 4	n	227	209
	Mean (SD)	-5.8 (12.2)	-4.4 (13.0)
	Median	-4.5	-4.5
	Min, max	-46.0, 47.0	-45.5, 54.0

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.

Table 14.2.2.1.2a
Summary of Sweat Chloride (mmol/L) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 16	n	231	225
	Mean (SD)	35.2 (18.0)	36.7 (19.0)
	Median	33.0	35.0
	Min, max	10.0, 108.0	10.0, 106.5
Change at OL Part A Week 16	n	227	224
	Mean (SD)	-6.6 (14.0)	-5.9 (12.6)
	Median	-6.8	-6.8
	Min, max	-54.8, 66.3	-49.0, 64.5
OL Part A Week 24	n	231	220
	Mean (SD)	35.9 (18.1)	38.1 (19.1)
	Median	33.5	36.0
	Min, max	10.0, 105.0	10.0, 112.0
Change at OL Part A Week 24	n	228	219
	Mean (SD)	-6.0 (14.7)	-5.3 (13.9)
	Median	-6.3	-5.5
	Min, max	-50.0, 71.8	-67.3, 64.0
OL Part A Week 48	n	223	218
	Mean (SD)	35.7 (18.4)	35.8 (18.4)
	Median	33.0	33.0
	Min, max	10.0, 113.0	10.0, 108.5
Change at OL Part A Week 48	n	222	217
	Mean (SD)	-6.2 (14.0)	-7.3 (12.3)
	Median	-6.4	-7.0
	Min, max	-44.0, 68.5	-39.8, 28.8

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.

Table 14.2.2.1.2a
Summary of Sweat Chloride (mmol/L) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 72	n	218	209
	Mean (SD)	35.3 (18.3)	38.0 (19.4)
	Median	33.3	35.5
	Min, max	10.0, 116.0	10.0, 99.5
Change at OL Part A Week 72	n	213	208
	Mean (SD)	-6.8 (14.4)	-5.5 (12.4)
	Median	-6.0	-5.8
	Min, max	-53.5, 52.8	-44.0, 29.5
OL Part A Week 96	n	214	202
	Mean (SD)	35.5 (20.0)	36.1 (19.1)
	Median	32.5	34.0
	Min, max	10.0, 151.0	10.0, 105.5
Change at OL Part A Week 96	n	210	201
	Mean (SD)	-7.5 (14.2)	-6.8 (12.7)
	Median	-7.4	-6.5
	Min, max	-51.5, 68.0	-54.5, 39.8

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.

Table 14.2.2.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in Sweat Chloride (mmol/L) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	201	194
Mean (SD)	54.3 (18.2)	53.6 (17.0)
Absolute change at Day 15		
n	189	182
LS mean (SE)	1.4 (0.7)	-6.3 (0.7)
95% CI of LS mean	(0.0, 2.7)	(-7.7, -4.9)
Absolute change at Week 4		
n	187	173
LS mean (SE)	1.9 (0.7)	-5.8 (0.8)
95% CI of LS mean	(0.5, 3.4)	(-7.3, -4.3)
Absolute change at Week 16		
n	188	179
LS mean (SE)	0.7 (0.8)	-7.9 (0.8)
95% CI of LS mean	(-0.8, 2.3)	(-9.5, -6.3)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.2.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in Sweat Chloride (mmol/L) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	185	180
LS mean (SE)	0.9 (1.0)	-7.0 (1.0)
95% CI of LS mean	(-1.0, 2.8)	(-9.0, -5.1)
Absolute change at Week 36		
n	186	172
LS mean (SE)	0.9 (0.9)	-6.9 (0.9)
95% CI of LS mean	(-0.9, 2.7)	(-8.8, -5.0)
Absolute change at Week 52		
n	184	167
LS mean (SE)	-0.5 (0.9)	-8.2 (0.9)
95% CI of LS mean	(-2.3, 1.2)	(-10.0, -6.3)
OL Efficacy Period for Part A		
N	170	166
Absolute change at OL Part A Day 15		
n	152	152
LS mean (SE)	-8.1 (0.9)	-8.4 (0.9)
95% CI of LS mean	(-9.9, -6.2)	(-10.2, -6.5)
Absolute change at OL Part A Week 4		
n	156	155
LS mean (SE)	-6.7 (0.9)	-5.9 (0.9)
95% CI of LS mean	(-8.6, -4.9)	(-7.7, -4.0)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.2.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in Sweat Chloride (mmol/L) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 16		
n	157	153
LS mean (SE)	-7.4 (1.0)	-7.7 (1.0)
95% CI of LS mean	(-9.4, -5.5)	(-9.7, -5.7)
Absolute change at OL Part A Week 24		
n	153	154
LS mean (SE)	-6.6 (0.9)	-7.9 (0.9)
95% CI of LS mean	(-8.4, -4.7)	(-9.7, -6.1)
Absolute change at OL Part A Week 48		
n	152	149
LS mean (SE)	-8.0 (1.0)	-8.2 (1.0)
95% CI of LS mean	(-10.1, -6.0)	(-10.3, -6.2)
Absolute change at OL Part A Week 72		
n	147	144
LS mean (SE)	-5.9 (1.1)	-8.8 (1.2)
95% CI of LS mean	(-8.2, -3.7)	(-11.0, -6.5)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.2.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in Sweat Chloride (mmol/L) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 96		
n	145	139
LS mean (SE)	-8.8 (1.0)	-9.3 (1.1)
95% CI of LS mean	(-10.8, -6.7)	(-11.4, -7.2)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.2.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in Sweat Chloride (mmol/L) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	282	282
Mean (SD)	42.1 (17.9)	43.4 (18.5)
Absolute change at Day 15		
n	264	256
LS mean (SE)	-0.4 (0.6)	-4.0 (0.6)
95% CI of LS mean	(-1.6, 0.7)	(-5.2, -2.8)
Absolute change at Week 4		
n	262	255
LS mean (SE)	0.9 (0.7)	-3.9 (0.7)
95% CI of LS mean	(-0.4, 2.2)	(-5.3, -2.6)
Absolute change at Week 16		
n	269	255
LS mean (SE)	-2.4 (0.7)	-5.7 (0.8)
95% CI of LS mean	(-3.8, -0.9)	(-7.2, -4.2)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.2.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in Sweat Chloride (mmol/L) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	258	258
LS mean (SE)	-2.2 (0.8)	-4.4 (0.9)
95% CI of LS mean	(-3.8, -0.5)	(-6.0, -2.7)
Absolute change at Week 36		
n	266	249
LS mean (SE)	-2.1 (0.8)	-5.4 (0.9)
95% CI of LS mean	(-3.7, -0.4)	(-7.1, -3.7)
Absolute change at Week 52		
n	263	249
LS mean (SE)	-2.2 (0.9)	-4.4 (0.9)
95% CI of LS mean	(-3.9, -0.5)	(-6.2, -2.6)
OL Efficacy Period for Part A		
N	248	238
Absolute change at OL Part A Day 15		
n	218	217
LS mean (SE)	-8.4 (0.7)	-6.6 (0.7)
95% CI of LS mean	(-9.8, -7.0)	(-8.0, -5.1)
Absolute change at OL Part A Week 4		
n	225	205
LS mean (SE)	-5.8 (0.8)	-4.4 (0.8)
95% CI of LS mean	(-7.3, -4.3)	(-5.9, -2.8)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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Table 14.2.2.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in Sweat Chloride (mmol/L) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 16		
n	224	220
LS mean (SE)	-7.0 (0.8)	-5.9 (0.8)
95% CI of LS mean	(-8.7, -5.4)	(-7.6, -4.2)
Absolute change at OL Part A Week 24		
n	225	215
LS mean (SE)	-6.4 (0.9)	-5.1 (0.9)
95% CI of LS mean	(-8.2, -4.7)	(-6.9, -3.3)
Absolute change at OL Part A Week 48		
n	219	213
LS mean (SE)	-6.3 (0.8)	-7.0 (0.8)
95% CI of LS mean	(-8.0, -4.7)	(-8.7, -5.4)
Absolute change at OL Part A Week 72		
n	210	204
LS mean (SE)	-6.9 (0.8)	-5.1 (0.9)
95% CI of LS mean	(-8.6, -5.3)	(-6.8, -3.4)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.2.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in Sweat Chloride (mmol/L) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 96		
n	207	197
LS mean (SE)	-7.4 (0.9)	-6.6 (0.9)
95% CI of LS mean	(-9.1, -5.7)	(-8.4, -4.9)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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Table 14.2.3.1.1a
Summary of Pulmonary Exacerbations During the Cumulative Efficacy Period for Part A
Cumulative Efficacy Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 196	Any VNZ/TEZ/D-IVA N = 366
Total number of days (years) in the Cumulative Efficacy Period for Part A	107380 (319.6)	174891 (520.5)	282271 (840.1)
Pulmonary Exacerbations			
Number of subjects with events, n (%)	58 (34.1)	83 (42.3)	141 (38.5)
Total number of events	104	180	284
Observed event rate per year	0.33	0.35	0.34

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms
- Cumulative Efficacy Period for Part A includes the time from the first dose date of VNZ/TEZ/D-IVA in Study 102 (for subjects randomized to VNZ/TEZ/D-IVA in Study 102) or in the OL study (for subjects not randomized to VNZ/TEZ/D-IVA in Study 102) until the last efficacy assessment in Part A of the OL study. For subjects who did not enroll in the OL study and were randomized to VNZ/TEZ/D-IVA in Study 102, this is the same as the PEx analysis period defined in the Study 102 SAP.
- Total number of days = sum of the individual duration (actual number of days) in the Cumulative Efficacy Period for Part A across all subjects in the analysis set. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days in the Cumulative Efficacy Period for Part A

Zusatzanalysen zur Studie VX20-121-104

Table 14.2.3.1.2a
Summary of Pulmonary Exacerbations During the Cumulative Efficacy Period for Part A
Cumulative Efficacy Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 284	Any VNZ/TEZ/D-IVA N = 532
Total number of days (years) in the Cumulative Efficacy Period for Part A	156837 (466.8)	249311 (742.0)	406148 (1208.8)
Pulmonary Exacerbations			
Number of subjects with events, n (%)	79 (31.9)	101 (35.6)	180 (33.8)
Total number of events	123	186	309
Observed event rate per year	0.26	0.25	0.26

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms
- Cumulative Efficacy Period for Part A includes the time from the first dose date of VNZ/TEZ/D-IVA in Study 103 (for subjects randomized to VNZ/TEZ/D-IVA in Study 103) or in the OL study (for subjects not randomized to VNZ/TEZ/D-IVA in Study 103) until the last efficacy assessment in Part A of the OL study. For subjects who did not enroll in the OL study and were randomized to VNZ/TEZ/D-IVA in Study 103, this is the same as the PEx analysis period defined in the Study 103 SAP.
- Total number of days = sum of the individual duration (actual number of days) in the Cumulative Efficacy Period for Part A across all subjects in the analysis set. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days in the Cumulative Efficacy Period for Part A

Zusatzanalysen zur Studie VX20-121-104

Table 14.2.3.2.1a
Summary of Pulmonary Exacerbations by Subcategory During the Cumulative Efficacy Period for Part A
Cumulative Efficacy Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 196	Any VNZ/TEZ/D-IVA N = 366
Total number of days (years) in the Cumulative Efficacy Period for Part A	107380 (319.6)	174891 (520.5)	282271 (840.1)
PEx requiring hospitalization			
Number of subjects with events, n (%)	16 (9.4)	17 (8.7)	33 (9.0)
Total number of events	21	24	45
Observed event rate per year	0.07	0.05	0.05
PEx requiring IV antibiotic therapy			
Number of subjects with events, n (%)	23 (13.5)	24 (12.2)	47 (12.8)
Total number of events	35	35	70
Observed event rate per year	0.11	0.07	0.08
PEx requiring hospitalization or IV antibiotic therapy			
Number of subjects with events, n (%)	23 (13.5)	24 (12.2)	47 (12.8)
Total number of events	35	36	71
Observed event rate per year	0.11	0.07	0.08

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms
- Cumulative Efficacy Period for Part A includes the time from the first dose date of VNZ/TEZ/D-IVA in Study 102 (for subjects randomized to VNZ/TEZ/D-IVA in Study 102) or in the OL study (for subjects not randomized to VNZ/TEZ/D-IVA in Study 102) until the last efficacy assessment in Part A of the OL study. For subjects who did not enroll in the OL study and were randomized to VNZ/TEZ/D-IVA in Study 102, this is the same as the PEx analysis period defined in the Study 102 SAP.
- Total number of days = sum of the individual duration (actual number of days) in the Cumulative Efficacy Period for Part A across all subjects in the analysis set. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days in the Cumulative Efficacy Period for Part A

Zusatzanalysen zur Studie VX20-121-104

Table 14.2.3.2.2a
Summary of Pulmonary Exacerbations by Subcategory During the Cumulative Efficacy Period for Part A
Cumulative Efficacy Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 284	Any VNZ/TEZ/D-IVA N = 532
Total number of days (years) in the Cumulative Efficacy Period for Part A	156837 (466.8)	249311 (742.0)	406148 (1208.8)
PEx requiring hospitalization			
Number of subjects with events, n (%)	16 (6.5)	25 (8.8)	41 (7.7)
Total number of events	20	38	58
Observed event rate per year	0.04	0.05	0.05
PEx requiring IV antibiotic therapy			
Number of subjects with events, n (%)	19 (7.7)	30 (10.6)	49 (9.2)
Total number of events	23	48	71
Observed event rate per year	0.05	0.06	0.06
PEx requiring hospitalization or IV antibiotic therapy			
Number of subjects with events, n (%)	19 (7.7)	31 (10.9)	50 (9.4)
Total number of events	23	53	76
Observed event rate per year	0.05	0.07	0.06

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms
- Cumulative Efficacy Period for Part A includes the time from the first dose date of VNZ/TEZ/D-IVA in Study 103 (for subjects randomized to VNZ/TEZ/D-IVA in Study 103) or in the OL study (for subjects not randomized to VNZ/TEZ/D-IVA in Study 103) until the last efficacy assessment in Part A of the OL study. For subjects who did not enroll in the OL study and were randomized to VNZ/TEZ/D-IVA in Study 103, this is the same as the PEx analysis period defined in the Study 103 SAP.
- Total number of days = sum of the individual duration (actual number of days) in the Cumulative Efficacy Period for Part A across all subjects in the analysis set. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days in the Cumulative Efficacy Period for Part A

Table 14.2.4a
Proportion of Subjects with Sweat Chloride <60 mmol/L at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Pooled Full Analysis Set and OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 or 121-103	VNZ/TEZ/D-IVA in 121-102 or 121-103
Parent Study Efficacy Period		
N	491	480
Parent study baseline		
N1	483	476
n	358	361
Proportion, n/N1 (%)	74.1	75.8
95% CI for the proportion	(70.0, 78.0)	(71.7, 79.6)
Day 15		
N1	460	448
n	343	363
Proportion, n/N1 (%)	74.6	81.0
95% CI for the proportion	(70.3, 78.5)	(77.1, 84.6)
Week 4		
N1	457	438
n	324	360
Proportion, n/N1 (%)	70.9	82.2
95% CI for the proportion	(66.5, 75.0)	(78.3, 85.7)
Week 16		
N1	464	443
n	360	382
Proportion, n/N1 (%)	77.6	86.2
95% CI for the proportion	(73.5, 81.3)	(82.7, 89.3)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1: number of subjects with non-missing SwCl at the given visit
- n: number of subjects at a given visit with SwCl <60 mmol/L
- 95% CI is based on the Clopper-Pearson method.

Table 14.2.4a
Proportion of Subjects with Sweat Chloride <60 mmol/L at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Pooled Full Analysis Set and OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 or 121-103	VNZ/TEZ/D-IVA in 121-102 or 121-103
Week 24		
N1	450	447
n	343	372
Proportion, n/N1 (%)	76.2	83.2
95% CI for the proportion	(72.0, 80.1)	(79.4, 86.6)
Week 36		
N1	460	430
n	342	358
Proportion, n/N1 (%)	74.3	83.3
95% CI for the proportion	(70.1, 78.3)	(79.4, 86.7)
Week 52		
N1	455	425
n	351	355
Proportion, n/N1 (%)	77.1	83.5
95% CI for the proportion	(73.0, 80.9)	(79.7, 86.9)
OL Efficacy Period for Part A		
N	418	404
OL Part A Day 15		
N1	377	375
n	330	318
Proportion, n/N1 (%)	87.5	84.8
95% CI for the proportion	(83.8, 90.7)	(80.8, 88.3)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1: number of subjects with non-missing SwCl at the given visit
- n: number of subjects at a given visit with SwCl <60 mmol/L
- 95% CI is based on the Clopper-Pearson method.

Table 14.2.4a
Proportion of Subjects with Sweat Chloride <60 mmol/L at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Pooled Full Analysis Set and OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 or 121-103	VNZ/TEZ/D-IVA in 121-102 or 121-103
OL Part A Week 4		
N1	389	366
n	332	295
Proportion, n/N1 (%)	85.3	80.6
95% CI for the proportion	(81.4, 88.7)	(76.2, 84.5)
OL Part A Week 16		
N1	390	380
n	329	318
Proportion, n/N1 (%)	84.4	83.7
95% CI for the proportion	(80.4, 87.8)	(79.6, 87.3)
OL Part A Week 24		
N1	385	376
n	321	322
Proportion, n/N1 (%)	83.4	85.6
95% CI for the proportion	(79.3, 87.0)	(81.7, 89.0)
OL Part A Week 48		
N1	377	369
n	322	311
Proportion, n/N1 (%)	85.4	84.3
95% CI for the proportion	(81.4, 88.8)	(80.2, 87.8)
OL Part A Week 72		
N1	366	354
n	314	303
Proportion, n/N1 (%)	85.8	85.6
95% CI for the proportion	(81.8, 89.2)	(81.5, 89.1)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1: number of subjects with non-missing SwCl at the given visit
- n: number of subjects at a given visit with SwCl <60 mmol/L
- 95% CI is based on the Clopper-Pearson method.

Table 14.2.4a
Proportion of Subjects with Sweat Chloride <60 mmol/L at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Pooled Full Analysis Set and OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 or 121-103	VNZ/TEZ/D-IVA in 121-102 or 121-103
OL Part A Week 96		
N1	361	342
n	313	291
Proportion, n/N1 (%)	86.7	85.1
95% CI for the proportion	(82.8, 90.0)	(80.9, 88.7)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1: number of subjects with non-missing SwCl at the given visit
- n: number of subjects at a given visit with SwCl <60 mmol/L
- 95% CI is based on the Clopper-Pearson method.

Table 14.2.5a
Proportion of Subjects with Sweat Chloride <30 mmol/L at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Pooled Full Analysis Set and OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 or 121-103	VNZ/TEZ/D-IVA in 121-102 or 121-103
Parent Study Efficacy Period		
N	491	480
Parent study baseline		
N1	483	476
n	99	89
Proportion, n/N1 (%)	20.5	18.7
95% CI for the proportion	(17.0, 24.4)	(15.3, 22.5)
Day 15		
N1	460	448
n	87	119
Proportion, n/N1 (%)	18.9	26.6
95% CI for the proportion	(15.4, 22.8)	(22.5, 30.9)
Week 4		
N1	457	438
n	78	118
Proportion, n/N1 (%)	17.1	26.9
95% CI for the proportion	(13.7, 20.8)	(22.8, 31.4)
Week 16		
N1	464	443
n	101	141
Proportion, n/N1 (%)	21.8	31.8
95% CI for the proportion	(18.1, 25.8)	(27.5, 36.4)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1: number of subjects with non-missing SwCl at the given visit
- n: number of subjects at a given visit with SwCl <30 mmol/L
- 95% CI is based on the Clopper-Pearson method.

Table 14.2.5a
Proportion of Subjects with Sweat Chloride <30 mmol/L at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Pooled Full Analysis Set and OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 or 121-103	VNZ/TEZ/D-IVA in 121-102 or 121-103
Week 24		
N1	450	447
n	101	130
Proportion, n/N1 (%)	22.4	29.1
95% CI for the proportion	(18.7, 26.6)	(24.9, 33.5)
Week 36		
N1	460	430
n	110	138
Proportion, n/N1 (%)	23.9	32.1
95% CI for the proportion	(20.1, 28.1)	(27.7, 36.7)
Week 52		
N1	455	425
n	118	141
Proportion, n/N1 (%)	25.9	33.2
95% CI for the proportion	(22.0, 30.2)	(28.7, 37.9)
OL Efficacy Period for Part A		
N	418	404
OL Part A Day 15		
N1	377	375
n	127	121
Proportion, n/N1 (%)	33.7	32.3
95% CI for the proportion	(28.9, 38.7)	(27.6, 37.3)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1: number of subjects with non-missing SwCl at the given visit
- n: number of subjects at a given visit with SwCl <30 mmol/L
- 95% CI is based on the Clopper-Pearson method.

Table 14.2.5a
Proportion of Subjects with Sweat Chloride <30 mmol/L at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Pooled Full Analysis Set and OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 or 121-103	VNZ/TEZ/D-IVA in 121-102 or 121-103
OL Part A Week 4		
N1	389	366
n	119	113
Proportion, n/N1 (%)	30.6	30.9
95% CI for the proportion	(26.0, 35.4)	(26.2, 35.9)
OL Part A Week 16		
N1	390	380
n	122	124
Proportion, n/N1 (%)	31.3	32.6
95% CI for the proportion	(26.7, 36.1)	(27.9, 37.6)
OL Part A Week 24		
N1	385	376
n	124	111
Proportion, n/N1 (%)	32.2	29.5
95% CI for the proportion	(27.6, 37.1)	(25.0, 34.4)
OL Part A Week 48		
N1	377	369
n	117	128
Proportion, n/N1 (%)	31.0	34.7
95% CI for the proportion	(26.4, 36.0)	(29.8, 39.8)
OL Part A Week 72		
N1	366	354
n	113	116
Proportion, n/N1 (%)	30.9	32.8
95% CI for the proportion	(26.2, 35.9)	(27.9, 37.9)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1: number of subjects with non-missing SwCl at the given visit
- n: number of subjects at a given visit with SwCl <30 mmol/L
- 95% CI is based on the Clopper-Pearson method.

Table 14.2.5a
Proportion of Subjects with Sweat Chloride <30 mmol/L at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Pooled Full Analysis Set and OL Full Analysis Set

	ELX/TEZ/IVA in 121-102 or 121-103	VNZ/TEZ/D-IVA in 121-102 or 121-103
OL Part A Week 96		
N1	361	342
n	125	116
Proportion, n/N1 (%)	34.6	33.9
95% CI for the proportion	(29.7, 39.8)	(28.9, 39.2)

- Parent study baseline is defined as the average of the two most recent pre-dose, non-missing values on or after the parent study Day -14 visit, including unscheduled visits. If only 1 non-missing value is available during this interval, the available value is considered as baseline.
- N1: number of subjects with non-missing SwCl at the given visit
- n: number of subjects at a given visit with SwCl <30 mmol/L
- 95% CI is based on the Clopper-Pearson method.

Table 14.2.6.1.1a
Summary of CFQ-R Respiratory Domain Score and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	166	164
	Mean (SD)	82.8 (15.3)	85.7 (14.9)
	Median	83.3	88.9
	Min, max	22.2, 100.0	27.8, 100.0
OL Part A Week 8	n	170	166
	Mean (SD)	83.7 (15.9)	87.5 (14.2)
	Median	88.9	88.9
	Min, max	27.8, 100.0	38.9, 100.0
Change at OL Part A Week 8	n	166	164
	Mean (SD)	0.9 (16.1)	1.7 (16.4)
	Median	0.0	0.0
	Min, max	-55.6, 50.0	-50.0, 72.2
OL Part A Week 16	n	169	163
	Mean (SD)	83.4 (16.6)	86.2 (17.0)
	Median	88.9	88.9
	Min, max	11.1, 100.0	0.0, 100.0
Change at OL Part A Week 16	n	165	162
	Mean (SD)	0.8 (15.8)	0.7 (18.7)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-100.0, 72.2

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.1.1a
Summary of CFQ-R Respiratory Domain Score and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 24	n	166	161
	Mean (SD)	85.0 (16.3)	87.7 (13.4)
	Median	88.9	88.9
	Min, max	16.7, 100.0	33.3, 100.0
Change at OL Part A Week 24	n	162	160
	Mean (SD)	2.1 (15.6)	2.2 (15.5)
	Median	0.0	0.0
	Min, max	-61.1, 61.1	-44.4, 66.7
OL Part A Week 48	n	159	160
	Mean (SD)	85.6 (16.1)	86.4 (15.5)
	Median	88.9	88.9
	Min, max	27.8, 100.0	16.7, 100.0
Change at OL Part A Week 48	n	155	159
	Mean (SD)	2.9 (14.8)	0.7 (16.2)
	Median	0.0	0.0
	Min, max	-50.0, 38.9	-66.7, 66.7
OL Part A Week 96	n	150	149
	Mean (SD)	82.8 (18.6)	85.2 (16.2)
	Median	88.9	88.9
	Min, max	16.7, 100.0	22.2, 100.0
Change at OL Part A Week 96	n	147	149
	Mean (SD)	0.1 (17.9)	-0.2 (16.3)
	Median	0.0	0.0
	Min, max	-66.7, 50.0	-61.1, 72.2

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.1.2a
Summary of CFQ-R Respiratory Domain Score and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	243	235
	Mean (SD)	85.5 (13.5)	85.8 (13.6)
	Median	88.9	88.9
	Min, max	27.8, 100.0	33.3, 100.0
OL Part A Week 8	n	247	237
	Mean (SD)	86.6 (14.4)	86.7 (14.5)
	Median	88.9	88.9
	Min, max	33.3, 100.0	16.7, 100.0
Change at OL Part A Week 8	n	242	234
	Mean (SD)	1.2 (14.9)	0.8 (13.8)
	Median	0.0	0.0
	Min, max	-66.7, 50.0	-55.6, 50.0
OL Part A Week 16	n	241	231
	Mean (SD)	85.2 (15.1)	86.2 (16.5)
	Median	88.9	94.4
	Min, max	27.8, 100.0	27.8, 100.0
Change at OL Part A Week 16	n	237	228
	Mean (SD)	-0.2 (15.4)	0.5 (15.2)
	Median	0.0	0.0
	Min, max	-66.7, 55.6	-61.1, 44.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.1.2a
Summary of CFQ-R Respiratory Domain Score and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 24	n	241	229
	Mean (SD)	84.3 (17.1)	86.6 (15.5)
	Median	88.9	88.9
	Min, max	16.7, 100.0	11.1, 100.0
Change at OL Part A Week 24	n	237	226
	Mean (SD)	-0.9 (17.2)	1.0 (14.5)
	Median	0.0	0.0
	Min, max	-72.2, 61.1	-61.1, 44.4
OL Part A Week 48	n	232	221
	Mean (SD)	86.2 (15.4)	87.3 (14.2)
	Median	88.9	88.9
	Min, max	16.7, 100.0	16.7, 100.0
Change at OL Part A Week 48	n	228	218
	Mean (SD)	0.5 (15.7)	1.5 (13.3)
	Median	0.0	0.0
	Min, max	-61.1, 58.3	-61.1, 44.4
OL Part A Week 96	n	226	212
	Mean (SD)	87.2 (15.2)	87.7 (17.2)
	Median	88.9	94.4
	Min, max	16.7, 100.0	0.0, 100.0
Change at OL Part A Week 96	n	222	209
	Mean (SD)	1.5 (16.4)	1.7 (14.8)
	Median	0.0	0.0
	Min, max	-83.3, 50.0	-94.4, 50.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Respiratory Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	197	192
Mean (SD)	82.9 (15.7)	85.8 (14.7)
Absolute change at Week 8		
n	192	186
LS mean (SE)	-2.2 (1.2)	-0.8 (1.2)
95% CI of LS mean	(-4.5, 0.2)	(-3.3, 1.6)
Absolute change at Week 16		
n	192	186
LS mean (SE)	-2.2 (1.2)	0.8 (1.2)
95% CI of LS mean	(-4.5, 0.2)	(-1.6, 3.2)
Absolute change at Week 24		
n	192	184
LS mean (SE)	-1.2 (1.2)	0.3 (1.3)
95% CI of LS mean	(-3.7, 1.2)	(-2.2, 2.8)
Absolute change at Week 52		
n	186	177
LS mean (SE)	-1.4 (1.1)	1.3 (1.1)
95% CI of LS mean	(-3.5, 0.8)	(-0.9, 3.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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Table 14.2.6.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Respiratory Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
OL Efficacy Period for Part A		
N	170	166
Absolute change at OL Part A Week 8		
n	164	162
LS mean (SE)	0.9 (1.3)	1.8 (1.3)
95% CI of LS mean	(-1.6, 3.4)	(-0.7, 4.4)
Absolute change at OL Part A Week 16		
n	163	160
LS mean (SE)	0.6 (1.4)	0.8 (1.4)
95% CI of LS mean	(-2.1, 3.2)	(-1.9, 3.5)
Absolute change at OL Part A Week 24		
n	160	158
LS mean (SE)	2.0 (1.2)	2.3 (1.2)
95% CI of LS mean	(-0.4, 4.4)	(-0.1, 4.7)
Absolute change at OL Part A Week 48		
n	153	157
LS mean (SE)	2.7 (1.3)	0.5 (1.2)
95% CI of LS mean	(0.2, 5.1)	(-1.9, 3.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Respiratory Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 96		
n	145	148
LS mean (SE)	-0.6 (1.4)	-0.5 (1.4)
95% CI of LS mean	(-3.4, 2.2)	(-3.3, 2.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Respiratory Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-104

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	282	280
Mean (SD)	85.6 (13.2)	85.7 (13.2)
Absolute change at Week 8		
n	270	271
LS mean (SE)	-0.5 (1.0)	-1.2 (1.0)
95% CI of LS mean	(-2.5, 1.4)	(-3.1, 0.8)
Absolute change at Week 16		
n	265	265
LS mean (SE)	-0.4 (1.0)	-0.6 (1.0)
95% CI of LS mean	(-2.3, 1.5)	(-2.5, 1.3)
Absolute change at Week 24		
n	267	262
LS mean (SE)	-1.9 (0.9)	-1.8 (0.9)
95% CI of LS mean	(-3.7, -0.2)	(-3.6, 0.0)
Absolute change at Week 52		
n	262	254
LS mean (SE)	-0.7 (1.0)	1.4 (1.0)
95% CI of LS mean	(-2.6, 1.2)	(-0.5, 3.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Respiratory Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
OL Efficacy Period for Part A		
N	248	238
Absolute change at OL Part A Week 8		
n	233	229
LS mean (SE)	1.1 (0.9)	0.7 (1.0)
95% CI of LS mean	(-0.8, 2.9)	(-1.1, 2.6)
Absolute change at OL Part A Week 16		
n	228	223
LS mean (SE)	-0.4 (1.0)	0.2 (1.0)
95% CI of LS mean	(-2.4, 1.6)	(-1.8, 2.2)
Absolute change at OL Part A Week 24		
n	228	221
LS mean (SE)	-1.2 (1.1)	0.7 (1.1)
95% CI of LS mean	(-3.3, 0.9)	(-1.5, 2.8)
Absolute change at OL Part A Week 48		
n	219	213
LS mean (SE)	0.1 (1.0)	1.1 (1.0)
95% CI of LS mean	(-1.8, 2.1)	(-0.9, 3.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Respiratory Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 96		
n	213	204
LS mean (SE)	1.3 (1.1)	1.4 (1.1)
95% CI of LS mean	(-0.8, 3.4)	(-0.8, 3.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Physical

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	166	164
	Mean (SD)	82.3 (18.8)	82.9 (19.7)
	Median	87.5	91.7
	Min, max	20.8, 100.0	4.2, 100.0
OL Part A Week 8	n	170	166
	Mean (SD)	84.4 (18.5)	84.7 (18.6)
	Median	91.7	91.7
	Min, max	16.7, 100.0	12.5, 100.0
Change at OL Part A Week 8	n	166	164
	Mean (SD)	2.0 (13.8)	1.9 (15.2)
	Median	0.0	0.0
	Min, max	-45.8, 62.5	-74.4, 66.7
OL Part A Week 16	n	169	163
	Mean (SD)	82.9 (18.7)	84.0 (19.7)
	Median	87.5	91.7
	Min, max	20.8, 100.0	8.3, 100.0
Change at OL Part A Week 16	n	165	162
	Mean (SD)	0.4 (14.7)	1.4 (14.3)
	Median	0.0	0.0
	Min, max	-62.5, 62.5	-58.3, 50.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Physical

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 24	n	166	161
	Mean (SD)	84.5 (19.8)	83.8 (19.1)
	Median	91.7	91.7
	Min, max	16.7, 100.0	16.7, 100.0
Change at OL Part A Week 24	n	162	160
	Mean (SD)	1.8 (15.4)	1.3 (13.3)
	Median	0.0	0.0
	Min, max	-62.5, 62.5	-54.2, 45.8
OL Part A Week 48	n	159	160
	Mean (SD)	84.6 (19.6)	85.8 (17.2)
	Median	91.7	91.7
	Min, max	16.7, 100.0	20.8, 100.0
Change at OL Part A Week 48	n	155	159
	Mean (SD)	1.6 (15.5)	2.9 (14.6)
	Median	0.0	0.0
	Min, max	-54.2, 58.3	-70.8, 54.2

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Physical

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 96	n	150	150
	Mean (SD)	83.5 (21.5)	84.7 (18.9)
	Median	93.8	91.7
	Min, max	0.0, 100.0	4.2, 100.0
Change at OL Part A Week 96	n	147	150
	Mean (SD)	0.4 (19.1)	2.5 (13.1)
	Median	0.0	0.0
	Min, max	-91.7, 58.3	-41.7, 41.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Vitality

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	159	160
	Mean (SD)	66.8 (17.8)	69.6 (20.8)
	Median	66.7	75.0
	Min, max	16.7, 100.0	0.0, 100.0
OL Part A Week 8	n	165	164
	Mean (SD)	65.9 (19.9)	68.6 (19.6)
	Median	66.7	66.7
	Min, max	25.0, 100.0	8.3, 100.0
Change at OL Part A Week 8	n	158	160
	Mean (SD)	-1.6 (15.1)	-0.9 (18.2)
	Median	0.0	0.0
	Min, max	-50.0, 50.0	-50.0, 58.3
OL Part A Week 16	n	165	161
	Mean (SD)	65.0 (20.7)	67.5 (19.7)
	Median	66.7	66.7
	Min, max	0.0, 100.0	8.3, 100.0
Change at OL Part A Week 16	n	158	158
	Mean (SD)	-1.9 (15.9)	-2.3 (19.3)
	Median	0.0	0.0
	Min, max	-66.7, 33.3	-58.3, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Vitality

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 24	n	163	159
	Mean (SD)	65.6 (21.6)	66.7 (20.5)
	Median	66.7	66.7
	Min, max	8.3, 100.0	16.7, 100.0
Change at OL Part A Week 24	n	155	156
	Mean (SD)	-1.9 (17.7)	-2.6 (18.7)
	Median	0.0	0.0
	Min, max	-50.0, 33.3	-50.0, 50.0
OL Part A Week 48	n	158	157
	Mean (SD)	66.0 (19.7)	67.5 (20.9)
	Median	66.7	66.7
	Min, max	25.0, 100.0	8.3, 100.0
Change at OL Part A Week 48	n	149	155
	Mean (SD)	-2.2 (15.5)	-2.1 (18.2)
	Median	0.0	0.0
	Min, max	-50.0, 41.7	-58.3, 58.3

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Vitality

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 96	n	150	150
	Mean (SD)	65.0 (20.8)	67.7 (21.6)
	Median	66.7	66.7
	Min, max	16.7, 100.0	0.0, 100.0
Change at OL Part A Week 96	n	140	146
	Mean (SD)	-3.2 (18.5)	-0.7 (17.9)
	Median	0.0	0.0
	Min, max	-58.3, 33.3	-50.0, 58.3

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Emotion

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	166	164
	Mean (SD)	80.8 (18.6)	81.6 (18.0)
	Median	86.7	86.7
	Min, max	6.7, 100.0	20.0, 100.0
OL Part A Week 8	n	170	166
	Mean (SD)	80.8 (18.1)	83.6 (15.2)
	Median	86.7	86.7
	Min, max	6.7, 100.0	40.0, 100.0
Change at OL Part A Week 8	n	166	164
	Mean (SD)	-0.4 (13.3)	2.1 (14.5)
	Median	0.0	0.0
	Min, max	-53.3, 46.7	-40.0, 60.0
OL Part A Week 16	n	169	163
	Mean (SD)	80.1 (19.3)	83.0 (15.9)
	Median	86.7	86.7
	Min, max	0.0, 100.0	20.0, 100.0
Change at OL Part A Week 16	n	165	162
	Mean (SD)	-1.1 (14.3)	1.4 (12.6)
	Median	0.0	0.0
	Min, max	-73.3, 33.3	-33.3, 51.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Emotion

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 24	n	166	161
	Mean (SD)	81.3 (19.0)	83.7 (16.4)
	Median	86.7	86.7
	Min, max	6.7, 100.0	6.7, 100.0
Change at OL Part A Week 24	n	162	160
	Mean (SD)	0.2 (14.9)	2.1 (13.8)
	Median	0.0	0.0
	Min, max	-53.3, 50.0	-33.3, 60.0
OL Part A Week 48	n	159	160
	Mean (SD)	80.7 (18.6)	84.0 (14.4)
	Median	86.7	86.7
	Min, max	6.7, 100.0	6.7, 100.0
Change at OL Part A Week 48	n	155	159
	Mean (SD)	-1.4 (14.0)	2.0 (15.3)
	Median	0.0	0.0
	Min, max	-53.3, 33.3	-40.0, 73.3

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Emotion

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 96	n	150	150
	Mean (SD)	81.1 (18.0)	82.7 (16.4)
	Median	83.3	86.7
	Min, max	6.7, 100.0	20.0, 100.0
Change at OL Part A Week 96	n	147	150
	Mean (SD)	-0.3 (14.3)	1.0 (14.3)
	Median	0.0	0.0
	Min, max	-46.7, 40.0	-53.3, 60.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Body

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	166	164
	Mean (SD)	76.4 (22.0)	78.3 (22.4)
	Median	77.8	88.9
	Min, max	11.1, 100.0	0.0, 100.0
OL Part A Week 8	n	170	166
	Mean (SD)	78.8 (21.0)	81.4 (20.0)
	Median	77.8	88.9
	Min, max	22.2, 100.0	11.1, 100.0
Change at OL Part A Week 8	n	166	164
	Mean (SD)	2.8 (15.4)	3.0 (15.2)
	Median	0.0	0.0
	Min, max	-33.3, 44.4	-44.4, 55.6
OL Part A Week 16	n	169	163
	Mean (SD)	78.5 (21.8)	80.2 (20.3)
	Median	77.8	88.9
	Min, max	22.2, 100.0	11.1, 100.0
Change at OL Part A Week 16	n	165	162
	Mean (SD)	2.3 (17.5)	2.1 (14.7)
	Median	0.0	0.0
	Min, max	-44.4, 44.4	-44.4, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Body

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 24	n	166	161
	Mean (SD)	79.3 (21.7)	81.0 (19.6)
	Median	77.8	88.9
	Min, max	22.2, 100.0	22.2, 100.0
Change at OL Part A Week 24	n	162	160
	Mean (SD)	3.6 (17.8)	3.1 (15.3)
	Median	0.0	0.0
	Min, max	-55.6, 66.7	-55.6, 55.6
OL Part A Week 48	n	159	160
	Mean (SD)	80.5 (20.4)	80.3 (20.4)
	Median	88.9	88.9
	Min, max	22.2, 100.0	22.2, 100.0
Change at OL Part A Week 48	n	155	159
	Mean (SD)	4.4 (18.4)	2.1 (15.3)
	Median	0.0	0.0
	Min, max	-44.4, 66.7	-66.7, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Body

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 96	n	150	150
	Mean (SD)	81.2 (19.6)	81.1 (19.0)
	Median	88.9	88.9
	Min, max	33.3, 100.0	22.2, 100.0
Change at OL Part A Week 96	n	147	150
	Mean (SD)	4.1 (17.8)	3.3 (16.4)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-44.4, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Eat

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	166	164
	Mean (SD)	92.6 (14.9)	91.5 (16.3)
	Median	100.0	100.0
	Min, max	33.3, 100.0	0.0, 100.0
OL Part A Week 8	n	170	166
	Mean (SD)	93.0 (14.3)	91.6 (16.0)
	Median	100.0	100.0
	Min, max	33.3, 100.0	0.0, 100.0
Change at OL Part A Week 8	n	166	164
	Mean (SD)	0.2 (12.7)	0.3 (11.6)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-33.3, 55.6
OL Part A Week 16	n	169	163
	Mean (SD)	93.2 (14.4)	91.5 (17.7)
	Median	100.0	100.0
	Min, max	44.4, 100.0	0.0, 100.0
Change at OL Part A Week 16	n	165	162
	Mean (SD)	0.5 (13.0)	0.0 (12.9)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-66.7, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Eat

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 24	n	166	161
	Mean (SD)	92.9 (14.7)	91.6 (16.2)
	Median	100.0	100.0
	Min, max	22.2, 100.0	0.0, 100.0
Change at OL Part A Week 24	n	162	160
	Mean (SD)	0.3 (14.3)	0.0 (12.7)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-44.4, 66.7
OL Part A Week 48	n	159	160
	Mean (SD)	93.4 (13.0)	91.9 (14.4)
	Median	100.0	100.0
	Min, max	44.4, 100.0	33.3, 100.0
Change at OL Part A Week 48	n	155	159
	Mean (SD)	0.9 (13.3)	0.3 (11.5)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-44.4, 44.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Eat

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 96	n	150	150
	Mean (SD)	93.6 (12.8)	91.0 (17.2)
	Median	100.0	100.0
	Min, max	44.4, 100.0	11.1, 100.0
Change at OL Part A Week 96	n	147	150
	Mean (SD)	0.9 (13.5)	-0.3 (11.7)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-44.4, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Treatment Burden

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	166	164
	Mean (SD)	70.5 (20.6)	72.6 (19.5)
	Median	66.7	77.8
	Min, max	11.1, 100.0	0.0, 100.0
OL Part A Week 8	n	170	166
	Mean (SD)	76.1 (20.2)	76.4 (19.8)
	Median	77.8	77.8
	Min, max	22.2, 100.0	11.1, 100.0
Change at OL Part A Week 8	n	166	164
	Mean (SD)	5.5 (16.6)	3.9 (15.6)
	Median	0.0	0.0
	Min, max	-44.4, 66.7	-55.6, 77.8
OL Part A Week 16	n	169	163
	Mean (SD)	74.6 (19.7)	76.6 (19.5)
	Median	77.8	77.8
	Min, max	22.2, 100.0	11.1, 100.0
Change at OL Part A Week 16	n	165	162
	Mean (SD)	3.9 (16.4)	3.7 (17.0)
	Median	0.0	0.0
	Min, max	-44.4, 77.8	-77.8, 100.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Treatment Burden

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 24	n	166	161
	Mean (SD)	75.0 (19.5)	76.3 (20.5)
	Median	77.8	77.8
	Min, max	11.1, 100.0	11.1, 100.0
Change at OL Part A Week 24	n	162	160
	Mean (SD)	4.6 (17.3)	3.3 (15.8)
	Median	0.0	0.0
	Min, max	-33.3, 88.9	-55.6, 88.9
OL Part A Week 48	n	159	160
	Mean (SD)	77.6 (19.0)	77.4 (20.0)
	Median	77.8	77.8
	Min, max	22.2, 100.0	11.1, 100.0
Change at OL Part A Week 48	n	155	159
	Mean (SD)	7.3 (16.4)	4.1 (16.9)
	Median	0.0	0.0
	Min, max	-33.3, 77.8	-66.7, 100.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Treatment Burden

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 96	n	150	150
	Mean (SD)	77.3 (20.1)	78.4 (19.4)
	Median	77.8	77.8
	Min, max	22.2, 100.0	11.1, 100.0
Change at OL Part A Week 96	n	147	150
	Mean (SD)	7.1 (19.5)	5.4 (17.1)
	Median	11.1	0.0
	Min, max	-55.6, 88.9	-55.6, 100.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Health Perceptions

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	159	160
	Mean (SD)	71.6 (19.2)	73.5 (19.7)
	Median	66.7	77.8
	Min, max	22.2, 100.0	0.0, 100.0
OL Part A Week 8	n	165	164
	Mean (SD)	73.8 (20.1)	74.6 (20.2)
	Median	77.8	77.8
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 8	n	158	160
	Mean (SD)	1.8 (14.7)	1.0 (15.0)
	Median	0.0	0.0
	Min, max	-44.4, 44.4	-55.6, 55.6
OL Part A Week 16	n	165	161
	Mean (SD)	71.3 (19.9)	73.2 (20.7)
	Median	66.7	77.8
	Min, max	11.1, 100.0	0.0, 100.0
Change at OL Part A Week 16	n	158	158
	Mean (SD)	-0.8 (13.9)	-0.6 (16.3)
	Median	0.0	0.0
	Min, max	-33.3, 44.4	-66.7, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Health Perceptions

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 24	n	163	159
	Mean (SD)	72.7 (20.2)	74.1 (19.6)
	Median	66.7	66.7
	Min, max	22.2, 100.0	11.1, 100.0
Change at OL Part A Week 24	n	155	156
	Mean (SD)	0.5 (15.6)	0.9 (15.8)
	Median	0.0	0.0
	Min, max	-66.7, 44.4	-33.3, 44.4
OL Part A Week 48	n	158	157
	Mean (SD)	73.7 (20.4)	74.9 (20.1)
	Median	72.2	77.8
	Min, max	11.1, 100.0	11.1, 100.0
Change at OL Part A Week 48	n	149	155
	Mean (SD)	1.0 (15.3)	0.9 (17.6)
	Median	0.0	0.0
	Min, max	-44.4, 44.4	-55.6, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Health Perceptions

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 96	n	150	150
	Mean (SD)	71.9 (21.3)	73.7 (23.0)
	Median	72.2	77.8
	Min, max	11.1, 100.0	0.0, 100.0
Change at OL Part A Week 96	n	140	146
	Mean (SD)	-1.4 (18.9)	0.6 (17.4)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-66.7, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Weight

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	159	160
	Mean (SD)	84.5 (27.2)	82.7 (28.2)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
OL Part A Week 8	n	165	164
	Mean (SD)	87.9 (24.4)	85.2 (24.8)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 8	n	158	160
	Mean (SD)	3.2 (25.5)	2.5 (22.6)
	Median	0.0	0.0
	Min, max	-66.7, 100.0	-66.7, 100.0
OL Part A Week 16	n	165	161
	Mean (SD)	87.3 (23.1)	84.7 (25.5)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 16	n	158	158
	Mean (SD)	2.7 (26.1)	2.1 (25.1)
	Median	0.0	0.0
	Min, max	-100.0, 100.0	-100.0, 100.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Weight

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 24	n	163	159
	Mean (SD)	87.1 (23.8)	81.8 (27.5)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 24	n	155	156
	Mean (SD)	3.0 (25.9)	-1.1 (25.2)
	Median	0.0	0.0
	Min, max	-66.7, 100.0	-100.0, 66.7
OL Part A Week 48	n	158	157
	Mean (SD)	88.0 (25.3)	80.3 (30.2)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 48	n	149	155
	Mean (SD)	4.0 (25.7)	-2.4 (26.6)
	Median	0.0	0.0
	Min, max	-100.0, 100.0	-100.0, 100.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Weight

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 96	n	150	149
	Mean (SD)	86.4 (27.3)	86.1 (25.7)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 96	n	140	145
	Mean (SD)	2.9 (26.4)	4.1 (23.9)
	Median	0.0	0.0
	Min, max	-100.0, 100.0	-66.7, 100.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Digestion

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	166	163
	Mean (SD)	81.4 (19.0)	85.0 (15.7)
	Median	88.9	88.9
	Min, max	22.2, 100.0	33.3, 100.0
OL Part A Week 8	n	169	166
	Mean (SD)	80.7 (21.3)	84.1 (16.6)
	Median	88.9	88.9
	Min, max	0.0, 100.0	33.3, 100.0
Change at OL Part A Week 8	n	165	163
	Mean (SD)	-1.4 (17.1)	-0.7 (12.6)
	Median	0.0	0.0
	Min, max	-66.7, 33.3	-33.3, 33.3
OL Part A Week 16	n	168	163
	Mean (SD)	80.0 (21.3)	85.1 (15.8)
	Median	88.9	88.9
	Min, max	0.0, 100.0	22.2, 100.0
Change at OL Part A Week 16	n	164	161
	Mean (SD)	-1.6 (18.5)	0.2 (13.0)
	Median	0.0	0.0
	Min, max	-77.8, 44.4	-44.4, 33.3

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Digestion

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 24	n	166	161
	Mean (SD)	81.9 (20.4)	84.3 (16.7)
	Median	88.9	88.9
	Min, max	0.0, 100.0	22.2, 100.0
Change at OL Part A Week 24	n	162	159
	Mean (SD)	0.2 (18.7)	-0.6 (12.7)
	Median	0.0	0.0
	Min, max	-77.8, 55.6	-33.3, 44.4
OL Part A Week 48	n	159	159
	Mean (SD)	80.9 (20.0)	85.6 (15.6)
	Median	88.9	88.9
	Min, max	0.0, 100.0	33.3, 100.0
Change at OL Part A Week 48	n	155	157
	Mean (SD)	-1.2 (17.6)	0.6 (12.9)
	Median	0.0	0.0
	Min, max	-77.8, 55.6	-33.3, 44.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Digestion

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 96	n	150	149
	Mean (SD)	81.3 (19.7)	84.0 (18.3)
	Median	88.9	88.9
	Min, max	0.0, 100.0	11.1, 100.0
Change at OL Part A Week 96	n	147	148
	Mean (SD)	-1.1 (18.4)	0.0 (15.7)
	Median	0.0	0.0
	Min, max	-77.8, 55.6	-55.6, 33.3

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Role

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	159	159
	Mean (SD)	87.5 (17.2)	87.2 (15.3)
	Median	91.7	91.7
	Min, max	8.3, 100.0	16.7, 100.0
OL Part A Week 8	n	165	164
	Mean (SD)	88.8 (15.0)	89.6 (13.8)
	Median	91.7	91.7
	Min, max	16.7, 100.0	50.0, 100.0
Change at OL Part A Week 8	n	158	159
	Mean (SD)	1.3 (14.5)	2.4 (12.8)
	Median	0.0	0.0
	Min, max	-41.7, 75.0	-50.0, 41.7
OL Part A Week 16	n	165	161
	Mean (SD)	87.7 (15.4)	89.1 (14.7)
	Median	91.7	91.7
	Min, max	16.7, 100.0	25.0, 100.0
Change at OL Part A Week 16	n	158	157
	Mean (SD)	0.1 (13.7)	1.9 (13.7)
	Median	0.0	0.0
	Min, max	-41.7, 58.3	-50.0, 50.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Role

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 24	n	163	159
	Mean (SD)	88.4 (15.2)	88.0 (15.0)
	Median	91.7	91.7
	Min, max	16.7, 100.0	25.0, 100.0
Change at OL Part A Week 24	n	155	155
	Mean (SD)	1.0 (13.9)	0.8 (14.8)
	Median	0.0	0.0
	Min, max	-50.0, 50.0	-66.7, 50.0
OL Part A Week 48	n	158	157
	Mean (SD)	89.6 (15.0)	89.4 (13.7)
	Median	91.7	91.7
	Min, max	8.3, 100.0	41.7, 100.0
Change at OL Part A Week 48	n	149	154
	Mean (SD)	1.3 (13.2)	1.8 (12.4)
	Median	0.0	0.0
	Min, max	-66.7, 58.3	-41.7, 50.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Role

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 96	n	150	149
	Mean (SD)	88.3 (16.6)	88.4 (15.1)
	Median	91.7	91.7
	Min, max	0.0, 100.0	25.0, 100.0
Change at OL Part A Week 96	n	140	144
	Mean (SD)	0.7 (16.5)	1.3 (12.8)
	Median	0.0	0.0
	Min, max	-100.0, 66.7	-41.7, 41.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Social

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	166	164
	Mean (SD)	74.2 (17.3)	74.7 (18.1)
	Median	77.8	77.8
	Min, max	22.2, 100.0	16.7, 100.0
OL Part A Week 8	n	170	166
	Mean (SD)	77.7 (17.6)	77.7 (17.4)
	Median	80.6	77.8
	Min, max	16.7, 100.0	33.3, 100.0
Change at OL Part A Week 8	n	166	164
	Mean (SD)	3.2 (13.9)	3.1 (13.0)
	Median	0.0	0.0
	Min, max	-33.3, 61.1	-44.4, 55.6
OL Part A Week 16	n	169	163
	Mean (SD)	76.2 (18.4)	78.0 (18.2)
	Median	77.8	77.8
	Min, max	22.2, 100.0	22.2, 100.0
Change at OL Part A Week 16	n	165	162
	Mean (SD)	1.9 (15.0)	3.2 (13.6)
	Median	0.0	0.0
	Min, max	-50.0, 61.1	-66.7, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Social

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 24	n	166	161
	Mean (SD)	78.7 (17.1)	78.3 (17.6)
	Median	83.3	77.8
	Min, max	27.8, 100.0	22.2, 100.0
Change at OL Part A Week 24	n	162	160
	Mean (SD)	4.3 (13.9)	3.5 (12.2)
	Median	5.2	0.0
	Min, max	-27.8, 44.4	-33.3, 44.4
OL Part A Week 48	n	159	160
	Mean (SD)	80.3 (15.2)	78.7 (16.7)
	Median	83.3	83.3
	Min, max	27.8, 100.0	33.3, 100.0
Change at OL Part A Week 48	n	155	159
	Mean (SD)	5.5 (14.0)	3.4 (13.5)
	Median	5.6	0.0
	Min, max	-40.5, 61.1	-38.9, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.1a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Social

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 96	n	150	150
	Mean (SD)	78.1 (16.0)	76.9 (16.8)
	Median	83.3	77.8
	Min, max	33.3, 100.0	22.2, 100.0
Change at OL Part A Week 96	n	147	150
	Mean (SD)	3.3 (13.8)	1.6 (14.6)
	Median	5.6	0.0
	Min, max	-44.4, 38.9	-61.1, 50.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Physical

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	243	235
	Mean (SD)	80.6 (21.1)	82.7 (18.9)
	Median	87.5	87.5
	Min, max	8.3, 100.0	4.2, 100.0
OL Part A Week 8	n	247	237
	Mean (SD)	80.4 (22.2)	83.3 (19.3)
	Median	87.5	91.7
	Min, max	4.2, 100.0	4.2, 100.0
Change at OL Part A Week 8	n	242	234
	Mean (SD)	0.0 (16.7)	0.5 (12.5)
	Median	0.0	0.0
	Min, max	-58.3, 58.3	-54.2, 34.7
OL Part A Week 16	n	241	231
	Mean (SD)	82.1 (20.3)	81.6 (21.0)
	Median	87.5	87.5
	Min, max	16.7, 100.0	8.3, 100.0
Change at OL Part A Week 16	n	237	228
	Mean (SD)	1.7 (14.7)	-0.9 (15.7)
	Median	0.0	0.0
	Min, max	-62.5, 57.1	-66.7, 38.9

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Physical

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 24	n	241	230
	Mean (SD)	82.0 (20.9)	83.2 (19.5)
	Median	91.7	91.7
	Min, max	8.3, 100.0	20.8, 100.0
Change at OL Part A Week 24	n	237	227
	Mean (SD)	1.7 (16.4)	0.8 (13.0)
	Median	0.0	0.0
	Min, max	-58.3, 58.3	-41.7, 54.2
OL Part A Week 48	n	232	221
	Mean (SD)	80.9 (22.0)	83.2 (20.3)
	Median	87.5	91.7
	Min, max	4.2, 100.0	4.2, 100.0
Change at OL Part A Week 48	n	228	218
	Mean (SD)	0.8 (18.2)	0.5 (14.0)
	Median	0.0	0.0
	Min, max	-79.2, 62.5	-58.3, 38.9

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Physical

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 96	n	226	213
	Mean (SD)	82.8 (21.4)	84.0 (20.5)
	Median	91.7	95.8
	Min, max	4.2, 100.0	0.0, 100.0
Change at OL Part A Week 96	n	222	210
	Mean (SD)	2.5 (18.6)	1.2 (14.6)
	Median	0.0	0.0
	Min, max	-87.5, 66.7	-62.5, 37.5

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Vitality

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	231	223
	Mean (SD)	66.5 (19.5)	67.9 (18.8)
	Median	66.7	66.7
	Min, max	8.3, 100.0	16.7, 100.0
OL Part A Week 8	n	244	230
	Mean (SD)	64.4 (20.7)	67.8 (19.6)
	Median	66.7	66.7
	Min, max	0.0, 100.0	8.3, 100.0
Change at OL Part A Week 8	n	230	222
	Mean (SD)	-2.0 (17.1)	-0.5 (16.1)
	Median	0.0	0.0
	Min, max	-58.3, 41.7	-58.3, 50.0
OL Part A Week 16	n	241	226
	Mean (SD)	64.2 (19.9)	66.2 (21.7)
	Median	66.7	66.7
	Min, max	8.3, 100.0	0.0, 100.0
Change at OL Part A Week 16	n	225	217
	Mean (SD)	-2.0 (17.0)	-2.0 (18.9)
	Median	0.0	0.0
	Min, max	-50.0, 50.0	-66.7, 58.3

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Vitality

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 24	n	241	225
	Mean (SD)	65.1 (21.4)	66.1 (21.4)
	Median	66.7	66.7
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 24	n	225	216
	Mean (SD)	-1.6 (18.5)	-1.9 (17.1)
	Median	0.0	0.0
	Min, max	-50.0, 50.0	-50.0, 50.0
OL Part A Week 48	n	230	220
	Mean (SD)	65.4 (20.6)	66.0 (20.9)
	Median	66.7	66.7
	Min, max	8.3, 100.0	0.0, 100.0
Change at OL Part A Week 48	n	216	207
	Mean (SD)	-1.2 (16.2)	-2.4 (16.8)
	Median	0.0	0.0
	Min, max	-66.7, 41.7	-66.7, 50.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Vitality

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 96	n	226	213
	Mean (SD)	66.8 (20.3)	68.0 (20.2)
	Median	66.7	75.0
	Min, max	0.0, 100.0	8.3, 100.0
Change at OL Part A Week 96	n	210	199
	Mean (SD)	-0.2 (18.4)	-0.5 (16.4)
	Median	0.0	0.0
	Min, max	-100.0, 50.0	-50.0, 50.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Emotion

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	243	235
	Mean (SD)	82.1 (16.9)	82.2 (17.3)
	Median	86.7	86.7
	Min, max	26.7, 100.0	6.7, 100.0
OL Part A Week 8	n	247	237
	Mean (SD)	82.3 (17.5)	82.7 (18.0)
	Median	86.7	86.7
	Min, max	20.0, 100.0	0.0, 100.0
Change at OL Part A Week 8	n	242	234
	Mean (SD)	0.2 (14.2)	0.6 (14.2)
	Median	0.0	0.0
	Min, max	-53.3, 53.3	-53.3, 46.7
OL Part A Week 16	n	241	231
	Mean (SD)	82.2 (17.1)	82.8 (16.6)
	Median	86.7	86.7
	Min, max	13.3, 100.0	13.3, 100.0
Change at OL Part A Week 16	n	237	228
	Mean (SD)	0.1 (14.4)	0.7 (14.5)
	Median	0.0	0.0
	Min, max	-66.7, 53.3	-46.7, 54.2

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Emotion

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 24	n	241	230
	Mean (SD)	82.6 (16.8)	83.0 (17.6)
	Median	86.7	86.7
	Min, max	0.0, 100.0	6.7, 100.0
Change at OL Part A Week 24	n	237	227
	Mean (SD)	0.7 (14.0)	1.1 (13.3)
	Median	0.0	0.0
	Min, max	-53.3, 53.3	-46.7, 46.7
OL Part A Week 48	n	232	221
	Mean (SD)	83.5 (15.9)	82.9 (18.8)
	Median	86.7	86.7
	Min, max	6.7, 100.0	13.3, 100.0
Change at OL Part A Week 48	n	228	218
	Mean (SD)	1.5 (14.5)	0.7 (14.8)
	Median	0.0	0.0
	Min, max	-46.7, 46.7	-53.3, 65.8

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Emotion

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 96	n	226	213
	Mean (SD)	84.7 (15.9)	84.4 (17.9)
	Median	86.7	93.3
	Min, max	20.0, 100.0	0.0, 100.0
Change at OL Part A Week 96	n	222	210
	Mean (SD)	2.6 (14.0)	2.1 (14.2)
	Median	0.0	0.0
	Min, max	-60.0, 46.7	-46.7, 46.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Body

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	243	235
	Mean (SD)	76.0 (23.8)	78.5 (21.4)
	Median	77.8	77.8
	Min, max	0.0, 100.0	11.1, 100.0
OL Part A Week 8	n	247	236
	Mean (SD)	79.7 (20.5)	81.0 (21.8)
	Median	88.9	88.9
	Min, max	11.1, 100.0	0.0, 100.0
Change at OL Part A Week 8	n	242	233
	Mean (SD)	3.5 (17.5)	2.1 (16.0)
	Median	0.0	0.0
	Min, max	-55.6, 77.8	-55.6, 55.6
OL Part A Week 16	n	241	231
	Mean (SD)	78.9 (21.3)	79.9 (22.6)
	Median	88.9	88.9
	Min, max	11.1, 100.0	0.0, 100.0
Change at OL Part A Week 16	n	237	228
	Mean (SD)	2.9 (17.8)	1.2 (15.3)
	Median	0.0	0.0
	Min, max	-66.7, 66.7	-66.7, 44.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Body

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 24	n	241	229
	Mean (SD)	79.3 (21.9)	82.0 (21.2)
	Median	88.9	88.9
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 24	n	237	226
	Mean (SD)	3.1 (18.6)	3.5 (16.3)
	Median	0.0	0.0
	Min, max	-44.4, 77.8	-55.6, 55.6
OL Part A Week 48	n	232	221
	Mean (SD)	79.8 (20.8)	80.5 (20.9)
	Median	88.9	88.9
	Min, max	11.1, 100.0	11.1, 100.0
Change at OL Part A Week 48	n	228	218
	Mean (SD)	3.9 (17.9)	1.6 (15.2)
	Median	0.0	0.0
	Min, max	-55.6, 55.6	-55.6, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Body

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 96	n	226	213
	Mean (SD)	81.0 (21.2)	83.6 (19.6)
	Median	88.9	88.9
	Min, max	0.0, 100.0	11.1, 100.0
Change at OL Part A Week 96	n	222	210
	Mean (SD)	5.3 (20.1)	3.9 (15.6)
	Median	0.0	0.0
	Min, max	-55.6, 77.8	-55.6, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Eat

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	243	235
	Mean (SD)	92.1 (15.1)	94.4 (12.0)
	Median	100.0	100.0
	Min, max	22.2, 100.0	44.4, 100.0
OL Part A Week 8	n	247	237
	Mean (SD)	91.5 (14.9)	93.3 (14.2)
	Median	100.0	100.0
	Min, max	22.2, 100.0	33.3, 100.0
Change at OL Part A Week 8	n	242	234
	Mean (SD)	-0.4 (14.0)	-1.1 (13.1)
	Median	0.0	0.0
	Min, max	-55.6, 55.6	-66.7, 55.6
OL Part A Week 16	n	241	231
	Mean (SD)	93.1 (14.6)	93.3 (13.5)
	Median	100.0	100.0
	Min, max	0.0, 100.0	33.3, 100.0
Change at OL Part A Week 16	n	237	228
	Mean (SD)	1.1 (12.9)	-1.1 (12.1)
	Median	0.0	0.0
	Min, max	-100.0, 55.6	-55.6, 44.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Eat

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 24	n	241	229
	Mean (SD)	93.2 (14.8)	94.2 (12.6)
	Median	100.0	100.0
	Min, max	22.2, 100.0	22.2, 100.0
Change at OL Part A Week 24	n	237	226
	Mean (SD)	1.4 (12.3)	0.0 (11.0)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-44.4, 44.4
OL Part A Week 48	n	232	221
	Mean (SD)	92.5 (15.3)	94.5 (12.8)
	Median	100.0	100.0
	Min, max	33.3, 100.0	33.3, 100.0
Change at OL Part A Week 48	n	228	218
	Mean (SD)	0.5 (13.4)	0.2 (10.5)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-44.4, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Eat

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 96	n	226	213
	Mean (SD)	92.2 (14.7)	95.3 (11.2)
	Median	100.0	100.0
	Min, max	33.3, 100.0	44.4, 100.0
Change at OL Part A Week 96	n	222	210
	Mean (SD)	-0.1 (14.4)	0.4 (11.6)
	Median	0.0	0.0
	Min, max	-55.6, 66.7	-44.4, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Treatment Burden

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	243	235
	Mean (SD)	70.8 (20.1)	70.8 (19.5)
	Median	66.7	66.7
	Min, max	22.2, 100.0	22.2, 100.0
OL Part A Week 8	n	247	237
	Mean (SD)	75.3 (20.6)	76.1 (19.7)
	Median	77.8	77.8
	Min, max	11.1, 100.0	22.2, 100.0
Change at OL Part A Week 8	n	242	234
	Mean (SD)	4.5 (16.8)	5.1 (15.3)
	Median	0.0	0.0
	Min, max	-77.8, 66.7	-44.4, 55.6
OL Part A Week 16	n	241	231
	Mean (SD)	74.6 (20.5)	75.5 (21.8)
	Median	77.8	77.8
	Min, max	11.1, 100.0	0.0, 100.0
Change at OL Part A Week 16	n	237	228
	Mean (SD)	3.8 (17.0)	4.4 (16.3)
	Median	0.0	0.0
	Min, max	-66.7, 55.6	-66.7, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Treatment Burden

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 24	n	241	229
	Mean (SD)	75.5 (20.8)	77.6 (20.6)
	Median	77.8	77.8
	Min, max	22.2, 100.0	22.2, 100.0
Change at OL Part A Week 24	n	237	226
	Mean (SD)	4.6 (17.7)	6.4 (16.2)
	Median	0.0	0.0
	Min, max	-66.7, 66.7	-55.6, 66.7
OL Part A Week 48	n	232	221
	Mean (SD)	76.2 (21.1)	77.4 (19.4)
	Median	77.8	77.8
	Min, max	0.0, 100.0	22.2, 100.0
Change at OL Part A Week 48	n	228	218
	Mean (SD)	5.9 (17.6)	6.2 (15.2)
	Median	0.0	0.0
	Min, max	-55.6, 55.6	-50.0, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Treatment Burden

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 96	n	226	213
	Mean (SD)	77.4 (20.2)	79.3 (20.4)
	Median	77.8	77.8
	Min, max	0.0, 100.0	22.2, 100.0
Change at OL Part A Week 96	n	222	210
	Mean (SD)	7.0 (18.4)	7.6 (17.5)
	Median	11.1	11.1
	Min, max	-55.6, 66.7	-55.6, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Health Perceptions

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	231	223
	Mean (SD)	71.8 (20.3)	73.0 (19.8)
	Median	77.8	77.8
	Min, max	11.1, 100.0	22.2, 100.0
OL Part A Week 8	n	244	229
	Mean (SD)	72.8 (21.3)	74.6 (21.1)
	Median	77.8	77.8
	Min, max	0.0, 100.0	11.1, 100.0
Change at OL Part A Week 8	n	230	221
	Mean (SD)	0.9 (17.7)	0.9 (14.3)
	Median	0.0	0.0
	Min, max	-66.7, 55.6	-66.7, 44.4
OL Part A Week 16	n	241	226
	Mean (SD)	73.0 (19.7)	73.2 (21.8)
	Median	77.8	77.8
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 16	n	225	217
	Mean (SD)	0.8 (16.7)	-0.3 (14.9)
	Median	0.0	0.0
	Min, max	-55.6, 55.6	-44.4, 44.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Health Perceptions

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 24	n	241	224
	Mean (SD)	72.6 (20.2)	73.5 (21.2)
	Median	66.7	77.8
	Min, max	0.0, 100.0	11.1, 100.0
Change at OL Part A Week 24	n	225	215
	Mean (SD)	0.5 (16.2)	0.0 (15.0)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-55.6, 33.3
OL Part A Week 48	n	229	220
	Mean (SD)	73.4 (20.4)	75.4 (19.5)
	Median	77.8	77.8
	Min, max	0.0, 100.0	22.2, 100.0
Change at OL Part A Week 48	n	215	207
	Mean (SD)	1.3 (16.3)	1.8 (14.2)
	Median	0.0	0.0
	Min, max	-44.4, 55.6	-44.4, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Health Perceptions

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 96	n	226	213
	Mean (SD)	75.4 (20.7)	76.4 (21.0)
	Median	77.8	77.8
	Min, max	11.1, 100.0	22.2, 100.0
Change at OL Part A Week 96	n	210	199
	Mean (SD)	3.8 (18.8)	3.0 (15.5)
	Median	0.0	0.0
	Min, max	-88.9, 66.7	-44.4, 55.6

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Weight

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	228	223
	Mean (SD)	88.6 (24.2)	83.6 (27.7)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
OL Part A Week 8	n	244	230
	Mean (SD)	85.8 (26.2)	85.9 (28.6)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 8	n	227	222
	Mean (SD)	-2.3 (20.2)	1.8 (23.4)
	Median	0.0	0.0
	Min, max	-66.7, 66.7	-100.0, 66.7
OL Part A Week 16	n	241	226
	Mean (SD)	86.7 (26.5)	83.6 (29.0)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 16	n	223	217
	Mean (SD)	-1.0 (20.6)	-0.3 (23.8)
	Median	0.0	0.0
	Min, max	-100.0, 66.7	-100.0, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Weight

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 24	n	241	224
	Mean (SD)	87.1 (25.9)	86.2 (26.4)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 24	n	223	215
	Mean (SD)	-1.2 (22.1)	2.3 (23.5)
	Median	0.0	0.0
	Min, max	-100.0, 66.7	-66.7, 100.0
OL Part A Week 48	n	230	220
	Mean (SD)	85.1 (29.0)	86.5 (26.9)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 48	n	214	207
	Mean (SD)	-3.4 (23.5)	2.6 (24.2)
	Median	0.0	0.0
	Min, max	-100.0, 66.7	-66.7, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Weight

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 96	n	226	212
	Mean (SD)	85.0 (28.1)	87.6 (24.9)
	Median	100.0	100.0
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 96	n	209	198
	Mean (SD)	-2.9 (24.5)	2.7 (22.1)
	Median	0.0	0.0
	Min, max	-100.0, 100.0	-66.7, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Digestion

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	243	235
	Mean (SD)	80.9 (17.2)	81.8 (18.4)
	Median	77.8	88.9
	Min, max	33.3, 100.0	22.2, 100.0
OL Part A Week 8	n	247	237
	Mean (SD)	78.9 (20.9)	80.6 (19.5)
	Median	77.8	88.9
	Min, max	11.1, 100.0	11.1, 100.0
Change at OL Part A Week 8	n	242	234
	Mean (SD)	-1.9 (17.6)	-1.3 (16.4)
	Median	0.0	0.0
	Min, max	-55.6, 44.4	-66.7, 66.7
OL Part A Week 16	n	241	231
	Mean (SD)	79.1 (20.4)	80.5 (20.3)
	Median	77.8	88.9
	Min, max	11.1, 100.0	11.1, 100.0
Change at OL Part A Week 16	n	237	228
	Mean (SD)	-1.7 (16.6)	-1.3 (17.2)
	Median	0.0	0.0
	Min, max	-66.7, 55.6	-55.6, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Digestion

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 24	n	241	229
	Mean (SD)	78.8 (20.7)	80.1 (20.6)
	Median	77.8	88.9
	Min, max	11.1, 100.0	0.0, 100.0
Change at OL Part A Week 24	n	237	226
	Mean (SD)	-2.0 (17.2)	-1.7 (17.0)
	Median	0.0	0.0
	Min, max	-66.7, 44.4	-55.6, 66.7
OL Part A Week 48	n	232	221
	Mean (SD)	79.4 (20.4)	81.1 (19.5)
	Median	88.9	88.9
	Min, max	22.2, 100.0	22.2, 100.0
Change at OL Part A Week 48	n	228	218
	Mean (SD)	-1.3 (17.8)	-0.7 (17.8)
	Median	0.0	0.0
	Min, max	-66.7, 66.7	-55.6, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Digestion

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 96	n	225	212
	Mean (SD)	80.0 (19.2)	80.8 (18.9)
	Median	88.9	88.9
	Min, max	11.1, 100.0	22.2, 100.0
Change at OL Part A Week 96	n	221	209
	Mean (SD)	-1.1 (17.7)	-0.8 (17.8)
	Median	0.0	0.0
	Min, max	-44.4, 44.4	-55.6, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Role

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	231	223
	Mean (SD)	86.1 (16.3)	87.0 (15.7)
	Median	91.7	91.7
	Min, max	25.0, 100.0	8.3, 100.0
OL Part A Week 8	n	243	230
	Mean (SD)	87.8 (17.1)	89.1 (16.2)
	Median	91.7	100.0
	Min, max	8.3, 100.0	8.3, 100.0
Change at OL Part A Week 8	n	229	222
	Mean (SD)	1.9 (15.7)	1.9 (13.4)
	Median	0.0	0.0
	Min, max	-83.3, 58.3	-50.0, 66.7
OL Part A Week 16	n	241	225
	Mean (SD)	87.9 (15.0)	88.6 (15.7)
	Median	91.7	91.7
	Min, max	25.0, 100.0	16.7, 100.0
Change at OL Part A Week 16	n	225	216
	Mean (SD)	2.2 (12.8)	1.2 (14.1)
	Median	0.0	0.0
	Min, max	-41.7, 58.3	-41.7, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Role

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 24	n	241	224
	Mean (SD)	87.7 (16.2)	87.9 (15.2)
	Median	91.7	91.7
	Min, max	25.0, 100.0	25.0, 100.0
Change at OL Part A Week 24	n	225	215
	Mean (SD)	1.9 (14.6)	1.0 (13.5)
	Median	0.0	0.0
	Min, max	-75.0, 58.3	-50.0, 58.3
OL Part A Week 48	n	230	220
	Mean (SD)	88.0 (15.8)	89.0 (14.6)
	Median	91.7	95.8
	Min, max	16.7, 100.0	33.3, 100.0
Change at OL Part A Week 48	n	216	207
	Mean (SD)	2.5 (15.2)	1.8 (14.0)
	Median	0.0	0.0
	Min, max	-55.6, 58.3	-50.0, 66.7

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Role

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 96	n	225	212
	Mean (SD)	89.2 (15.3)	89.4 (15.6)
	Median	100.0	100.0
	Min, max	25.0, 100.0	8.3, 100.0
Change at OL Part A Week 96	n	209	198
	Mean (SD)	3.8 (14.6)	1.9 (13.8)
	Median	0.0	0.0
	Min, max	-50.0, 58.3	-66.7, 50.0

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Social

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	243	235
	Mean (SD)	72.5 (18.0)	76.0 (18.0)
	Median	72.2	77.8
	Min, max	11.1, 100.0	23.8, 100.0
OL Part A Week 8	n	247	236
	Mean (SD)	75.9 (17.4)	79.8 (18.0)
	Median	77.8	83.3
	Min, max	0.0, 100.0	27.8, 100.0
Change at OL Part A Week 8	n	242	233
	Mean (SD)	3.4 (15.1)	3.6 (12.8)
	Median	5.2	5.6
	Min, max	-50.0, 44.4	-50.0, 38.9
OL Part A Week 16	n	241	231
	Mean (SD)	76.1 (17.4)	79.0 (19.1)
	Median	77.8	83.3
	Min, max	0.0, 100.0	11.1, 100.0
Change at OL Part A Week 16	n	237	228
	Mean (SD)	3.5 (14.8)	3.2 (14.6)
	Median	5.6	0.0
	Min, max	-50.0, 45.2	-66.7, 42.9

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Social

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 24	n	241	229
	Mean (SD)	76.8 (18.0)	79.7 (18.0)
	Median	77.8	83.3
	Min, max	5.6, 100.0	16.7, 100.0
Change at OL Part A Week 24	n	237	226
	Mean (SD)	4.3 (14.9)	3.8 (15.0)
	Median	5.6	5.6
	Min, max	-50.0, 45.2	-83.3, 52.4
OL Part A Week 48	n	232	221
	Mean (SD)	77.7 (18.1)	81.0 (17.5)
	Median	83.3	83.3
	Min, max	5.6, 100.0	27.8, 100.0
Change at OL Part A Week 48	n	228	218
	Mean (SD)	5.5 (16.3)	5.1 (13.6)
	Median	5.6	5.6
	Min, max	-66.7, 50.0	-33.3, 44.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.6.3.2a
Summary of CFQ-R Non-Respiratory Domain Scores and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Version: Pooled Children Ages 12 and 13 and Adolescents and Adults

Domain: Social

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 96	n	226	213
	Mean (SD)	78.9 (16.5)	81.8 (17.4)
	Median	83.3	88.9
	Min, max	22.2, 100.0	16.7, 100.0
Change at OL Part A Week 96	n	222	210
	Mean (SD)	6.6 (15.6)	5.7 (12.5)
	Median	5.6	5.6
	Min, max	-55.6, 50.8	-44.4, 44.4

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.1a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Domain: Effectiveness

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 22	VNZ/TEZ/D-IVA in 121-102 N = 23
Parent Study Baseline	n	22	22
	Mean (SD)	80.6 (13.7)	79.3 (28.4)
	Median	83.3	91.7
	Min, max	50.0, 100.0	0.0, 100.0
OL Part A Week 24	n	21	22
	Mean (SD)	76.7 (24.6)	76.5 (25.7)
	Median	83.3	83.3
	Min, max	11.1, 100.0	0.0, 100.0
Change at OL Part A Week 24	n	21	21
	Mean (SD)	-3.4 (24.4)	1.1 (35.9)
	Median	0.0	0.0
	Min, max	-72.2, 22.2	-100.0, 94.4
OL Part A Week 48	n	22	22
	Mean (SD)	81.3 (23.2)	79.0 (27.6)
	Median	86.1	83.3
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 48	n	22	21
	Mean (SD)	0.8 (24.0)	-0.5 (28.1)
	Median	5.6	0.0
	Min, max	-83.3, 33.3	-100.0, 55.6

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.1a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Domain: Effectiveness

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 22	VNZ/TEZ/D-IVA in 121-102 N = 23
OL Part A Week 96	n	21	23
	Mean (SD)	86.5 (13.6)	87.2 (20.1)
	Median	88.9	100.0
	Min, max	61.1, 100.0	16.7, 100.0
Change at OL Part A Week 96	n	21	22
	Mean (SD)	6.3 (15.5)	9.1 (24.5)
	Median	5.6	5.6
	Min, max	-27.8, 50.0	-27.8, 94.4

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.1a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Domain: Side Effects

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 22	VNZ/TEZ/D-IVA in 121-102 N = 23
Parent Study Baseline	n	22	21
	Mean (SD)	97.2 (12.0)	98.5 (4.4)
	Median	100.0	100.0
	Min, max	43.8, 100.0	81.3, 100.0
OL Part A Week 24	n	21	22
	Mean (SD)	99.4 (2.7)	97.4 (12.0)
	Median	100.0	100.0
	Min, max	87.5, 100.0	43.8, 100.0
Change at OL Part A Week 24	n	21	20
	Mean (SD)	2.4 (12.7)	-1.3 (13.7)
	Median	0.0	0.0
	Min, max	-12.5, 56.3	-56.3, 18.8
OL Part A Week 48	n	22	22
	Mean (SD)	96.6 (7.6)	97.4 (12.0)
	Median	100.0	100.0
	Min, max	75.0, 100.0	43.8, 100.0
Change at OL Part A Week 48	n	22	20
	Mean (SD)	-0.6 (12.5)	-1.3 (8.7)
	Median	0.0	0.0
	Min, max	-25.0, 43.8	-37.5, 6.3

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.1a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Domain: Side Effects

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 22	VNZ/TEZ/D-IVA in 121-102 N = 23
OL Part A Week 96	n	21	23
	Mean (SD)	94.3 (15.4)	92.4 (17.5)
	Median	100.0	100.0
	Min, max	43.8, 100.0	43.8, 100.0
Change at OL Part A Week 96	n	21	21
	Mean (SD)	-2.7 (20.6)	-5.4 (15.8)
	Median	0.0	0.0
	Min, max	-56.3, 56.3	-56.3, 6.3

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.1a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Domain: Convenience

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 22	VNZ/TEZ/D-IVA in 121-102 N = 23
Parent Study Baseline	n	22	22
	Mean (SD)	76.8 (13.9)	83.8 (15.2)
	Median	75.0	88.9
	Min, max	50.0, 100.0	55.6, 100.0
OL Part A Week 24	n	21	22
	Mean (SD)	83.1 (14.3)	88.9 (11.1)
	Median	83.3	88.9
	Min, max	55.6, 100.0	55.6, 100.0
Change at OL Part A Week 24	n	21	21
	Mean (SD)	7.4 (13.1)	5.6 (17.6)
	Median	5.6	0.0
	Min, max	-11.1, 38.9	-33.3, 38.9
OL Part A Week 48	n	22	22
	Mean (SD)	83.1 (13.9)	90.9 (11.6)
	Median	80.6	100.0
	Min, max	55.6, 100.0	66.7, 100.0
Change at OL Part A Week 48	n	22	21
	Mean (SD)	6.3 (12.7)	6.9 (18.2)
	Median	5.6	5.6
	Min, max	-16.7, 38.9	-22.2, 44.4

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.1a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Domain: Convenience

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 22	VNZ/TEZ/D-IVA in 121-102 N = 23
OL Part A Week 96	n	21	23
	Mean (SD)	83.9 (13.6)	91.1 (13.1)
	Median	83.3	100.0
	Min, max	50.0, 100.0	61.1, 100.0
Change at OL Part A Week 96	n	21	22
	Mean (SD)	6.9 (16.0)	6.8 (19.6)
	Median	5.6	0.0
	Min, max	-22.2, 50.0	-22.2, 44.4

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.1a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Domain: Global Satisfaction

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 22	VNZ/TEZ/D-IVA in 121-102 N = 23
Parent Study Baseline	n	22	22
	Mean (SD)	81.8 (16.0)	88.0 (13.7)
	Median	85.7	92.9
	Min, max	42.9, 100.0	57.1, 100.0
OL Part A Week 24	n	21	22
	Mean (SD)	84.4 (19.4)	84.1 (13.6)
	Median	92.9	85.7
	Min, max	14.3, 100.0	42.9, 100.0
Change at OL Part A Week 24	n	21	21
	Mean (SD)	2.7 (16.0)	-2.7 (18.1)
	Median	0.0	0.0
	Min, max	-50.0, 28.6	-57.1, 28.6
OL Part A Week 48	n	22	22
	Mean (SD)	89.0 (14.9)	86.4 (16.2)
	Median	100.0	89.3
	Min, max	57.1, 100.0	42.9, 100.0
Change at OL Part A Week 48	n	22	21
	Mean (SD)	7.1 (15.9)	-1.0 (20.0)
	Median	7.1	0.0
	Min, max	-28.6, 35.7	-57.1, 42.9

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.1a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Domain: Global Satisfaction

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 22	VNZ/TEZ/D-IVA in 121-102 N = 23
OL Part A Week 96	n	21	23
	Mean (SD)	92.2 (10.6)	89.1 (15.8)
	Median	100.0	100.0
	Min, max	71.4, 100.0	50.0, 100.0
Change at OL Part A Week 96	n	21	22
	Mean (SD)	10.2 (15.4)	2.9 (18.7)
	Median	7.1	0.0
	Min, max	-14.3, 57.1	-35.7, 42.9

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.2a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set for Part A - Subjects from Study 103

Domain: Effectiveness

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 33	VNZ/TEZ/D-IVA in 121-103 N = 31
Parent Study Baseline	n	31	28
	Mean (SD)	81.9 (17.1)	81.9 (15.8)
	Median	83.3	83.3
	Min, max	33.3, 100.0	44.4, 100.0
OL Part A Week 24	n	31	29
	Mean (SD)	86.0 (20.6)	85.8 (15.8)
	Median	94.4	88.9
	Min, max	11.1, 100.0	55.6, 100.0
Change at OL Part A Week 24	n	30	27
	Mean (SD)	3.9 (24.7)	4.9 (16.9)
	Median	0.0	5.6
	Min, max	-72.2, 61.1	-33.3, 33.3
OL Part A Week 48	n	33	27
	Mean (SD)	84.2 (25.1)	74.3 (35.4)
	Median	94.4	83.3
	Min, max	0.0, 100.0	0.0, 100.0
Change at OL Part A Week 48	n	31	24
	Mean (SD)	1.3 (26.7)	-9.3 (35.4)
	Median	0.0	0.0
	Min, max	-83.3, 66.7	-100.0, 33.3

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.2a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set for Part A - Subjects from Study 103

Domain: Effectiveness

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 33	VNZ/TEZ/D-IVA in 121-103 N = 31
OL Part A Week 96	n	33	29
	Mean (SD)	90.4 (17.4)	88.3 (20.1)
	Median	100.0	94.4
	Min, max	27.8, 100.0	0.0, 100.0
Change at OL Part A Week 96	n	31	26
	Mean (SD)	7.9 (21.9)	6.2 (23.3)
	Median	0.0	2.8
	Min, max	-44.4, 66.7	-77.8, 44.4

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.2a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set for Part A - Subjects from Study 103

Domain: Side Effects

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 33	VNZ/TEZ/D-IVA in 121-103 N = 31
Parent Study Baseline	n	31	28
	Mean (SD)	100.0 (0.0)	96.2 (12.5)
	Median	100.0	100.0
	Min, max	100.0, 100.0	37.5, 100.0
OL Part A Week 24	n	31	29
	Mean (SD)	98.8 (6.7)	98.5 (7.0)
	Median	100.0	100.0
	Min, max	62.5, 100.0	62.5, 100.0
Change at OL Part A Week 24	n	30	27
	Mean (SD)	-1.3 (6.8)	2.3 (13.2)
	Median	0.0	0.0
	Min, max	-37.5, 0.0	-18.8, 62.5
OL Part A Week 48	n	32	27
	Mean (SD)	97.9 (10.0)	98.4 (6.4)
	Median	100.0	100.0
	Min, max	43.8, 100.0	68.8, 100.0
Change at OL Part A Week 48	n	30	24
	Mean (SD)	-2.3 (10.3)	-1.6 (6.5)
	Median	0.0	0.0
	Min, max	-56.3, 0.0	-31.3, 0.0

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.2a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set for Part A - Subjects from Study 103

Domain: Side Effects

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 33	VNZ/TEZ/D-IVA in 121-103 N = 31
OL Part A Week 96	n	33	29
	Mean (SD)	99.1 (5.4)	99.8 (1.2)
	Median	100.0	100.0
	Min, max	68.8, 100.0	93.8, 100.0
Change at OL Part A Week 96	n	31	26
	Mean (SD)	-1.0 (5.6)	0.7 (3.7)
	Median	0.0	0.0
	Min, max	-31.3, 0.0	0.0, 18.8

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.2a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set for Part A - Subjects from Study 103

Domain: Convenience

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 33	VNZ/TEZ/D-IVA in 121-103 N = 31
Parent Study Baseline	n	31	27
	Mean (SD)	83.0 (15.0)	84.4 (14.6)
	Median	88.9	88.9
	Min, max	44.4, 100.0	50.0, 100.0
OL Part A Week 24	n	31	29
	Mean (SD)	88.7 (13.3)	88.7 (14.1)
	Median	94.4	94.4
	Min, max	50.0, 100.0	50.0, 100.0
Change at OL Part A Week 24	n	30	26
	Mean (SD)	5.4 (19.0)	5.3 (17.7)
	Median	0.0	5.6
	Min, max	-27.8, 55.6	-33.3, 44.4
OL Part A Week 48	n	33	27
	Mean (SD)	92.4 (10.5)	88.5 (13.4)
	Median	94.4	88.9
	Min, max	55.6, 100.0	44.4, 100.0
Change at OL Part A Week 48	n	31	24
	Mean (SD)	9.0 (16.8)	2.8 (16.9)
	Median	5.6	0.0
	Min, max	-44.4, 55.6	-27.8, 44.4

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.2a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set for Part A - Subjects from Study 103

Domain: Convenience

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 33	VNZ/TEZ/D-IVA in 121-103 N = 31
OL Part A Week 96	n	33	29
	Mean (SD)	89.7 (13.0)	90.8 (11.4)
	Median	100.0	94.4
	Min, max	55.6, 100.0	61.1, 100.0
Change at OL Part A Week 96	n	31	26
	Mean (SD)	6.5 (16.7)	6.4 (17.3)
	Median	5.6	2.8
	Min, max	-22.2, 55.6	-27.8, 38.9

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.2a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set for Part A - Subjects from Study 103

Domain: Global Satisfaction

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 33	VNZ/TEZ/D-IVA in 121-103 N = 31
Parent Study Baseline	n	31	28
	Mean (SD)	86.4 (13.1)	87.7 (14.4)
	Median	85.7	92.9
	Min, max	50.0, 100.0	50.0, 100.0
OL Part A Week 24	n	31	29
	Mean (SD)	90.8 (13.6)	89.2 (14.9)
	Median	100.0	100.0
	Min, max	57.1, 100.0	50.0, 100.0
Change at OL Part A Week 24	n	30	27
	Mean (SD)	4.3 (12.2)	2.0 (14.3)
	Median	0.0	0.0
	Min, max	-28.6, 28.6	-35.7, 28.6
OL Part A Week 48	n	33	27
	Mean (SD)	92.4 (11.1)	93.7 (10.5)
	Median	100.0	100.0
	Min, max	50.0, 100.0	57.1, 100.0
Change at OL Part A Week 48	n	31	24
	Mean (SD)	5.5 (15.2)	5.7 (14.6)
	Median	0.0	3.6
	Min, max	-35.7, 50.0	-28.6, 35.7

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.2a
Summary of TSQM Domain Scores and Change from Parent Study Baseline at Each Visit
for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent in the Parent Study - OL Efficacy Period for Part A
OL Full Analysis Set for Part A - Subjects from Study 103

Domain: Global Satisfaction

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 33	VNZ/TEZ/D-IVA in 121-103 N = 31
OL Part A Week 96	n	33	29
	Mean (SD)	93.1 (12.4)	94.8 (8.5)
	Median	100.0	100.0
	Min, max	50.0, 100.0	71.4, 100.0
Change at OL Part A Week 96	n	31	26
	Mean (SD)	6.2 (16.6)	7.1 (13.7)
	Median	0.0	0.0
	Min, max	-35.7, 42.9	-14.3, 42.9

- N is the number of subjects in the specified analysis set who are ≥12 to <18 years of age at the date of informed consent in the parent study.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.7.3a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

Domain: Effectiveness

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	31	26
Parent study baseline		
n	31	25
Mean (SD)	80.6 (14.6)	79.6 (27.7)
Absolute change at Week 52		
n	28	22
LS mean (SE)	2.1 (4.8)	7.3 (5.4)
95% CI of LS mean	(-7.6, 11.8)	(-3.5, 18.2)
OL Efficacy Period for Part A		
N	22	23
Absolute change at OL Part A Week 24		
n	21	21
LS mean (SE)	-3.8 (6.8)	0.9 (6.8)
95% CI of LS mean	(-17.5, 9.9)	(-12.9, 14.8)
Absolute change at OL Part A Week 48		
n	22	20
LS mean (SE)	0.7 (5.8)	-0.6 (6.0)
95% CI of LS mean	(-11.1, 12.4)	(-12.7, 11.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.3a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

Domain: Effectiveness

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 96		
n	21	21
LS mean (SE)	5.9 (4.4)	9.4 (4.4)
95% CI of LS mean	(-3.1, 14.9)	(0.3, 18.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.3a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

Domain: Side Effects

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	31	26
Parent study baseline		
n	31	24
Mean (SD)	96.2 (13.3)	98.7 (4.1)
Absolute change at Week 52		
n	28	21
LS mean (SE)	-0.8 (1.9)	-2.5 (2.2)
95% CI of LS mean	(-4.7, 3.0)	(-6.9, 2.0)
OL Efficacy Period for Part A		
N	22	23
Absolute change at OL Part A Week 24		
n	21	20
LS mean (SE)	2.5 (2.9)	-1.2 (3.0)
95% CI of LS mean	(-3.4, 8.4)	(-7.2, 4.9)
Absolute change at OL Part A Week 48		
n	22	19
LS mean (SE)	-0.6 (2.3)	-1.2 (2.5)
95% CI of LS mean	(-5.4, 4.1)	(-6.2, 3.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.3a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

Domain: Side Effects

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 96		
n	21	20
LS mean (SE)	-2.7 (4.0)	-5.5 (4.1)
95% CI of LS mean	(-10.8, 5.4)	(-13.9, 2.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.3a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

Domain: Convenience

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	31	26
Parent study baseline		
n	31	25
Mean (SD)	78.7 (14.8)	83.1 (15.5)
Absolute change at Week 52		
n	28	22
LS mean (SE)	3.4 (3.3)	3.7 (3.6)
95% CI of LS mean	(-3.2, 9.9)	(-3.6, 11.1)
OL Efficacy Period for Part A		
N	22	23
Absolute change at OL Part A Week 24		
n	21	21
LS mean (SE)	6.4 (3.3)	5.4 (3.3)
95% CI of LS mean	(-0.2, 13.0)	(-1.3, 12.0)
Absolute change at OL Part A Week 48		
n	22	20
LS mean (SE)	5.8 (3.5)	6.5 (3.5)
95% CI of LS mean	(-1.2, 12.8)	(-0.7, 13.7)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.3a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

Domain: Convenience

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 96		
n	21	21
LS mean (SE)	6.5 (3.9)	6.9 (3.9)
95% CI of LS mean	(-1.3, 14.3)	(-1.0, 14.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.3a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

Domain: Global Satisfaction

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	31	26
Parent study baseline		
n	31	25
Mean (SD)	81.8 (16.0)	86.6 (14.9)
Absolute change at Week 52		
n	28	22
LS mean (SE)	5.9 (2.9)	1.4 (3.3)
95% CI of LS mean	(0.1, 11.8)	(-5.2, 7.9)
OL Efficacy Period for Part A		
N	22	23
Absolute change at OL Part A Week 24		
n	21	21
LS mean (SE)	3.0 (3.8)	-2.6 (3.8)
95% CI of LS mean	(-4.7, 10.7)	(-10.3, 5.1)
Absolute change at OL Part A Week 48		
n	22	20
LS mean (SE)	7.5 (3.9)	-1.1 (4.0)
95% CI of LS mean	(-0.3, 15.3)	(-9.2, 6.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.3a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

Domain: Global Satisfaction

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 96		
n	21	21
LS mean (SE)	9.8 (3.8)	3.2 (3.9)
95% CI of LS mean	(2.0, 17.5)	(-4.6, 11.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.4a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Domain: Effectiveness

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), genotype group (F/F, F/G, F/RF, TCR/non-F), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	38	41
Parent study baseline		
n	35	38
Mean (SD)	81.3 (17.3)	79.2 (17.7)
Absolute change at Week 52		
n	31	36
LS mean (SE)	5.0 (3.9)	3.1 (3.6)
95% CI of LS mean	(-2.7, 12.7)	(-4.0, 10.3)
OL Efficacy Period for Part A		
N	33	31
Absolute change at OL Part A Week 24		
n	28	27
LS mean (SE)	3.4 (4.4)	4.7 (4.4)
95% CI of LS mean	(-5.4, 12.2)	(-4.2, 13.5)
Absolute change at OL Part A Week 48		
n	29	24
LS mean (SE)	-0.4 (5.8)	-9.0 (6.3)
95% CI of LS mean	(-12.0, 11.3)	(-21.5, 3.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), genotype group (F/F, F/G, F/RF, TCR/non-F), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.4a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Domain: Effectiveness

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 96		
n	29	26
LS mean (SE)	8.8 (4.3)	6.0 (4.5)
95% CI of LS mean	(0.1, 17.5)	(-3.0, 15.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), genotype group (F/F, F/G, F/RF, TCR/non-F), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.4a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Domain: Side Effects

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), genotype group (F/F, F/G, F/RF, TCR/non-F), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-104

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	38	41
Parent study baseline		
n	35	38
Mean (SD)	100.0 (0.0)	95.2 (12.1)
Absolute change at Week 52		
n	31	36
LS mean (SE)	-6.1 (2.6)	0.0 (2.4)
95% CI of LS mean	(-11.4, -0.9)	(-4.9, 4.8)
OL Efficacy Period for Part A		
N	33	31
Absolute change at OL Part A Week 24		
n	28	27
LS mean (SE)	-1.2 (2.0)	2.0 (2.0)
95% CI of LS mean	(-5.1, 2.7)	(-2.0, 6.0)
Absolute change at OL Part A Week 48		
n	28	24
LS mean (SE)	-2.3 (2.8)	1.1 (2.9)
95% CI of LS mean	(-8.1, 3.5)	(-4.8, 7.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), genotype group (F/F, F/G, F/RF, TCR/non-F), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.4a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Domain: Side Effects

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 96		
n	29	26
LS mean (SE)	-1.0 (1.0)	0.7 (1.0)
95% CI of LS mean	(-3.0, 1.0)	(-1.4, 2.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), genotype group (F/F, F/G, F/RF, TCR/non-F), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.4a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Domain: Convenience

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), genotype group (F/F, F/G, F/RF, TCR/non-F), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-104

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	38	41
Parent study baseline		
n	35	37
Mean (SD)	82.2 (15.4)	83.0 (16.2)
Absolute change at Week 52		
n	31	35
LS mean (SE)	2.0 (3.0)	0.0 (2.8)
95% CI of LS mean	(-4.0, 8.1)	(-5.7, 5.7)
OL Efficacy Period for Part A		
N	33	31
Absolute change at OL Part A Week 24		
n	28	26
LS mean (SE)	4.7 (3.7)	5.3 (3.8)
95% CI of LS mean	(-2.7, 12.1)	(-2.3, 12.8)
Absolute change at OL Part A Week 48		
n	29	24
LS mean (SE)	7.5 (3.3)	3.4 (3.4)
95% CI of LS mean	(0.9, 14.0)	(-3.4, 10.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), genotype group (F/F, F/G, F/RF, TCR/non-F), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.4a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Domain: Convenience

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 96		
n	29	26
LS mean (SE)	7.1 (3.3)	6.7 (3.4)
95% CI of LS mean	(0.4, 13.7)	(-0.2, 13.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), genotype group (F/F, F/G, F/RF, TCR/non-F), visit, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.4a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Domain: Global Satisfaction

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), genotype group (F/F, F/G, F/RF, TCR/non-F), visit, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-104

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	38	41
Parent study baseline		
n	35	38
Mean (SD)	86.3 (12.7)	86.0 (15.0)
Absolute change at Week 52		
n	31	36
LS mean (SE)	2.6 (3.1)	2.0 (2.8)
95% CI of LS mean	(-3.5, 8.7)	(-3.7, 7.7)
OL Efficacy Period for Part A		
N	33	31
Absolute change at OL Part A Week 24		
n	28	27
LS mean (SE)	3.0 (2.6)	2.7 (2.7)
95% CI of LS mean	(-2.4, 8.3)	(-2.6, 8.1)
Absolute change at OL Part A Week 48		
n	29	24
LS mean (SE)	3.8 (2.8)	6.8 (2.9)
95% CI of LS mean	(-1.7, 9.4)	(1.1, 12.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), genotype group (F/F, F/G, F/RF, TCR/non-F), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.4a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Domain: Global Satisfaction

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 96		
n	29	26
LS mean (SE)	6.3 (2.7)	8.2 (2.8)
95% CI of LS mean	(0.8, 11.7)	(2.6, 13.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis with weights based on all subjects 12 to <18 years old and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), genotype group (F/F, F/G, F/RF, TCR/non-F), visit, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.8.1.1a
Summary of BMI (kg/m^2) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	170	165
	Mean (SD)	23.01 (3.88)	22.86 (3.46)
	Median	22.40	22.39
	Min, max	15.81, 44.72	14.28, 35.31
OL Part A Day 15	n	167	162
	Mean (SD)	23.06 (3.74)	23.05 (3.12)
	Median	22.31	22.74
	Min, max	15.62, 41.96	15.81, 33.47
Change at OL Part A Day 15	n	167	161
	Mean (SD)	0.09 (1.36)	0.33 (1.27)
	Median	0.00	0.31
	Min, max	-5.40, 3.84	-3.73, 3.72
OL Part A Week 4	n	167	162
	Mean (SD)	23.16 (3.73)	23.18 (3.25)
	Median	22.47	22.79
	Min, max	15.22, 41.40	16.18, 34.76
Change at OL Part A Week 4	n	167	161
	Mean (SD)	0.10 (1.38)	0.32 (1.28)
	Median	0.00	0.29
	Min, max	-5.40, 3.91	-3.73, 3.72

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.1.1a
Summary of BMI (kg/m^2) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 8	n	169	164
	Mean (SD)	23.11 (3.68)	23.06 (3.27)
	Median	22.43	22.81
	Min, max	15.43, 42.14	15.43, 33.71
Change at OL Part A Week 8	n	169	163
	Mean (SD)	0.07 (1.44)	0.23 (1.34)
	Median	0.00	0.13
	Min, max	-5.79, 4.73	-3.73, 3.57
OL Part A Week 16	n	168	163
	Mean (SD)	23.22 (3.63)	23.14 (3.28)
	Median	22.53	22.88
	Min, max	15.82, 41.96	15.43, 33.22
Change at OL Part A Week 16	n	168	162
	Mean (SD)	0.22 (1.60)	0.28 (1.31)
	Median	0.07	0.27
	Min, max	-5.79, 4.60	-2.81, 3.96
OL Part A Week 24	n	166	160
	Mean (SD)	23.27 (3.74)	23.10 (3.25)
	Median	22.78	22.70
	Min, max	16.02, 42.88	15.97, 33.35
Change at OL Part A Week 24	n	166	159
	Mean (SD)	0.25 (1.66)	0.26 (1.51)
	Median	0.31	0.10
	Min, max	-6.42, 5.11	-4.67, 3.97

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.1.1a
Summary of BMI (kg/m^2) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 36	n	162	160
	Mean (SD)	23.25 (3.84)	23.16 (3.32)
	Median	22.52	22.83
	Min, max	16.33, 42.69	16.28, 34.82
Change at OL Part A Week 36	n	162	159
	Mean (SD)	0.21 (1.72)	0.35 (1.55)
	Median	0.00	0.30
	Min, max	-6.07, 6.38	-4.38, 4.97
OL Part A Week 48	n	157	157
	Mean (SD)	23.32 (3.82)	23.12 (3.23)
	Median	22.66	22.66
	Min, max	16.33, 41.96	16.30, 35.29
Change at OL Part A Week 48	n	157	156
	Mean (SD)	0.35 (1.75)	0.36 (1.69)
	Median	0.33	0.32
	Min, max	-5.79, 7.66	-6.17, 6.14
OL Part A Week 60	n	156	153
	Mean (SD)	23.40 (3.92)	23.11 (3.34)
	Median	22.56	22.41
	Min, max	15.59, 44.35	16.28, 36.05
Change at OL Part A Week 60	n	156	152
	Mean (SD)	0.36 (1.77)	0.34 (1.59)
	Median	0.08	0.32
	Min, max	-5.02, 6.06	-3.88, 6.93

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.1.1a
Summary of BMI (kg/m^2) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 72	n	155	153
	Mean (SD)	23.51 (3.87)	23.19 (3.27)
	Median	22.89	22.72
	Min, max	15.92, 44.90	16.65, 36.33
Change at OL Part A Week 72	n	155	152
	Mean (SD)	0.44 (1.92)	0.43 (1.66)
	Median	0.21	0.29
	Min, max	-5.02, 6.38	-4.00, 7.32
OL Part A Week 84	n	153	147
	Mean (SD)	23.52 (3.79)	23.14 (3.20)
	Median	22.66	22.66
	Min, max	15.22, 43.06	16.28, 36.67
Change at OL Part A Week 84	n	153	146
	Mean (SD)	0.42 (1.94)	0.43 (1.72)
	Median	0.28	0.30
	Min, max	-5.79, 7.02	-5.64, 7.33
OL Part A Week 96	n	151	145
	Mean (SD)	23.63 (3.76)	23.09 (3.18)
	Median	22.95	22.59
	Min, max	16.46, 41.77	16.28, 36.18
Change at OL Part A Week 96	n	151	144
	Mean (SD)	0.48 (2.07)	0.37 (1.73)
	Median	0.32	0.06
	Min, max	-5.79, 7.66	-5.30, 8.49

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.1.2a
Summary of BMI (kg/m^2) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	248	236
	Mean (SD)	22.90 (3.35)	23.24 (3.80)
	Median	22.77	22.48
	Min, max	15.43, 35.42	15.56, 39.84
OL Part A Day 15	n	240	235
	Mean (SD)	23.17 (3.49)	23.67 (3.86)
	Median	22.86	22.94
	Min, max	15.99, 34.85	15.93, 37.11
Change at OL Part A Day 15	n	240	233
	Mean (SD)	0.22 (1.23)	0.39 (1.28)
	Median	0.31	0.33
	Min, max	-5.27, 4.30	-4.39, 4.99
OL Part A Week 4	n	243	230
	Mean (SD)	23.17 (3.51)	23.65 (3.81)
	Median	23.01	22.98
	Min, max	15.43, 35.25	15.64, 36.39
Change at OL Part A Week 4	n	243	228
	Mean (SD)	0.24 (1.26)	0.40 (1.26)
	Median	0.32	0.32
	Min, max	-5.65, 4.69	-4.39, 4.63

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.1.2a
Summary of BMI (kg/m^2) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 8	n	245	234
	Mean (SD)	23.18 (3.47)	23.64 (3.83)
	Median	22.86	22.99
	Min, max	15.24, 34.85	16.07, 37.89
Change at OL Part A Week 8	n	245	232
	Mean (SD)	0.26 (1.23)	0.38 (1.30)
	Median	0.33	0.29
	Min, max	-6.40, 4.30	-4.73, 5.02
OL Part A Week 16	n	241	229
	Mean (SD)	23.22 (3.52)	23.72 (3.83)
	Median	22.84	23.04
	Min, max	15.44, 35.65	16.07, 36.33
Change at OL Part A Week 16	n	241	227
	Mean (SD)	0.30 (1.30)	0.47 (1.35)
	Median	0.33	0.38
	Min, max	-6.50, 4.30	-4.06, 5.79
OL Part A Week 24	n	240	230
	Mean (SD)	23.30 (3.52)	23.69 (3.75)
	Median	23.08	23.04
	Min, max	15.16, 35.65	16.07, 37.20
Change at OL Part A Week 24	n	240	228
	Mean (SD)	0.36 (1.34)	0.46 (1.49)
	Median	0.37	0.35
	Min, max	-6.40, 4.30	-5.08, 6.17

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.1.2a
Summary of BMI (kg/m^2) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 36	n	235	225
	Mean (SD)	23.24 (3.53)	23.76 (3.69)
	Median	23.05	23.14
	Min, max	15.73, 35.64	16.07, 36.85
Change at OL Part A Week 36	n	235	223
	Mean (SD)	0.33 (1.49)	0.47 (1.54)
	Median	0.33	0.42
	Min, max	-5.39, 5.75	-5.13, 5.14
OL Part A Week 48	n	232	222
	Mean (SD)	23.21 (3.53)	23.81 (3.67)
	Median	22.99	23.07
	Min, max	15.44, 35.29	16.07, 37.73
Change at OL Part A Week 48	n	232	220
	Mean (SD)	0.33 (1.48)	0.52 (1.57)
	Median	0.33	0.40
	Min, max	-4.89, 5.09	-5.69, 4.46
OL Part A Week 60	n	229	219
	Mean (SD)	23.33 (3.62)	23.88 (3.66)
	Median	22.94	23.33
	Min, max	15.83, 35.99	15.96, 37.02
Change at OL Part A Week 60	n	229	217
	Mean (SD)	0.41 (1.62)	0.56 (1.72)
	Median	0.35	0.38
	Min, max	-6.16, 6.99	-6.64, 5.14

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.1.2a
Summary of BMI (kg/m^2) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 72	n	226	216
	Mean (SD)	23.36 (3.54)	24.04 (3.65)
	Median	23.21	23.56
	Min, max	16.01, 36.68	16.28, 36.85
Change at OL Part A Week 72	n	226	214
	Mean (SD)	0.44 (1.47)	0.70 (1.78)
	Median	0.37	0.41
	Min, max	-3.16, 5.58	-5.47, 5.14
OL Part A Week 84	n	226	213
	Mean (SD)	23.45 (3.56)	24.04 (3.61)
	Median	23.39	23.46
	Min, max	16.30, 37.02	16.65, 36.49
Change at OL Part A Week 84	n	226	211
	Mean (SD)	0.54 (1.58)	0.71 (1.85)
	Median	0.39	0.62
	Min, max	-3.59, 6.89	-4.69, 5.79
OL Part A Week 96	n	222	211
	Mean (SD)	23.57 (4.14)	24.08 (3.63)
	Median	22.93	23.46
	Min, max	16.59, 55.40	16.65, 37.38
Change at OL Part A Week 96	n	222	209
	Mean (SD)	0.70 (2.65)	0.71 (1.91)
	Median	0.50	0.62
	Min, max	-3.25, 31.79	-5.47, 5.49

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.8.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI (kg/m^2) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	202	195
Mean (SD)	23.03 (3.85)	22.71 (3.40)
Absolute change at Day 15		
n	196	190
LS mean (SE)	0.07 (0.03)	0.02 (0.03)
95% CI of LS mean	(0.01, 0.13)	(-0.04, 0.09)
Absolute change at Week 4		
n	195	183
LS mean (SE)	0.05 (0.04)	0.01 (0.04)
95% CI of LS mean	(-0.02, 0.12)	(-0.06, 0.08)
Absolute change at Week 8		
n	194	188
LS mean (SE)	0.08 (0.04)	0.09 (0.04)
95% CI of LS mean	(0.00, 0.16)	(0.01, 0.17)
Absolute change at Week 16		
n	195	187
LS mean (SE)	0.11 (0.05)	0.11 (0.06)
95% CI of LS mean	(0.01, 0.22)	(0.00, 0.22)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.8.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI (kg/m^2) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	195	186
LS mean (SE)	0.11 (0.07)	0.09 (0.07)
95% CI of LS mean	(-0.02, 0.24)	(-0.04, 0.22)
Absolute change at Week 36		
n	193	182
LS mean (SE)	0.08 (0.08)	0.16 (0.08)
95% CI of LS mean	(-0.08, 0.23)	(0.00, 0.32)
Absolute change at Week 52		
n	187	179
LS mean (SE)	0.08 (0.10)	0.30 (0.10)
95% CI of LS mean	(-0.11, 0.27)	(0.11, 0.49)
OL Efficacy Period for Part A		
N	170	166
Absolute change at OL Part A Day 15		
n	165	159
LS mean (SE)	0.12 (0.10)	0.31 (0.10)
95% CI of LS mean	(-0.07, 0.31)	(0.11, 0.50)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.8.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI (kg/m^2) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 4		
n	165	159
LS mean (SE)	0.13 (0.10)	0.31 (0.10)
95% CI of LS mean	(-0.06, 0.33)	(0.11, 0.50)
Absolute change at OL Part A Week 8		
n	167	161
LS mean (SE)	0.09 (0.10)	0.22 (0.11)
95% CI of LS mean	(-0.11, 0.29)	(0.02, 0.43)
Absolute change at OL Part A Week 16		
n	166	160
LS mean (SE)	0.24 (0.11)	0.28 (0.11)
95% CI of LS mean	(0.03, 0.45)	(0.07, 0.50)
Absolute change at OL Part A Week 24		
n	164	157
LS mean (SE)	0.27 (0.12)	0.26 (0.12)
95% CI of LS mean	(0.04, 0.50)	(0.02, 0.50)
Absolute change at OL Part A Week 36		
n	160	157
LS mean (SE)	0.23 (0.12)	0.32 (0.13)
95% CI of LS mean	(-0.01, 0.48)	(0.07, 0.57)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.8.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI (kg/m^2) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 48		
n	155	154
LS mean (SE)	0.33 (0.13)	0.35 (0.13)
95% CI of LS mean	(0.07, 0.58)	(0.09, 0.61)
Absolute change at OL Part A Week 60		
n	154	151
LS mean (SE)	0.35 (0.13)	0.33 (0.13)
95% CI of LS mean	(0.10, 0.59)	(0.08, 0.58)
Absolute change at OL Part A Week 72		
n	153	151
LS mean (SE)	0.42 (0.13)	0.44 (0.14)
95% CI of LS mean	(0.16, 0.69)	(0.17, 0.71)
Absolute change at OL Part A Week 84		
n	151	145
LS mean (SE)	0.41 (0.14)	0.47 (0.14)
95% CI of LS mean	(0.14, 0.69)	(0.20, 0.75)
Absolute change at OL Part A Week 96		
n	149	143
LS mean (SE)	0.47 (0.14)	0.42 (0.15)
95% CI of LS mean	(0.19, 0.76)	(0.13, 0.71)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-104

Table 14.2.8.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI (kg/m^2) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	289	280
Mean (SD)	22.92 (3.27)	23.27 (4.02)
Absolute change at Day 15		
n	275	270
LS mean (SE)	0.02 (0.02)	0.01 (0.02)
95% CI of LS mean	(-0.03, 0.07)	(-0.04, 0.06)
Absolute change at Week 4		
n	274	273
LS mean (SE)	0.01 (0.03)	0.06 (0.03)
95% CI of LS mean	(-0.04, 0.07)	(0.00, 0.12)
Absolute change at Week 8		
n	278	268
LS mean (SE)	0.07 (0.03)	0.09 (0.03)
95% CI of LS mean	(0.00, 0.14)	(0.03, 0.16)
Absolute change at Week 16		
n	276	262
LS mean (SE)	0.10 (0.05)	0.20 (0.05)
95% CI of LS mean	(0.00, 0.19)	(0.10, 0.29)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.8.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI (kg/m^2) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	274	259
LS mean (SE)	0.17 (0.06)	0.31 (0.06)
95% CI of LS mean	(0.06, 0.28)	(0.19, 0.42)
Absolute change at Week 36		
n	272	258
LS mean (SE)	0.17 (0.07)	0.33 (0.07)
95% CI of LS mean	(0.04, 0.31)	(0.19, 0.46)
Absolute change at Week 52		
n	266	248
LS mean (SE)	0.22 (0.07)	0.37 (0.08)
95% CI of LS mean	(0.07, 0.36)	(0.22, 0.52)
OL Efficacy Period for Part A		
N	248	238
Absolute change at OL Part A Day 15		
n	231	228
LS mean (SE)	0.19 (0.08)	0.40 (0.08)
95% CI of LS mean	(0.03, 0.35)	(0.24, 0.56)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.8.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI (kg/m^2) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 4		
n	234	223
LS mean (SE)	0.21 (0.08)	0.39 (0.08)
95% CI of LS mean	(0.05, 0.37)	(0.23, 0.56)
Absolute change at OL Part A Week 8		
n	236	227
LS mean (SE)	0.21 (0.08)	0.37 (0.08)
95% CI of LS mean	(0.05, 0.37)	(0.21, 0.54)
Absolute change at OL Part A Week 16		
n	232	222
LS mean (SE)	0.24 (0.09)	0.46 (0.09)
95% CI of LS mean	(0.07, 0.41)	(0.28, 0.63)
Absolute change at OL Part A Week 24		
n	231	223
LS mean (SE)	0.31 (0.09)	0.44 (0.09)
95% CI of LS mean	(0.13, 0.49)	(0.25, 0.62)
Absolute change at OL Part A Week 36		
n	226	218
LS mean (SE)	0.31 (0.10)	0.44 (0.10)
95% CI of LS mean	(0.11, 0.50)	(0.24, 0.63)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.8.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI (kg/m^2) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 48		
n	223	215
LS mean (SE)	0.29 (0.10)	0.51 (0.10)
95% CI of LS mean	(0.10, 0.48)	(0.31, 0.70)
Absolute change at OL Part A Week 60		
n	220	212
LS mean (SE)	0.39 (0.11)	0.54 (0.11)
95% CI of LS mean	(0.18, 0.60)	(0.32, 0.75)
Absolute change at OL Part A Week 72		
n	218	209
LS mean (SE)	0.42 (0.11)	0.67 (0.11)
95% CI of LS mean	(0.22, 0.63)	(0.46, 0.88)
Absolute change at OL Part A Week 84		
n	217	206
LS mean (SE)	0.49 (0.11)	0.68 (0.11)
95% CI of LS mean	(0.28, 0.71)	(0.45, 0.90)
Absolute change at OL Part A Week 96		
n	213	204
LS mean (SE)	0.68 (0.16)	0.67 (0.16)
95% CI of LS mean	(0.37, 0.98)	(0.36, 0.98)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.9.1.1a
Summary of BMI z-score and Change from Parent Study Baseline at Each Visit
for Subjects ≤20 Years at Parent Study Baseline - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 29	VNZ/TEZ/D-IVA in 121-102 N = 28
Parent study baseline	n	29	28
	Mean (SD)	-0.13 (0.77)	-0.43 (1.13)
	Median	-0.31	-0.35
	Min, max	-1.31, 1.56	-4.15, 1.92
OL Part A Day 15	n	23	25
	Mean (SD)	-0.14 (0.75)	-0.19 (0.99)
	Median	-0.19	-0.06
	Min, max	-1.81, 1.78	-3.14, 1.26
Change at OL Part A Day 15	n	23	25
	Mean (SD)	0.03 (0.41)	0.29 (0.55)
	Median	0.13	0.27
	Min, max	-0.73, 0.79	-0.67, 1.27
OL Part A Week 4	n	24	25
	Mean (SD)	-0.11 (0.86)	-0.17 (0.95)
	Median	-0.15	-0.16
	Min, max	-2.12, 1.77	-2.82, 1.26
Change at OL Part A Week 4	n	24	25
	Mean (SD)	0.01 (0.48)	0.31 (0.50)
	Median	0.11	0.27
	Min, max	-0.90, 0.96	-0.67, 1.32

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.9.1.1a
Summary of BMI z-score and Change from Parent Study Baseline at Each Visit
for Subjects ≤20 Years at Parent Study Baseline - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 29	VNZ/TEZ/D-IVA in 121-102 N = 28
OL Part A Week 8	n	24	25
	Mean (SD)	-0.13 (0.84)	-0.23 (1.07)
	Median	-0.16	-0.17
	Min, max	-1.99, 1.81	-3.51, 1.24
Change at OL Part A Week 8	n	24	25
	Mean (SD)	-0.01 (0.54)	0.25 (0.50)
	Median	0.09	0.25
	Min, max	-0.97, 1.05	-0.68, 1.23
OL Part A Week 16	n	23	25
	Mean (SD)	-0.11 (0.76)	-0.21 (1.07)
	Median	-0.16	-0.15
	Min, max	-1.76, 1.84	-3.58, 1.39
Change at OL Part A Week 16	n	23	25
	Mean (SD)	0.08 (0.64)	0.27 (0.49)
	Median	0.24	0.24
	Min, max	-1.56, 1.23	-0.63, 1.26
OL Part A Week 24	n	23	24
	Mean (SD)	-0.13 (0.79)	-0.18 (1.05)
	Median	-0.12	-0.03
	Min, max	-1.69, 1.79	-3.16, 1.26
Change at OL Part A Week 24	n	23	24
	Mean (SD)	0.05 (0.72)	0.28 (0.56)
	Median	0.08	0.35
	Min, max	-2.00, 1.16	-0.80, 1.08

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.9.1.1a
Summary of BMI z-score and Change from Parent Study Baseline at Each Visit
for Subjects ≤20 Years at Parent Study Baseline - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 29	VNZ/TEZ/D-IVA in 121-102 N = 28
OL Part A Week 36	n	22	24
	Mean (SD)	-0.28 (0.79)	-0.19 (1.04)
	Median	-0.44	-0.07
	Min, max	-1.54, 1.63	-2.77, 1.37
Change at OL Part A Week 36	n	22	24
	Mean (SD)	-0.06 (0.66)	0.27 (0.58)
	Median	0.10	0.28
	Min, max	-1.90, 1.20	-0.76, 1.38
OL Part A Week 48	n	22	23
	Mean (SD)	-0.22 (0.78)	-0.11 (0.99)
	Median	-0.16	0.03
	Min, max	-1.65, 1.56	-2.35, 1.49
Change at OL Part A Week 48	n	22	23
	Mean (SD)	0.00 (0.65)	0.33 (0.67)
	Median	0.05	0.42
	Min, max	-1.56, 1.02	-1.40, 1.79
OL Part A Week 60	n	19	21
	Mean (SD)	-0.22 (0.90)	-0.11 (1.04)
	Median	-0.17	-0.16
	Min, max	-1.99, 1.44	-2.33, 1.56
Change at OL Part A Week 60	n	19	21
	Mean (SD)	0.03 (0.66)	0.32 (0.62)
	Median	0.24	0.30
	Min, max	-1.10, 1.15	-0.83, 1.81

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.9.1.1a
Summary of BMI z-score and Change from Parent Study Baseline at Each Visit
for Subjects ≤20 Years at Parent Study Baseline - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 29	VNZ/TEZ/D-IVA in 121-102 N = 28
OL Part A Week 72	n	19	22
	Mean (SD)	-0.07 (0.80)	-0.14 (0.99)
	Median	-0.01	-0.12
	Min, max	-1.73, 1.48	-2.66, 1.59
Change at OL Part A Week 72	n	19	22
	Mean (SD)	0.18 (0.67)	0.25 (0.61)
	Median	0.49	0.21
	Min, max	-1.28, 1.01	-0.93, 1.49
OL Part A Week 84	n	19	21
	Mean (SD)	-0.08 (0.90)	-0.21 (1.00)
	Median	-0.01	-0.01
	Min, max	-2.29, 1.52	-2.63, 1.58
Change at OL Part A Week 84	n	19	21
	Mean (SD)	0.18 (0.80)	0.19 (0.68)
	Median	0.47	0.37
	Min, max	-1.52, 1.30	-1.38, 1.52
OL Part A Week 96	n	18	21
	Mean (SD)	-0.10 (0.86)	-0.22 (0.93)
	Median	-0.08	-0.01
	Min, max	-1.58, 1.60	-2.19, 1.67
Change at OL Part A Week 96	n	18	21
	Mean (SD)	0.18 (0.78)	0.18 (0.70)
	Median	0.44	0.20
	Min, max	-1.94, 0.92	-1.33, 1.95

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.9.1.2a
Summary of BMI z-score and Change from Parent Study Baseline at Each Visit
for Subjects ≤20 Years at Parent Study Baseline - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 36	VNZ/TEZ/D-IVA in 121-103 N = 42
Parent study baseline	n	36	42
	Mean (SD)	-0.33 (1.03)	-0.08 (0.98)
	Median	-0.26	-0.03
	Min, max	-3.07, 1.21	-2.62, 2.12
OL Part A Day 15	n	33	35
	Mean (SD)	-0.31 (0.93)	0.06 (1.04)
	Median	-0.22	0.01
	Min, max	-2.12, 1.00	-2.83, 2.21
Change at OL Part A Day 15	n	33	35
	Mean (SD)	-0.06 (0.55)	0.08 (0.33)
	Median	0.04	0.10
	Min, max	-1.78, 0.96	-0.72, 0.61
OL Part A Week 4	n	33	35
	Mean (SD)	-0.40 (1.00)	0.10 (1.00)
	Median	-0.23	-0.01
	Min, max	-2.60, 1.00	-2.21, 2.35
Change at OL Part A Week 4	n	33	35
	Mean (SD)	-0.06 (0.57)	0.13 (0.31)
	Median	0.03	0.14
	Min, max	-1.94, 0.93	-0.72, 0.59

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.9.1.2a
Summary of BMI z-score and Change from Parent Study Baseline at Each Visit
for Subjects ≤20 Years at Parent Study Baseline - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 36	VNZ/TEZ/D-IVA in 121-103 N = 42
OL Part A Week 8	n	34	35
	Mean (SD)	-0.38 (1.06)	0.11 (0.90)
	Median	-0.11	-0.05
	Min, max	-2.83, 1.07	-1.55, 2.21
Change at OL Part A Week 8	n	34	35
	Mean (SD)	-0.07 (0.59)	0.14 (0.38)
	Median	0.04	0.14
	Min, max	-2.31, 0.77	-0.72, 1.40
OL Part A Week 16	n	34	36
	Mean (SD)	-0.42 (1.04)	0.09 (0.91)
	Median	-0.05	0.10
	Min, max	-2.63, 1.05	-1.57, 2.20
Change at OL Part A Week 16	n	34	36
	Mean (SD)	-0.11 (0.68)	0.12 (0.40)
	Median	0.04	0.13
	Min, max	-2.40, 1.11	-0.82, 1.39
OL Part A Week 24	n	33	34
	Mean (SD)	-0.39 (1.02)	0.12 (0.94)
	Median	-0.11	0.12
	Min, max	-2.49, 0.94	-1.98, 2.22
Change at OL Part A Week 24	n	33	34
	Mean (SD)	-0.08 (0.65)	0.12 (0.51)
	Median	-0.05	0.22
	Min, max	-2.39, 0.87	-1.60, 0.92

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.9.1.2a
Summary of BMI z-score and Change from Parent Study Baseline at Each Visit
for Subjects ≤20 Years at Parent Study Baseline - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 36	VNZ/TEZ/D-IVA in 121-103 N = 42
OL Part A Week 36	n	33	33
	Mean (SD)	-0.41 (1.05)	0.25 (0.83)
	Median	-0.20	0.35
	Min, max	-2.68, 1.01	-1.64, 2.31
Change at OL Part A Week 36	n	33	33
	Mean (SD)	-0.10 (0.69)	0.16 (0.45)
	Median	0.11	0.16
	Min, max	-1.98, 1.11	-1.42, 0.88
OL Part A Week 48	n	33	28
	Mean (SD)	-0.38 (1.11)	0.25 (0.84)
	Median	-0.18	0.23
	Min, max	-4.01, 0.98	-1.67, 2.24
Change at OL Part A Week 48	n	33	28
	Mean (SD)	-0.07 (0.72)	0.10 (0.50)
	Median	0.02	0.17
	Min, max	-1.80, 1.60	-1.71, 0.77
OL Part A Week 60	n	33	28
	Mean (SD)	-0.35 (1.07)	0.31 (0.88)
	Median	-0.19	0.26
	Min, max	-3.81, 1.10	-1.95, 2.32
Change at OL Part A Week 60	n	33	28
	Mean (SD)	-0.04 (0.76)	0.14 (0.55)
	Median	0.04	0.23
	Min, max	-1.84, 1.44	-1.90, 0.85

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.9.1.2a
Summary of BMI z-score and Change from Parent Study Baseline at Each Visit
for Subjects ≤20 Years at Parent Study Baseline - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 36	VNZ/TEZ/D-IVA in 121-103 N = 42
OL Part A Week 72	n	30	27
	Mean (SD)	-0.31 (0.89)	0.30 (0.90)
	Median	-0.26	0.28
	Min, max	-2.07, 1.06	-1.97, 2.41
Change at OL Part A Week 72	n	30	27
	Mean (SD)	-0.01 (0.72)	0.12 (0.55)
	Median	0.02	0.33
	Min, max	-1.57, 1.57	-1.56, 0.86
OL Part A Week 84	n	28	26
	Mean (SD)	-0.34 (0.92)	0.27 (0.91)
	Median	-0.23	0.27
	Min, max	-2.13, 0.98	-2.26, 2.27
Change at OL Part A Week 84	n	28	26
	Mean (SD)	0.00 (0.69)	0.10 (0.59)
	Median	0.07	0.37
	Min, max	-1.44, 1.35	-1.27, 0.78
OL Part A Week 96	n	28	24
	Mean (SD)	-0.30 (0.87)	0.37 (0.74)
	Median	-0.09	0.27
	Min, max	-1.98, 0.99	-0.89, 2.14
Change at OL Part A Week 96	n	28	24
	Mean (SD)	0.04 (0.67)	0.10 (0.58)
	Median	0.06	0.29
	Min, max	-1.49, 1.29	-1.52, 0.86

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.9.2.1a

MMRM Analysis of Absolute Change from Parent Study Baseline in BMI z-score at Each Visit for Subjects ≤20 Years at Parent Study Baseline - Parent Study Efficacy Period and OL Efficacy Period for Part A

Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-104

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	40	32
Parent study baseline		
n	40	32
Mean (SD)	-0.14 (0.88)	-0.36 (1.09)
Absolute change at Day 15		
n	38	31
LS mean (SE)	-0.01 (0.03)	0.04 (0.03)
95% CI of LS mean	(-0.07, 0.05)	(-0.02, 0.11)
Absolute change at Week 4		
n	38	31
LS mean (SE)	0.01 (0.04)	0.02 (0.04)
95% CI of LS mean	(-0.06, 0.08)	(-0.06, 0.10)
Absolute change at Week 8		
n	38	31
LS mean (SE)	0.01 (0.04)	0.02 (0.05)
95% CI of LS mean	(-0.08, 0.09)	(-0.07, 0.12)
Absolute change at Week 16		
n	38	28
LS mean (SE)	0.04 (0.05)	0.08 (0.06)
95% CI of LS mean	(-0.07, 0.14)	(-0.04, 0.20)

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.9.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI z-score at Each Visit for Subjects ≤20 Years at Parent Study Baseline - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	36	28
LS mean (SE)	0.03 (0.06)	0.06 (0.06)
95% CI of LS mean	(-0.09, 0.14)	(-0.07, 0.19)
Absolute change at Week 36		
n	35	28
LS mean (SE)	-0.03 (0.07)	0.14 (0.08)
95% CI of LS mean	(-0.18, 0.11)	(-0.02, 0.31)
Absolute change at Week 52		
n	32	27
LS mean (SE)	-0.09 (0.09)	0.25 (0.10)
95% CI of LS mean	(-0.27, 0.09)	(0.05, 0.45)
OL Efficacy Period for Part A		
N	29	28
Absolute change at OL Part A Day 15		
n	23	24
LS mean (SE)	0.04 (0.10)	0.29 (0.10)
95% CI of LS mean	(-0.17, 0.24)	(0.09, 0.50)

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.9.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI z-score at Each Visit for Subjects ≤20 Years at Parent Study Baseline - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 4		
n	24	24
LS mean (SE)	0.01 (0.10)	0.31 (0.10)
95% CI of LS mean	(-0.20, 0.22)	(0.11, 0.52)
Absolute change at OL Part A Week 8		
n	24	24
LS mean (SE)	-0.01 (0.11)	0.25 (0.11)
95% CI of LS mean	(-0.23, 0.21)	(0.03, 0.47)
Absolute change at OL Part A Week 16		
n	23	24
LS mean (SE)	0.07 (0.12)	0.27 (0.12)
95% CI of LS mean	(-0.17, 0.31)	(0.04, 0.51)
Absolute change at OL Part A Week 24		
n	23	23
LS mean (SE)	0.04 (0.13)	0.30 (0.13)
95% CI of LS mean	(-0.23, 0.31)	(0.04, 0.57)
Absolute change at OL Part A Week 36		
n	22	23
LS mean (SE)	-0.09 (0.13)	0.29 (0.13)
95% CI of LS mean	(-0.36, 0.17)	(0.03, 0.55)

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.9.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI z-score at Each Visit for Subjects ≤20 Years at Parent Study Baseline - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 48		
n	22	22
LS mean (SE)	-0.02 (0.14)	0.31 (0.14)
95% CI of LS mean	(-0.30, 0.25)	(0.04, 0.59)
Absolute change at OL Part A Week 60		
n	19	20
LS mean (SE)	-0.08 (0.14)	0.29 (0.14)
95% CI of LS mean	(-0.37, 0.21)	(0.00, 0.57)
Absolute change at OL Part A Week 72		
n	19	21
LS mean (SE)	0.04 (0.15)	0.28 (0.15)
95% CI of LS mean	(-0.26, 0.34)	(-0.02, 0.57)
Absolute change at OL Part A Week 84		
n	19	20
LS mean (SE)	0.03 (0.17)	0.18 (0.17)
95% CI of LS mean	(-0.32, 0.38)	(-0.17, 0.52)
Absolute change at OL Part A Week 96		
n	18	20
LS mean (SE)	0.01 (0.17)	0.16 (0.17)
95% CI of LS mean	(-0.33, 0.36)	(-0.18, 0.50)

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.9.2.2a

MMRM Analysis of Absolute Change from Parent Study Baseline in BMI z-score at Each Visit for Subjects ≤20 Years at Parent Study Baseline - Parent Study Efficacy Period and OL Efficacy Period for Part A

Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, genotype group, and treatment-by-visit interaction, with parent study baseline ppFEV$_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-104

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	42	53
Parent study baseline		
n	42	53
Mean (SD)	-0.30 (0.98)	-0.17 (0.95)
Absolute change at Day 15		
n	39	52
LS mean (SE)	0.00 (0.03)	0.00 (0.02)
95% CI of LS mean	(-0.05, 0.06)	(-0.04, 0.05)
Absolute change at Week 4		
n	38	52
LS mean (SE)	-0.05 (0.03)	0.03 (0.03)
95% CI of LS mean	(-0.12, 0.02)	(-0.03, 0.09)
Absolute change at Week 8		
n	39	52
LS mean (SE)	-0.01 (0.04)	0.03 (0.03)
95% CI of LS mean	(-0.08, 0.07)	(-0.04, 0.10)
Absolute change at Week 16		
n	38	50
LS mean (SE)	-0.01 (0.05)	0.07 (0.05)
95% CI of LS mean	(-0.12, 0.10)	(-0.02, 0.16)

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.9.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI z-score at Each Visit for Subjects ≤20 Years at Parent Study Baseline - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	37	49
LS mean (SE)	-0.07 (0.06)	0.12 (0.05)
95% CI of LS mean	(-0.18, 0.04)	(0.03, 0.22)
Absolute change at Week 36		
n	36	43
LS mean (SE)	-0.17 (0.08)	0.12 (0.07)
95% CI of LS mean	(-0.33, -0.02)	(-0.01, 0.25)
Absolute change at Week 52		
n	35	42
LS mean (SE)	-0.13 (0.07)	0.11 (0.06)
95% CI of LS mean	(-0.27, 0.01)	(-0.01, 0.23)
OL Efficacy Period for Part A		
N	36	42
Absolute change at OL Part A Day 15		
n	31	35
LS mean (SE)	-0.09 (0.08)	0.05 (0.07)
95% CI of LS mean	(-0.24, 0.06)	(-0.09, 0.20)

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.9.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI z-score at Each Visit for Subjects ≤20 Years at Parent Study Baseline - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 4		
n	31	35
LS mean (SE)	-0.07 (0.08)	0.09 (0.07)
95% CI of LS mean	(-0.22, 0.08)	(-0.05, 0.24)
Absolute change at OL Part A Week 8		
n	32	35
LS mean (SE)	-0.10 (0.08)	0.12 (0.08)
95% CI of LS mean	(-0.26, 0.07)	(-0.04, 0.27)
Absolute change at OL Part A Week 16		
n	32	36
LS mean (SE)	-0.13 (0.09)	0.09 (0.09)
95% CI of LS mean	(-0.32, 0.06)	(-0.09, 0.26)
Absolute change at OL Part A Week 24		
n	31	34
LS mean (SE)	-0.07 (0.10)	0.07 (0.09)
95% CI of LS mean	(-0.27, 0.13)	(-0.12, 0.26)
Absolute change at OL Part A Week 36		
n	31	33
LS mean (SE)	-0.10 (0.10)	0.13 (0.09)
95% CI of LS mean	(-0.30, 0.10)	(-0.05, 0.32)

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.9.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in BMI z-score at Each Visit for Subjects ≤20 Years at Parent Study Baseline - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 48		
n	31	28
LS mean (SE)	-0.06 (0.11)	0.09 (0.11)
95% CI of LS mean	(-0.28, 0.15)	(-0.12, 0.30)
Absolute change at OL Part A Week 60		
n	31	28
LS mean (SE)	-0.03 (0.12)	0.08 (0.11)
95% CI of LS mean	(-0.26, 0.20)	(-0.14, 0.31)
Absolute change at OL Part A Week 72		
n	28	27
LS mean (SE)	-0.05 (0.12)	0.09 (0.12)
95% CI of LS mean	(-0.30, 0.20)	(-0.15, 0.32)
Absolute change at OL Part A Week 84		
n	26	26
LS mean (SE)	-0.08 (0.12)	0.07 (0.12)
95% CI of LS mean	(-0.33, 0.16)	(-0.16, 0.31)
Absolute change at OL Part A Week 96		
n	26	24
LS mean (SE)	-0.01 (0.12)	0.02 (0.12)
95% CI of LS mean	(-0.26, 0.23)	(-0.22, 0.25)

- N is the number of subjects in the specified analysis set who are ≤20 years of age at parent study baseline.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.10.1.1a
Summary of Weight (kg) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
Parent study baseline	n	170	165
	Mean (SD)	64.64 (13.94)	66.24 (13.64)
	Median	63.00	65.00
	Min, max	33.00, 116.57	33.00, 130.18
OL Part A Day 15	n	167	162
	Mean (SD)	65.10 (13.29)	66.84 (12.34)
	Median	63.00	65.00
	Min, max	38.00, 112.94	42.00, 123.38
Change at OL Part A Day 15	n	167	161
	Mean (SD)	0.57 (4.04)	1.13 (3.79)
	Median	0.45	1.00
	Min, max	-14.00, 13.00	-9.00, 12.00
OL Part A Week 4	n	167	162
	Mean (SD)	65.39 (13.34)	67.35 (12.69)
	Median	63.00	65.50
	Min, max	38.00, 114.00	43.00, 122.00
Change at OL Part A Week 4	n	167	161
	Mean (SD)	0.60 (4.08)	1.12 (3.88)
	Median	0.00	1.00
	Min, max	-14.00, 13.00	-10.00, 12.00

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.10.1.1a
Summary of Weight (kg) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 8	n	169	164
	Mean (SD)	65.29 (13.15)	66.97 (12.63)
	Median	63.00	65.39
	Min, max	39.00, 110.00	41.00, 123.38
Change at OL Part A Week 8	n	169	163
	Mean (SD)	0.54 (4.31)	0.85 (4.02)
	Median	0.00	0.93
	Min, max	-15.00, 16.00	-12.00, 12.00
OL Part A Week 16	n	168	163
	Mean (SD)	65.57 (12.90)	67.32 (12.67)
	Median	63.28	67.00
	Min, max	38.00, 109.00	42.00, 122.47
Change at OL Part A Week 16	n	168	162
	Mean (SD)	0.98 (4.77)	1.03 (4.04)
	Median	0.39	0.95
	Min, max	-15.00, 15.00	-9.00, 12.00
OL Part A Week 24	n	166	160
	Mean (SD)	65.76 (13.09)	67.23 (12.42)
	Median	63.98	66.00
	Min, max	38.00, 107.00	44.00, 122.92
Change at OL Part A Week 24	n	166	159
	Mean (SD)	1.09 (5.10)	0.98 (4.70)
	Median	1.00	0.91
	Min, max	-17.00, 16.00	-16.00, 14.00

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.10.1.1a
Summary of Weight (kg) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 36	n	162	160
	Mean (SD)	65.87 (13.29)	67.34 (12.50)
	Median	64.00	66.34
	Min, max	37.00, 106.00	44.00, 128.37
Change at OL Part A Week 36	n	162	159
	Mean (SD)	1.08 (5.35)	1.26 (4.82)
	Median	0.68	1.00
	Min, max	-16.00, 20.00	-15.00, 17.00
OL Part A Week 48	n	157	157
	Mean (SD)	66.12 (13.22)	67.31 (12.15)
	Median	64.00	67.00
	Min, max	38.00, 107.50	45.00, 128.82
Change at OL Part A Week 48	n	157	156
	Mean (SD)	1.52 (5.56)	1.31 (5.28)
	Median	1.00	1.00
	Min, max	-15.00, 24.00	-14.00, 19.00
OL Part A Week 60	n	156	153
	Mean (SD)	66.48 (13.49)	67.36 (12.57)
	Median	64.93	66.00
	Min, max	39.00, 109.32	45.00, 132.90
Change at OL Part A Week 60	n	156	152
	Mean (SD)	1.57 (5.71)	1.32 (5.10)
	Median	0.57	1.00
	Min, max	-13.00, 23.00	-13.00, 18.00

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.10.1.1a
Summary of Weight (kg) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 102

Visit	Statistic	ELX/TEZ/IVA in 121-102 N = 170	VNZ/TEZ/D-IVA in 121-102 N = 166
OL Part A Week 72	n	155	153
	Mean (SD)	66.82 (13.21)	67.61 (12.52)
	Median	65.00	66.00
	Min, max	39.00, 110.68	46.00, 132.45
Change at OL Part A Week 72	n	155	152
	Mean (SD)	1.83 (6.27)	1.63 (5.26)
	Median	1.00	1.00
	Min, max	-13.00, 24.00	-12.00, 18.00
OL Part A Week 84	n	153	147
	Mean (SD)	66.92 (13.04)	67.41 (12.48)
	Median	65.00	66.00
	Min, max	40.00, 108.86	45.00, 135.17
Change at OL Part A Week 84	n	153	146
	Mean (SD)	1.82 (6.39)	1.66 (5.45)
	Median	1.00	1.00
	Min, max	-15.00, 24.00	-11.44, 19.00
OL Part A Week 96	n	151	145
	Mean (SD)	67.29 (12.99)	67.29 (12.30)
	Median	65.00	66.00
	Min, max	40.00, 106.14	46.00, 133.36
Change at OL Part A Week 96	n	151	144
	Mean (SD)	2.01 (6.74)	1.50 (5.61)
	Median	1.00	0.50
	Min, max	-15.00, 26.00	-12.00, 21.00

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.10.1.2a
Summary of Weight (kg) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
Parent study baseline	n	248	236
	Mean (SD)	65.32 (13.68)	66.66 (13.63)
	Median	63.00	65.00
	Min, max	32.00, 106.00	34.00, 110.00
OL Part A Day 15	n	240	235
	Mean (SD)	66.47 (13.51)	68.21 (13.53)
	Median	64.00	67.00
	Min, max	37.00, 111.00	39.00, 109.00
Change at OL Part A Day 15	n	240	233
	Mean (SD)	0.90 (3.67)	1.34 (3.88)
	Median	1.00	1.00
	Min, max	-14.00, 12.00	-13.00, 16.00
OL Part A Week 4	n	243	230
	Mean (SD)	66.33 (13.56)	68.24 (13.42)
	Median	63.96	66.50
	Min, max	37.00, 110.00	40.00, 110.00
Change at OL Part A Week 4	n	243	228
	Mean (SD)	0.91 (3.73)	1.36 (3.87)
	Median	1.00	1.00
	Min, max	-15.00, 12.00	-13.00, 17.00

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.10.1.2a
Summary of Weight (kg) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 8	n	245	234
	Mean (SD)	66.36 (13.47)	68.25 (13.46)
	Median	64.00	66.00
	Min, max	37.00, 110.00	41.00, 112.00
Change at OL Part A Week 8	n	245	232
	Mean (SD)	1.01 (3.71)	1.33 (4.03)
	Median	1.00	1.00
	Min, max	-17.00, 13.00	-14.00, 17.00
OL Part A Week 16	n	241	229
	Mean (SD)	66.54 (13.61)	68.46 (13.55)
	Median	64.00	67.00
	Min, max	37.00, 109.00	41.00, 111.00
Change at OL Part A Week 16	n	241	227
	Mean (SD)	1.17 (3.91)	1.66 (4.20)
	Median	1.00	1.00
	Min, max	-16.00, 11.00	-12.00, 17.00
OL Part A Week 24	n	240	230
	Mean (SD)	66.75 (13.60)	68.26 (13.15)
	Median	64.00	66.00
	Min, max	39.00, 109.00	41.00, 109.00
Change at OL Part A Week 24	n	240	228
	Mean (SD)	1.36 (4.08)	1.65 (4.61)
	Median	1.00	1.00
	Min, max	-17.00, 13.00	-13.00, 17.00

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.10.1.2a
Summary of Weight (kg) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 36	n	235	225
	Mean (SD)	66.75 (13.72)	68.52 (12.96)
	Median	65.00	66.00
	Min, max	39.00, 112.00	41.00, 111.00
Change at OL Part A Week 36	n	235	223
	Mean (SD)	1.31 (4.54)	1.73 (4.77)
	Median	1.00	1.26
	Min, max	-15.00, 17.00	-14.00, 21.00
OL Part A Week 48	n	232	222
	Mean (SD)	66.67 (13.70)	68.61 (12.96)
	Median	65.00	67.00
	Min, max	40.00, 112.00	42.00, 110.00
Change at OL Part A Week 48	n	232	220
	Mean (SD)	1.32 (4.70)	1.88 (4.91)
	Median	1.00	1.26
	Min, max	-13.00, 16.00	-13.00, 24.00
OL Part A Week 60	n	229	219
	Mean (SD)	67.08 (13.83)	68.79 (12.81)
	Median	65.00	67.13
	Min, max	41.00, 112.00	42.00, 107.00
Change at OL Part A Week 60	n	229	217
	Mean (SD)	1.61 (5.12)	2.01 (5.31)
	Median	1.00	1.00
	Min, max	-20.00, 17.00	-17.00, 23.00

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.10.1.2a
Summary of Weight (kg) and Change from Parent Study Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Subjects from Study 103

Visit	Statistic	ELX/TEZ/IVA in 121-103 N = 248	VNZ/TEZ/D-IVA in 121-103 N = 238
OL Part A Week 72	n	226	216
	Mean (SD)	67.14 (13.82)	69.31 (12.78)
	Median	65.66	68.97
	Min, max	41.00, 110.00	42.00, 102.00
Change at OL Part A Week 72	n	226	214
	Mean (SD)	1.76 (4.72)	2.43 (5.54)
	Median	1.00	1.68
	Min, max	-9.00, 19.00	-14.00, 26.00
OL Part A Week 84	n	226	213
	Mean (SD)	67.52 (13.96)	69.36 (12.71)
	Median	66.00	68.00
	Min, max	42.00, 110.00	41.00, 101.00
Change at OL Part A Week 84	n	226	211
	Mean (SD)	2.11 (5.12)	2.50 (5.85)
	Median	1.00	2.00
	Min, max	-10.00, 23.00	-15.00, 29.00
OL Part A Week 96	n	222	211
	Mean (SD)	67.82 (14.97)	69.55 (12.71)
	Median	65.00	67.13
	Min, max	43.00, 149.00	43.00, 103.00
Change at OL Part A Week 96	n	222	209
	Mean (SD)	2.55 (7.72)	2.50 (5.99)
	Median	2.00	2.00
	Min, max	-8.62, 85.50	-14.00, 30.00

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.

Table 14.2.10.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in Weight (kg) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Parent Study Efficacy Period		
N	202	196
Parent study baseline		
n	202	195
Mean (SD)	64.54 (13.75)	65.08 (13.32)
Absolute change at Day 15		
n	196	190
LS mean (SE)	0.21 (0.09)	0.08 (0.09)
95% CI of LS mean	(0.03, 0.39)	(-0.10, 0.26)
Absolute change at Week 4		
n	195	183
LS mean (SE)	0.19 (0.10)	0.08 (0.10)
95% CI of LS mean	(0.00, 0.39)	(-0.12, 0.28)
Absolute change at Week 8		
n	194	188
LS mean (SE)	0.30 (0.12)	0.30 (0.12)
95% CI of LS mean	(0.07, 0.52)	(0.07, 0.53)
Absolute change at Week 16		
n	195	187
LS mean (SE)	0.43 (0.16)	0.36 (0.16)
95% CI of LS mean	(0.12, 0.74)	(0.05, 0.68)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.10.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in Weight (kg) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at Week 24		
n	195	186
LS mean (SE)	0.49 (0.19)	0.36 (0.20)
95% CI of LS mean	(0.11, 0.87)	(-0.03, 0.75)
Absolute change at Week 36		
n	193	182
LS mean (SE)	0.43 (0.23)	0.57 (0.24)
95% CI of LS mean	(-0.03, 0.89)	(0.10, 1.04)
Absolute change at Week 52		
n	187	179
LS mean (SE)	0.50 (0.28)	1.01 (0.29)
95% CI of LS mean	(-0.05, 1.06)	(0.44, 1.57)
OL Efficacy Period for Part A		
N	170	166
Absolute change at OL Part A Day 15		
n	165	159
LS mean (SE)	0.65 (0.28)	1.06 (0.28)
95% CI of LS mean	(0.10, 1.20)	(0.50, 1.61)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.10.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in Weight (kg) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 4		
n	165	159
LS mean (SE)	0.71 (0.28)	1.07 (0.28)
95% CI of LS mean	(0.16, 1.26)	(0.51, 1.63)
Absolute change at OL Part A Week 8		
n	167	161
LS mean (SE)	0.60 (0.30)	0.84 (0.30)
95% CI of LS mean	(0.01, 1.18)	(0.25, 1.44)
Absolute change at OL Part A Week 16		
n	166	160
LS mean (SE)	1.02 (0.31)	1.04 (0.32)
95% CI of LS mean	(0.40, 1.64)	(0.41, 1.67)
Absolute change at OL Part A Week 24		
n	164	157
LS mean (SE)	1.14 (0.35)	0.97 (0.36)
95% CI of LS mean	(0.45, 1.83)	(0.27, 1.67)
Absolute change at OL Part A Week 36		
n	160	157
LS mean (SE)	1.12 (0.37)	1.17 (0.38)
95% CI of LS mean	(0.39, 1.85)	(0.43, 1.91)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.10.2.1a
MMRM Analysis of Absolute Change from Parent Study Baseline in Weight (kg) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

	ELX/TEZ/IVA in 121-102	VNZ/TEZ/D-IVA in 121-102
Absolute change at OL Part A Week 48		
n	155	154
LS mean (SE)	1.44 (0.39)	1.29 (0.39)
95% CI of LS mean	(0.68, 2.21)	(0.52, 2.07)
Absolute change at OL Part A Week 60		
n	154	151
LS mean (SE)	1.54 (0.38)	1.29 (0.39)
95% CI of LS mean	(0.79, 2.30)	(0.52, 2.05)
Absolute change at OL Part A Week 72		
n	153	151
LS mean (SE)	1.78 (0.41)	1.65 (0.42)
95% CI of LS mean	(0.97, 2.59)	(0.83, 2.47)
Absolute change at OL Part A Week 84		
n	151	145
LS mean (SE)	1.78 (0.43)	1.75 (0.43)
95% CI of LS mean	(0.95, 2.62)	(0.91, 2.60)
Absolute change at OL Part A Week 96		
n	149	143
LS mean (SE)	1.97 (0.44)	1.62 (0.45)
95% CI of LS mean	(1.10, 2.85)	(0.73, 2.51)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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Table 14.2.10.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in Weight (kg) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Parent Study Efficacy Period		
N	289	284
Parent study baseline		
n	289	280
Mean (SD)	65.05 (13.35)	66.58 (13.98)
Absolute change at Day 15		
n	275	270
LS mean (SE)	0.07 (0.07)	0.02 (0.07)
95% CI of LS mean	(-0.06, 0.20)	(-0.11, 0.16)
Absolute change at Week 4		
n	274	273
LS mean (SE)	0.06 (0.08)	0.19 (0.08)
95% CI of LS mean	(-0.10, 0.21)	(0.03, 0.34)
Absolute change at Week 8		
n	278	268
LS mean (SE)	0.23 (0.10)	0.31 (0.10)
95% CI of LS mean	(0.03, 0.42)	(0.12, 0.51)
Absolute change at Week 16		
n	276	262
LS mean (SE)	0.34 (0.14)	0.65 (0.14)
95% CI of LS mean	(0.07, 0.61)	(0.37, 0.92)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.10.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in Weight (kg) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at Week 24		
n	274	259
LS mean (SE)	0.54 (0.16)	1.00 (0.17)
95% CI of LS mean	(0.22, 0.86)	(0.67, 1.33)
Absolute change at Week 36		
n	272	258
LS mean (SE)	0.63 (0.20)	1.09 (0.20)
95% CI of LS mean	(0.24, 1.01)	(0.70, 1.49)
Absolute change at Week 52		
n	266	248
LS mean (SE)	0.81 (0.22)	1.31 (0.23)
95% CI of LS mean	(0.38, 1.25)	(0.87, 1.76)
OL Efficacy Period for Part A		
N	248	238
Absolute change at OL Part A Day 15		
n	231	228
LS mean (SE)	0.79 (0.23)	1.36 (0.24)
95% CI of LS mean	(0.33, 1.24)	(0.90, 1.83)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.10.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in Weight (kg) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 4		
n	234	223
LS mean (SE)	0.84 (0.24)	1.35 (0.24)
95% CI of LS mean	(0.37, 1.30)	(0.88, 1.82)
Absolute change at OL Part A Week 8		
n	236	227
LS mean (SE)	0.87 (0.24)	1.32 (0.24)
95% CI of LS mean	(0.40, 1.33)	(0.84, 1.79)
Absolute change at OL Part A Week 16		
n	232	222
LS mean (SE)	0.97 (0.25)	1.61 (0.26)
95% CI of LS mean	(0.47, 1.47)	(1.10, 2.12)
Absolute change at OL Part A Week 24		
n	231	223
LS mean (SE)	1.17 (0.27)	1.57 (0.28)
95% CI of LS mean	(0.64, 1.71)	(1.03, 2.11)
Absolute change at OL Part A Week 36		
n	226	218
LS mean (SE)	1.18 (0.28)	1.62 (0.29)
95% CI of LS mean	(0.62, 1.74)	(1.05, 2.19)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.10.2.2a
MMRM Analysis of Absolute Change from Parent Study Baseline in Weight (kg) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

	ELX/TEZ/IVA in 121-103	VNZ/TEZ/D-IVA in 121-103
Absolute change at OL Part A Week 48		
n	223	215
LS mean (SE)	1.15 (0.29)	1.83 (0.30)
95% CI of LS mean	(0.58, 1.73)	(1.25, 2.41)
Absolute change at OL Part A Week 60		
n	220	212
LS mean (SE)	1.46 (0.32)	1.92 (0.32)
95% CI of LS mean	(0.84, 2.08)	(1.29, 2.55)
Absolute change at OL Part A Week 72		
n	218	209
LS mean (SE)	1.63 (0.31)	2.32 (0.32)
95% CI of LS mean	(1.02, 2.24)	(1.70, 2.94)
Absolute change at OL Part A Week 84		
n	217	206
LS mean (SE)	1.89 (0.33)	2.37 (0.34)
95% CI of LS mean	(1.24, 2.54)	(1.70, 3.03)
Absolute change at OL Part A Week 96		
n	213	204
LS mean (SE)	2.38 (0.44)	2.34 (0.45)
95% CI of LS mean	(1.51, 3.25)	(1.45, 3.23)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study. If the pre-dose Day 1 value is missing, the most recent pre-dose, non-missing value on or after the parent study Day -14 visit, including unscheduled visits, is used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ≥18 years), genotype group, and treatment-by-visit interaction, with parent study baseline $ppFEV_1$ and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Total duration of safety analysis period in 100 PY	--	5.15	--	5.00	--	15.43
Subjects with any TEAEs	469 (95.5)	736.87	459 (95.6)	709.91	796 (96.8)	617.07
Infections and infestations	392 (79.8)	223.10	349 (72.7)	198.52	703 (85.5)	185.56
Infective pulmonary exacerbation of cystic fibrosis	158 (32.2)	54.17	133 (27.7)	43.18	300 (36.5)	41.87
Nasopharyngitis	95 (19.3)	35.34	102 (21.3)	31.59	209 (25.4)	30.46
Upper respiratory tract infection	67 (13.6)	18.25	72 (15.0)	18.99	192 (23.4)	21.91
COVID-19	127 (25.9)	26.60	107 (22.3)	22.99	169 (20.6)	12.05
Influenza	26 (5.3)	5.24	52 (10.8)	10.80	116 (14.1)	8.75
Viral upper respiratory tract infection	35 (7.1)	7.96	37 (7.7)	9.00	72 (8.8)	7.71
Sinusitis	36 (7.3)	8.54	19 (4.0)	4.60	62 (7.5)	5.25
Rhinitis	17 (3.5)	4.27	16 (3.3)	3.80	53 (6.4)	5.51
Urinary tract infection	16 (3.3)	3.50	11 (2.3)	2.40	43 (5.2)	3.69
Pneumonia	10 (2.0)	2.14	9 (1.9)	2.20	36 (4.4)	3.37
Respiratory tract infection	16 (3.3)	4.85	13 (2.7)	4.00	36 (4.4)	3.56
Gastroenteritis	10 (2.0)	1.94	10 (2.1)	2.00	27 (3.3)	1.75
Lower respiratory tract infection	10 (2.0)	2.14	8 (1.7)	2.80	27 (3.3)	2.14
Vulvovaginal mycotic infection	9 (1.8)	1.75	6 (1.3)	1.40	25 (3.0)	1.94
Conjunctivitis	12 (2.4)	2.52	6 (1.3)	1.20	23 (2.8)	1.62
Bronchitis	9 (1.8)	2.52	8 (1.7)	2.40	20 (2.4)	2.20
Respiratory tract infection viral	5 (1.0)	1.17	6 (1.3)	2.80	19 (2.3)	1.43

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Gastroenteritis viral	4 (0.8)	0.78	4 (0.8)	0.80	16 (1.9)	1.10
Pharyngitis	8 (1.6)	1.55	8 (1.7)	1.80	15 (1.8)	1.10
Tonsillitis	6 (1.2)	1.55	6 (1.3)	1.80	15 (1.8)	1.17
Oral herpes	7 (1.4)	2.14	4 (0.8)	0.80	14 (1.7)	1.43
Ear infection	5 (1.0)	0.97	6 (1.3)	1.20	13 (1.6)	0.91
Pharyngitis streptococcal	4 (0.8)	0.78	3 (0.6)	0.60	13 (1.6)	0.84
Viral infection	6 (1.2)	1.17	3 (0.6)	0.60	12 (1.5)	1.04
Oral candidiasis	7 (1.4)	1.94	7 (1.5)	1.40	11 (1.3)	0.84
Chronic sinusitis	6 (1.2)	1.55	2 (0.4)	0.60	10 (1.2)	0.97
Laryngitis	6 (1.2)	1.17	1 (0.2)	0.20	10 (1.2)	0.65
Hordeolum	8 (1.6)	2.14	1 (0.2)	0.20	9 (1.1)	0.78
Fungal skin infection	1 (0.2)	0.39	0	0	8 (1.0)	0.52
Tooth infection	4 (0.8)	0.97	3 (0.6)	0.80	8 (1.0)	0.52
Acute sinusitis	4 (0.8)	0.78	3 (0.6)	0.60	7 (0.9)	0.52
Bacterial disease carrier	2 (0.4)	1.17	1 (0.2)	0.20	7 (0.9)	0.52
Cystitis	3 (0.6)	0.58	7 (1.5)	1.40	7 (0.9)	0.58
Suspected COVID-19	0	0	0	0	7 (0.9)	0.45
Vulvovaginal candidiasis	10 (2.0)	2.52	3 (0.6)	0.60	7 (0.9)	0.45
Herpes zoster	5 (1.0)	1.36	4 (0.8)	0.80	6 (0.7)	0.39
Otitis media	6 (1.2)	1.17	6 (1.3)	1.40	6 (0.7)	0.39
Pulpitis dental	0	0	1 (0.2)	0.20	6 (0.7)	0.39
Bacterial vaginosis	0	0	1 (0.2)	0.20	5 (0.6)	0.39
Cellulitis	2 (0.4)	0.39	1 (0.2)	0.20	5 (0.6)	0.32
Respiratory tract infection bacterial	1 (0.2)	0.19	5 (1.0)	1.40	5 (0.6)	0.32
Tinea pedis	1 (0.2)	0.39	1 (0.2)	0.20	5 (0.6)	0.32

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Bronchopulmonary aspergillosis allergic	1 (0.2)	0.19	0	0	4 (0.5)	0.39
Localised infection	2 (0.4)	0.39	1 (0.2)	0.20	4 (0.5)	0.26
Oral fungal infection	2 (0.4)	0.58	2 (0.4)	0.40	4 (0.5)	0.26
Respiratory syncytial virus infection	0	0	3 (0.6)	0.60	4 (0.5)	0.26
Tooth abscess	1 (0.2)	0.19	2 (0.4)	0.60	4 (0.5)	0.26
Upper respiratory tract infection bacterial	1 (0.2)	0.19	1 (0.2)	0.20	4 (0.5)	0.26
Atypical mycobacterial pneumonia	1 (0.2)	0.19	0	0	3 (0.4)	0.19
Bacteriuria	0	0	0	0	3 (0.4)	0.19
Bronchitis viral	0	0	0	0	3 (0.4)	0.19
Folliculitis	2 (0.4)	0.39	0	0	3 (0.4)	0.19
Gastroenteritis norovirus	0	0	0	0	3 (0.4)	0.19
Gastrointestinal viral infection	1 (0.2)	0.19	0	0	3 (0.4)	0.26
Genital infection fungal	1 (0.2)	0.19	0	0	3 (0.4)	0.19
Hand-foot-and-mouth disease	1 (0.2)	0.19	1 (0.2)	0.20	3 (0.4)	0.19
Infective exacerbation of bronchiectasis	3 (0.6)	0.58	2 (0.4)	0.60	3 (0.4)	0.32
Onychomycosis	1 (0.2)	0.19	1 (0.2)	0.20	3 (0.4)	0.19
Otitis media acute	1 (0.2)	0.19	0	0	3 (0.4)	0.19
Pneumonia staphylococcal	0	0	1 (0.2)	0.20	3 (0.4)	0.26
Pyelonephritis	1 (0.2)	0.39	1 (0.2)	0.20	3 (0.4)	0.26
Rhinovirus infection	3 (0.6)	0.58	2 (0.4)	0.40	3 (0.4)	0.19
Tinea versicolour	0	0	0	0	3 (0.4)	0.26
Viral rhinitis	1 (0.2)	0.19	0	0	3 (0.4)	0.19

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Wound infection	1 (0.2)	0.19	1 (0.2)	0.20	3 (0.4)	0.19
Bacterial vulvovaginitis	0	0	0	0	2 (0.2)	0.13
Escherichia urinary tract infection	0	0	2 (0.4)	0.40	2 (0.2)	0.13
Fungal infection	0	0	0	0	2 (0.2)	0.19
Gastric infection	0	0	0	0	2 (0.2)	0.13
Genital herpes	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Gingivitis	0	0	1 (0.2)	0.20	2 (0.2)	0.32
Impetigo	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Laryngopharyngitis	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Lower respiratory tract infection bacterial	2 (0.4)	0.39	0	0	2 (0.2)	0.13
Mycobacterial disease carrier	0	0	0	0	2 (0.2)	0.13
Norovirus infection	0	0	0	0	2 (0.2)	0.13
Otitis externa	0	0	1 (0.2)	0.20	2 (0.2)	0.19
Paronychia	0	0	0	0	2 (0.2)	0.13
Pharyngotonsillitis	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Pilonidal disease	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Pneumonia pseudomonal	0	0	0	0	2 (0.2)	0.13
Post procedural infection	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Postoperative abscess	0	0	0	0	2 (0.2)	0.13
Sepsis	0	0	0	0	2 (0.2)	0.13
Skin infection	3 (0.6)	0.58	0	0	2 (0.2)	0.13
Tinea infection	0	0	0	0	2 (0.2)	0.13
Tongue fungal infection	0	0	1 (0.2)	0.20	2 (0.2)	0.26
Tracheitis	0	0	1 (0.2)	0.20	2 (0.2)	0.13

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- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Urinary tract candidiasis	0	0	0	0	2 (0.2)	0.13
Vaginal infection	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Viral pharyngitis	0	0	0	0	2 (0.2)	0.13
Abscess limb	0	0	0	0	1 (0.1)	0.06
Adenoviral conjunctivitis	0	0	0	0	1 (0.1)	0.06
Anorectal cellulitis	0	0	0	0	1 (0.1)	0.06
Appendicitis	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
Aspergilloma	0	0	0	0	1 (0.1)	0.06
Bacterial rhinitis	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Body tinea	0	0	0	0	1 (0.1)	0.13
Bronchopulmonary aspergillosis	0	0	1 (0.2)	0.20	1 (0.1)	0.06
COVID-19 pneumonia	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
Campylobacter gastroenteritis	0	0	0	0	1 (0.1)	0.06
Conjunctivitis bacterial	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Conjunctivitis viral	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Croup infectious	0	0	0	0	1 (0.1)	0.06
Diarrhoea infectious	0	0	0	0	1 (0.1)	0.06
Ear, nose and throat infection	0	0	0	0	1 (0.1)	0.13
Enterobiasis	0	0	0	0	1 (0.1)	0.06
Epididymitis	0	0	0	0	1 (0.1)	0.06
Eye infection	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Fungal disease carrier	0	0	0	0	1 (0.1)	0.06
Fungal foot infection	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
Furuncle	0	0	0	0	1 (0.1)	0.06
Gastroenteritis clostridial	0	0	0	0	1 (0.1)	0.06

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Gastrointestinal infection	3 (0.6)	0.58	1 (0.2)	0.20	1 (0.1)	0.06
Gastrointestinal microorganism overgrowth	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
Giardiasis	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Hepatitis A	0	0	0	0	1 (0.1)	0.06
Herpangina	0	0	0	0	1 (0.1)	0.06
Herpes simplex	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Herpes virus infection	0	0	0	0	1 (0.1)	0.06
Infectious mononucleosis	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Kidney infection	0	0	0	0	1 (0.1)	0.06
Klebsiella urinary tract infection	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Laryngitis viral	0	0	0	0	1 (0.1)	0.06
Lower respiratory tract infection viral	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
Lung abscess	0	0	0	0	1 (0.1)	0.06
Nail bed infection	0	0	0	0	1 (0.1)	0.06
Oesophageal candidiasis	0	0	0	0	1 (0.1)	0.06
Oral infection	0	0	0	0	1 (0.1)	0.06
Oropharyngeal candidiasis	0	0	0	0	1 (0.1)	0.06
Pelvic infection	0	0	0	0	1 (0.1)	0.06
Periorbital cellulitis	0	0	0	0	1 (0.1)	0.06
Perirectal abscess	0	0	0	0	1 (0.1)	0.13
Pertussis	0	0	0	0	1 (0.1)	0.06
Pharyngeal pustule	0	0	0	0	1 (0.1)	0.06
Pneumonia aspiration	0	0	0	0	1 (0.1)	0.06

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- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Pneumonia bordetella	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Pneumonia haemophilus	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Pneumonia parainfluenzae viral	0	0	0	0	1 (0.1)	0.13
Pneumonia serratia	0	0	0	0	1 (0.1)	0.06
Pseudomonas infection	0	0	0	0	1 (0.1)	0.13
Pyuria	0	0	0	0	1 (0.1)	0.06
Scabies	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
Sialoadenitis	0	0	0	0	1 (0.1)	0.06
Sinusitis bacterial	0	0	0	0	1 (0.1)	0.06
Skin bacterial infection	0	0	0	0	1 (0.1)	0.06
Sputum purulent	0	0	0	0	1 (0.1)	0.06
Urinary tract infection enterococcal	0	0	0	0	1 (0.1)	0.06
Viral labyrinthitis	0	0	0	0	1 (0.1)	0.06
Viral sinusitis	0	0	0	0	1 (0.1)	0.06
Vulvovaginitis	0	0	0	0	1 (0.1)	0.06
Abscess neck	0	0	1 (0.2)	0.20	0	0
Adenoviral upper respiratory infection	1 (0.2)	0.19	0	0	0	0
Asymptomatic bacteriuria	0	0	1 (0.2)	0.20	0	0
Balanitis candida	1 (0.2)	0.19	1 (0.2)	0.40	0	0
Clostridium difficile colitis	0	0	1 (0.2)	0.20	0	0
Dermatophytosis	1 (0.2)	0.19	0	0	0	0
Diverticulitis	0	0	1 (0.2)	0.20	0	0
Erysipelas	0	0	1 (0.2)	0.20	0	0
Erythema migrans	0	0	1 (0.2)	0.20	0	0
Eye infection bacterial	1 (0.2)	0.19	1 (0.2)	0.20	0	0

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Eye infection staphylococcal	1 (0.2)	0.19	0	0	0	0
Gastritis viral	1 (0.2)	0.19	0	0	0	0
Genital candidiasis	1 (0.2)	0.19	2 (0.4)	0.40	0	0
Genital herpes simplex	0	0	1 (0.2)	0.20	0	0
Genital infection	1 (0.2)	0.19	0	0	0	0
Gingival abscess	0	0	1 (0.2)	0.20	0	0
Herpes dermatitis	1 (0.2)	0.58	0	0	0	0
Infected bite	0	0	1 (0.2)	0.20	0	0
Mastoiditis	0	0	1 (0.2)	0.20	0	0
Meningitis aseptic	1 (0.2)	0.19	0	0	0	0
Metapneumovirus infection	1 (0.2)	0.19	0	0	0	0
Metapneumovirus pneumonia	1 (0.2)	0.39	0	0	0	0
Nasal vestibulitis	0	0	1 (0.2)	0.20	0	0
Ocular demodicosis	1 (0.2)	0.19	0	0	0	0
Omphalitis	1 (0.2)	0.19	0	0	0	0
Pelvic inflammatory disease	0	0	1 (0.2)	0.20	0	0
Pneumonia moraxella	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Pneumonia respiratory syncytial viral	0	0	1 (0.2)	0.20	0	0
Pneumonia viral	1 (0.2)	0.19	0	0	0	0
Pulmonary nocardiosis	0	0	1 (0.2)	0.20	0	0
Rash pustular	1 (0.2)	0.19	0	0	0	0
Retinitis	1 (0.2)	0.19	0	0	0	0
Sexually transmitted disease	1 (0.2)	0.19	0	0	0	0
Staphylococcal skin infection	1 (0.2)	0.19	0	0	0	0
Streptococcal infection	0	0	1 (0.2)	0.20	0	0

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Subcutaneous abscess	1 (0.2)	0.19	0	0	0	0
Superinfection bacterial	0	0	1 (0.2)	0.20	0	0
Tinea faciei	0	0	1 (0.2)	0.20	0	0
Tonsillitis bacterial	1 (0.2)	0.19	0	0	0	0
Urinary tract infection bacterial	1 (0.2)	0.19	0	0	0	0
Urinary tract infection fungal	0	0	1 (0.2)	0.20	0	0
Urogenital infection fungal	0	0	1 (0.2)	0.20	0	0
Vascular device infection	0	0	1 (0.2)	0.20	0	0
Viral myocarditis	0	0	1 (0.2)	0.20	0	0
Viral tonsillitis	1 (0.2)	0.19	0	0	0	0
Respiratory, thoracic and mediastinal disorders	251 (51.1)	131.45	239 (49.8)	145.94	488 (59.4)	131.18
Cough	101 (20.6)	28.15	108 (22.5)	30.59	240 (29.2)	29.49
Oropharyngeal pain	60 (12.2)	15.34	69 (14.4)	18.39	154 (18.7)	13.93
Sputum increased	50 (10.2)	12.82	45 (9.4)	10.80	127 (15.5)	12.96
Nasal congestion	47 (9.6)	11.46	48 (10.0)	12.19	108 (13.1)	10.50
Rhinorrhoea	36 (7.3)	8.35	35 (7.3)	8.80	88 (10.7)	7.39
Productive cough	24 (4.9)	6.02	28 (5.8)	7.20	85 (10.3)	7.52
Dyspnoea	28 (5.7)	5.44	18 (3.8)	5.00	63 (7.7)	5.51
Haemoptysis	33 (6.7)	10.49	30 (6.3)	8.40	60 (7.3)	7.97
Sinus congestion	15 (3.1)	3.50	32 (6.7)	9.20	51 (6.2)	5.18
Lower respiratory tract congestion	8 (1.6)	3.30	14 (2.9)	3.40	37 (4.5)	3.11
Wheezing	11 (2.2)	2.14	13 (2.7)	3.00	32 (3.9)	2.98
Respiration abnormal	12 (2.4)	2.91	17 (3.5)	3.80	30 (3.6)	2.33
Rhinitis allergic	4 (0.8)	1.17	2 (0.4)	0.40	18 (2.2)	1.36

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Upper-airway cough syndrome	8 (1.6)	2.14	5 (1.0)	1.20	17 (2.1)	1.69
Paranasal sinus discomfort	4 (0.8)	0.78	4 (0.8)	0.80	16 (1.9)	1.43
Epistaxis	5 (1.0)	0.97	7 (1.5)	1.60	15 (1.8)	1.17
Throat irritation	4 (0.8)	0.78	2 (0.4)	0.40	15 (1.8)	1.17
Dyspnoea exertional	0	0	10 (2.1)	2.00	12 (1.5)	0.78
Dysphonia	4 (0.8)	0.78	6 (1.3)	1.20	11 (1.3)	0.84
Pleuritic pain	3 (0.6)	0.58	7 (1.5)	1.40	11 (1.3)	1.30
Sneezing	5 (1.0)	0.97	1 (0.2)	0.20	11 (1.3)	0.71
Bronchospasm	3 (0.6)	0.58	0	0	10 (1.2)	0.71
Paranasal sinus hypersecretion	6 (1.2)	1.17	7 (1.5)	1.60	10 (1.2)	0.78
Sputum discoloured	7 (1.4)	1.55	9 (1.9)	1.80	10 (1.2)	0.71
Asthma	5 (1.0)	0.97	6 (1.3)	1.40	9 (1.1)	0.58
Pulmonary congestion	2 (0.4)	0.58	1 (0.2)	0.40	9 (1.1)	0.65
Sinus pain	2 (0.4)	0.39	5 (1.0)	1.00	8 (1.0)	0.65
Rales	6 (1.2)	1.36	3 (0.6)	0.60	7 (0.9)	0.52
Nasal obstruction	1 (0.2)	0.19	4 (0.8)	1.00	6 (0.7)	0.45
Nasal polyps	2 (0.4)	0.58	0	0	6 (0.7)	0.39
Painful respiration	5 (1.0)	1.17	3 (0.6)	0.60	6 (0.7)	0.45
Respiratory symptom	0	0	2 (0.4)	0.60	5 (0.6)	0.39
Upper respiratory tract inflammation	0	0	0	0	5 (0.6)	0.52
Increased viscosity of bronchial secretion	2 (0.4)	0.39	2 (0.4)	0.40	4 (0.5)	0.26
Obstructive airways disorder	0	0	1 (0.2)	0.20	4 (0.5)	0.32
Upper respiratory tract congestion	3 (0.6)	0.78	3 (0.6)	0.60	4 (0.5)	0.39
Aphonia	3 (0.6)	0.58	4 (0.8)	1.00	3 (0.4)	0.19

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Dry throat	0	0	1 (0.2)	0.20	3 (0.4)	0.19
Nasal discomfort	0	0	0	0	3 (0.4)	0.26
Obstructive sleep apnoea syndrome	0	0	0	0	3 (0.4)	0.19
Pleurisy	0	0	1 (0.2)	0.20	3 (0.4)	0.19
Pulmonary pain	2 (0.4)	0.39	3 (0.6)	0.80	3 (0.4)	0.19
Bronchial secretion retention	1 (0.2)	0.19	2 (0.4)	0.40	2 (0.2)	0.13
Hypoxia	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Nasal septum deviation	0	0	0	0	2 (0.2)	0.13
Respiratory tract congestion	2 (0.4)	0.39	2 (0.4)	0.40	2 (0.2)	0.13
Rhonchi	0	0	0	0	2 (0.2)	0.13
Sputum retention	0	0	0	0	2 (0.2)	0.13
Tonsillar hypertrophy	0	0	0	0	2 (0.2)	0.13
Tonsillolith	0	0	0	0	2 (0.2)	0.13
Allergic cough	0	0	0	0	1 (0.1)	0.06
Bronchial artery hypertrophy	0	0	0	0	1 (0.1)	0.13
Bronchial disorder	0	0	0	0	1 (0.1)	0.06
Bronchial hyperreactivity	0	0	0	0	1 (0.1)	0.06
Bronchial obstruction	0	0	0	0	1 (0.1)	0.06
Bronchial wall thickening	0	0	0	0	1 (0.1)	0.06
Catarrh	0	0	0	0	1 (0.1)	0.06
Hiccups	0	0	0	0	1 (0.1)	0.06
Increased bronchial secretion	0	0	2 (0.4)	0.40	1 (0.1)	0.06
Lung infiltration	0	0	0	0	1 (0.1)	0.06
Nasal crusting	0	0	0	0	1 (0.1)	0.06
Nasal discharge discolouration	0	0	1 (0.2)	0.40	1 (0.1)	0.13

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Nasal dryness	2 (0.4)	0.39	1 (0.2)	0.20	1 (0.1)	0.06
Nasal oedema	0	0	0	0	1 (0.1)	0.06
Oropharyngeal plaque	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Paranasal sinus inflammation	0	0	0	0	1 (0.1)	0.06
Pneumonitis	0	0	0	0	1 (0.1)	0.06
Pneumothorax	0	0	0	0	1 (0.1)	0.06
Pulmonary cavitation	0	0	1 (0.2)	0.20	1 (0.1)	0.13
Pulmonary hypertension	0	0	0	0	1 (0.1)	0.06
Pulmonary mass	0	0	0	0	1 (0.1)	0.06
Reflux laryngitis	0	0	0	0	1 (0.1)	0.06
Sinonasal obstruction	0	0	0	0	1 (0.1)	0.06
Sinus disorder	0	0	0	0	1 (0.1)	0.06
Throat tightness	0	0	0	0	1 (0.1)	0.06
Bronchiectasis	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Bronchopulmonary disease	1 (0.2)	0.19	0	0	0	0
Diaphragmatic paralysis	1 (0.2)	0.19	0	0	0	0
Increased upper airway secretion	3 (0.6)	0.58	1 (0.2)	0.20	0	0
Lung opacity	0	0	1 (0.2)	0.20	0	0
Pharyngeal disorder	0	0	1 (0.2)	0.20	0	0
Pleural thickening	0	0	1 (0.2)	0.20	0	0
Respiratory tract irritation	0	0	1 (0.2)	0.20	0	0
Throat clearing	2 (0.4)	0.39	1 (0.2)	0.20	0	0
Gastrointestinal disorders	179 (36.5)	71.65	178 (37.1)	62.37	376 (45.7)	57.16
Diarrhoea	59 (12.0)	12.43	58 (12.1)	15.19	140 (17.0)	11.67
Abdominal pain	37 (7.5)	9.71	25 (5.2)	5.80	72 (8.8)	5.25

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Nausea	30 (6.1)	6.60	29 (6.0)	6.00	71 (8.6)	5.64
Abdominal pain upper	19 (3.9)	4.66	26 (5.4)	6.40	57 (6.9)	4.80
Constipation	30 (6.1)	6.99	22 (4.6)	5.20	55 (6.7)	5.06
Vomiting	27 (5.5)	6.99	15 (3.1)	3.40	53 (6.4)	3.95
Abdominal distension	15 (3.1)	3.11	11 (2.3)	2.20	31 (3.8)	2.27
Flatulence	15 (3.1)	3.11	8 (1.7)	1.60	23 (2.8)	1.62
Gastrooesophageal reflux disease	10 (2.0)	1.94	8 (1.7)	1.60	20 (2.4)	1.36
Toothache	5 (1.0)	1.17	8 (1.7)	1.60	20 (2.4)	1.36
Abdominal discomfort	2 (0.4)	0.39	2 (0.4)	0.40	12 (1.5)	0.78
Distal intestinal obstruction syndrome	6 (1.2)	1.36	2 (0.4)	1.00	11 (1.3)	0.97
Dental caries	1 (0.2)	0.19	3 (0.6)	0.60	9 (1.1)	0.84
Gastritis	6 (1.2)	1.17	2 (0.4)	0.40	9 (1.1)	0.71
Dyspepsia	2 (0.4)	0.39	4 (0.8)	0.80	8 (1.0)	0.52
Haemorrhoids	1 (0.2)	0.19	2 (0.4)	0.40	8 (1.0)	0.58
Haematochezia	2 (0.4)	0.39	2 (0.4)	0.40	7 (0.9)	0.58
Large intestine polyp	2 (0.4)	0.39	0	0	7 (0.9)	0.45
Intestinal obstruction	0	0	0	0	6 (0.7)	0.39
Odynophagia	1 (0.2)	0.19	2 (0.4)	0.40	6 (0.7)	0.52
Rectal haemorrhage	0	0	3 (0.6)	0.60	6 (0.7)	0.71
Abdominal pain lower	1 (0.2)	0.19	1 (0.2)	0.20	5 (0.6)	0.32
Food poisoning	6 (1.2)	1.17	4 (0.8)	0.80	5 (0.6)	0.32
Hiatus hernia	1 (0.2)	0.19	0	0	5 (0.6)	0.32
Steatorrhoea	0	0	5 (1.0)	1.00	5 (0.6)	0.32
Anal fissure	0	0	0	0	3 (0.4)	0.19
Gingival pain	1 (0.2)	0.19	0	0	3 (0.4)	0.19

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

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System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Inguinal hernia	1 (0.2)	0.19	0	0	3 (0.4)	0.19
Stomatitis	0	0	0	0	3 (0.4)	0.32
Abdominal hernia	0	0	0	0	2 (0.2)	0.13
Aphthous ulcer	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Dysphagia	4 (0.8)	1.17	0	0	2 (0.2)	0.19
Epigastric discomfort	0	0	0	0	2 (0.2)	0.13
Faecaloma	5 (1.0)	1.55	1 (0.2)	0.20	2 (0.2)	0.13
Faeces pale	0	0	0	0	2 (0.2)	0.13
Faeces soft	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Gingival bleeding	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Lip swelling	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Malabsorption	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Mouth ulceration	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Oral mucosal blistering	0	0	0	0	2 (0.2)	0.13
Proctalgia	0	0	0	0	2 (0.2)	0.13
Small intestinal obstruction	0	0	1 (0.2)	0.40	2 (0.2)	0.26
Abnormal faeces	0	0	0	0	1 (0.1)	0.06
Aerophagia	0	0	0	0	1 (0.1)	0.06
Angular cheilitis	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Anorectal polyp	0	0	0	0	1 (0.1)	0.06
Barrett's oesophagus	0	0	0	0	1 (0.1)	0.06
Bowel movement irregularity	0	0	0	0	1 (0.1)	0.06
Colitis	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Colitis ischaemic	0	0	0	0	1 (0.1)	0.06
Duodenitis	0	0	0	0	1 (0.1)	0.06

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Eructation	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Faeces discoloured	0	0	1 (0.2)	0.20	1 (0.1)	0.13
Frequent bowel movements	0	0	4 (0.8)	0.80	1 (0.1)	0.06
Gastritis erosive	0	0	0	0	1 (0.1)	0.06
Gastrointestinal inflammation	0	0	0	0	1 (0.1)	0.06
Gastrointestinal motility disorder	0	0	0	0	1 (0.1)	0.06
Gastrointestinal tract irritation	0	0	0	0	1 (0.1)	0.06
Gingival swelling	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Haemorrhoids thrombosed	0	0	0	0	1 (0.1)	0.06
Hyperaesthesia teeth	0	0	0	0	1 (0.1)	0.06
Intestinal metaplasia	0	0	0	0	1 (0.1)	0.06
Irritable bowel syndrome	0	0	0	0	1 (0.1)	0.06
Lip pain	0	0	0	0	1 (0.1)	0.06
Loose tooth	0	0	0	0	1 (0.1)	0.06
Malpositioned teeth	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Mucous stools	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Oral discomfort	0	0	0	0	1 (0.1)	0.06
Oral disorder	0	0	0	0	1 (0.1)	0.06
Oral pain	0	0	0	0	1 (0.1)	0.06
Palatal disorder	0	0	0	0	1 (0.1)	0.06
Pancreatic steatosis	0	0	0	0	1 (0.1)	0.06
Pancreatitis	2 (0.4)	0.39	0	0	1 (0.1)	0.06
Proctitis ulcerative	0	0	0	0	1 (0.1)	0.06
Rectal prolapse	0	0	1 (0.2)	0.20	1 (0.1)	0.19
Salivary hypersecretion	1 (0.2)	0.39	1 (0.2)	0.20	1 (0.1)	0.06

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Tongue blistering	0	0	0	0	1 (0.1)	0.06
Tongue coated	0	0	0	0	1 (0.1)	0.13
Tongue discomfort	0	0	0	0	1 (0.1)	0.06
Tongue geographic	0	0	0	0	1 (0.1)	0.06
Tooth disorder	0	0	0	0	1 (0.1)	0.06
Tooth impacted	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Umbilical hernia	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Change of bowel habit	2 (0.4)	0.39	0	0	0	0
Chronic gastritis	1 (0.2)	0.19	0	0	0	0
Coeliac disease	0	0	1 (0.2)	0.20	0	0
Colitis ulcerative	1 (0.2)	0.19	0	0	0	0
Dental discomfort	1 (0.2)	0.19	0	0	0	0
Dental plaque	1 (0.2)	0.19	0	0	0	0
Diverticulum intestinal	1 (0.2)	0.19	0	0	0	0
Dry mouth	2 (0.4)	0.39	1 (0.2)	0.20	0	0
Faeces hard	0	0	1 (0.2)	0.20	0	0
Gastrointestinal pain	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Glossitis	0	0	1 (0.2)	0.20	0	0
Haemorrhoidal haemorrhage	1 (0.2)	0.19	0	0	0	0
Hyperchlorhydria	1 (0.2)	0.97	0	0	0	0
Intestinal prolapse	0	0	1 (0.2)	0.20	0	0
Mechanical ileus	0	0	1 (0.2)	0.20	0	0
Melaena	0	0	1 (0.2)	0.40	0	0
Pancreatic cyst	0	0	1 (0.2)	0.60	0	0
Post-tussive vomiting	0	0	1 (0.2)	0.20	0	0

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Subileus	1 (0.2)	0.19	0	0	0	0
Varices oesophageal	1 (0.2)	0.19	0	0	0	0
Investigations	166 (33.8)	74.95	176 (36.7)	80.77	338 (41.1)	52.30
Blood creatine phosphokinase increased	41 (8.4)	8.93	43 (9.0)	10.00	68 (8.3)	5.44
Alanine aminotransferase increased	29 (5.9)	6.80	38 (7.9)	8.80	56 (6.8)	4.73
Aspartate aminotransferase increased	27 (5.5)	6.02	33 (6.9)	7.40	56 (6.8)	4.34
Weight decreased	6 (1.2)	1.17	15 (3.1)	3.00	35 (4.3)	2.33
Bacterial test positive	19 (3.9)	3.88	14 (2.9)	3.20	31 (3.8)	2.72
Blood glucose increased	8 (1.6)	2.14	8 (1.7)	2.40	30 (3.6)	2.53
Forced expiratory volume decreased	4 (0.8)	0.78	9 (1.9)	2.00	24 (2.9)	1.75
Gamma-glutamyltransferase increased	13 (2.6)	3.30	9 (1.9)	2.20	23 (2.8)	1.81
Glycosylated haemoglobin increased	8 (1.6)	1.75	3 (0.6)	0.80	21 (2.6)	1.43
SARS-CoV-2 test positive	11 (2.2)	2.14	14 (2.9)	3.20	20 (2.4)	1.36
Pulmonary function test decreased	11 (2.2)	2.33	7 (1.5)	1.40	18 (2.2)	1.30
Blood alkaline phosphatase increased	9 (1.8)	1.75	9 (1.9)	1.80	14 (1.7)	1.04
Blood creatinine increased	2 (0.4)	0.39	2 (0.4)	0.40	13 (1.6)	0.84
Crystal urine present	7 (1.4)	1.94	9 (1.9)	2.40	13 (1.6)	1.10
Blood lactate dehydrogenase increased	3 (0.6)	0.58	3 (0.6)	0.80	12 (1.5)	0.84
Glucose urine present	6 (1.2)	1.17	6 (1.3)	1.20	12 (1.5)	1.23
Weight increased	2 (0.4)	0.39	4 (0.8)	0.80	12 (1.5)	0.84
White blood cells urine positive	8 (1.6)	2.14	5 (1.0)	1.60	10 (1.2)	1.10
Blood bilirubin increased	17 (3.5)	3.69	9 (1.9)	1.80	8 (1.0)	0.65
Blood cholesterol increased	1 (0.2)	0.19	1 (0.2)	0.20	7 (0.9)	0.45
Blood urea increased	1 (0.2)	0.19	1 (0.2)	0.20	6 (0.7)	0.39
Protein urine present	1 (0.2)	0.19	2 (0.4)	0.60	6 (0.7)	0.45

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Vitamin D decreased	2 (0.4)	0.39	1 (0.2)	0.20	6 (0.7)	0.39
Blood glucose decreased	6 (1.2)	1.36	1 (0.2)	0.40	5 (0.6)	0.39
Blood glucose fluctuation	0	0	5 (1.0)	1.00	5 (0.6)	0.32
Blood pressure increased	4 (0.8)	0.78	2 (0.4)	0.40	5 (0.6)	0.32
Body temperature increased	2 (0.4)	0.78	2 (0.4)	0.60	5 (0.6)	0.32
International normalised ratio increased	6 (1.2)	1.17	6 (1.3)	1.40	5 (0.6)	0.32
Specific gravity urine increased	0	0	2 (0.4)	0.60	5 (0.6)	0.39
Activated partial thromboplastin time prolonged	2 (0.4)	0.39	2 (0.4)	0.40	4 (0.5)	0.26
Blood bilirubin unconjugated increased	7 (1.4)	1.55	5 (1.0)	1.00	4 (0.5)	0.32
Eosinophil count increased	1 (0.2)	0.39	1 (0.2)	0.20	4 (0.5)	0.26
Fungal test positive	0	0	3 (0.6)	0.80	4 (0.5)	0.26
Human rhinovirus test positive	2 (0.4)	0.39	1 (0.2)	0.40	4 (0.5)	0.26
Influenza A virus test positive	4 (0.8)	0.78	1 (0.2)	0.20	4 (0.5)	0.26
Staphylococcus test positive	1 (0.2)	0.19	0	0	4 (0.5)	0.32
Urine bilirubin increased	0	0	0	0	4 (0.5)	0.26
Urine ketone body present	3 (0.6)	0.58	2 (0.4)	0.60	4 (0.5)	0.26
Viral test positive	0	0	0	0	4 (0.5)	0.26
White blood cell count decreased	1 (0.2)	0.19	2 (0.4)	0.40	4 (0.5)	0.26
Amylase increased	0	0	1 (0.2)	0.60	3 (0.4)	0.26
Blood iron decreased	0	0	0	0	3 (0.4)	0.19
Blood sodium decreased	0	0	0	0	3 (0.4)	0.26
Blood urine present	2 (0.4)	0.39	1 (0.2)	0.20	3 (0.4)	0.19
C-reactive protein increased	1 (0.2)	0.19	1 (0.2)	0.20	3 (0.4)	0.19

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Glucose tolerance test abnormal	0	0	0	0	3 (0.4)	0.19
Lymphocyte count decreased	2 (0.4)	0.39	1 (0.2)	0.40	3 (0.4)	0.19
Neutrophil count decreased	1 (0.2)	0.19	3 (0.6)	0.80	3 (0.4)	0.19
Pseudomonas test positive	2 (0.4)	0.39	2 (0.4)	0.40	3 (0.4)	0.19
Red blood cells urine positive	3 (0.6)	0.58	1 (0.2)	0.20	3 (0.4)	0.26
Respiratory syncytial virus test positive	1 (0.2)	0.19	1 (0.2)	0.20	3 (0.4)	0.19
Stenotrophomonas test positive	1 (0.2)	0.19	0	0	3 (0.4)	0.19
Streptococcus test positive	2 (0.4)	0.39	1 (0.2)	0.20	3 (0.4)	0.19
Urinary squamous epithelial cells increased	1 (0.2)	0.19	1 (0.2)	0.20	3 (0.4)	0.26
Vitamin E decreased	0	0	0	0	3 (0.4)	0.19
Atypical mycobacterium test positive	1 (0.2)	0.39	2 (0.4)	0.40	2 (0.2)	0.13
Bilirubin conjugated increased	5 (1.0)	0.97	1 (0.2)	0.20	2 (0.2)	0.13
Bilirubin urine present	0	0	0	0	2 (0.2)	0.13
Blood bicarbonate decreased	0	0	0	0	2 (0.2)	0.13
Blood potassium decreased	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Blood potassium increased	0	0	3 (0.6)	0.60	2 (0.2)	0.13
Breath sounds abnormal	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Clostridium test positive	0	0	0	0	2 (0.2)	0.13
Electrocardiogram QT shortened	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Glomerular filtration rate decreased	0	0	0	0	2 (0.2)	0.13
Haemoglobin increased	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Heart rate increased	0	0	0	0	2 (0.2)	0.13
Lipase increased	0	0	1 (0.2)	0.20	2 (0.2)	0.13

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Nitrite urine present	0	0	0	0	2 (0.2)	0.13
Platelet count decreased	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Spirometry abnormal	0	0	0	0	2 (0.2)	0.13
Urinary casts	0	0	2 (0.4)	0.40	2 (0.2)	0.19
White blood cell count increased	5 (1.0)	1.17	2 (0.4)	0.60	2 (0.2)	0.13
Acinetobacter test positive	0	0	0	0	1 (0.1)	0.06
Aspergillus test positive	0	0	0	0	1 (0.1)	0.06
Biopsy thyroid gland abnormal	0	0	0	0	1 (0.1)	0.06
Bleeding time prolonged	0	0	0	0	1 (0.1)	0.06
Blood calcium increased	0	0	0	0	1 (0.1)	0.06
Blood chloride increased	0	0	0	0	1 (0.1)	0.06
Blood immunoglobulin E increased	0	0	0	0	1 (0.1)	0.06
Blood magnesium decreased	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Blood phosphorus increased	0	0	0	0	1 (0.1)	0.06
Blood pressure diastolic increased	2 (0.4)	0.58	2 (0.4)	0.40	1 (0.1)	0.06
Blood sodium increased	0	0	0	0	1 (0.1)	0.06
Blood testosterone decreased	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Blood thyroid stimulating hormone increased	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Blood triglycerides increased	0	0	0	0	1 (0.1)	0.06
Blood urine	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Citric acid urine decreased	0	0	0	0	1 (0.1)	0.06
Eosinophil percentage increased	0	0	0	0	1 (0.1)	0.06
Faecal occult blood positive	0	0	0	0	1 (0.1)	0.06
Gastric pH decreased	0	0	1 (0.2)	0.20	1 (0.1)	0.06

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	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Glucose urine	0	0	0	0	1 (0.1)	0.06
Influenza B virus test positive	0	0	0	0	1 (0.1)	0.06
Influenza virus test positive	0	0	0	0	1 (0.1)	0.06
Lymphocyte percentage decreased	0	0	0	0	1 (0.1)	0.06
Moraxella test positive	0	0	0	0	1 (0.1)	0.06
Neutrophil count increased	3 (0.6)	0.78	3 (0.6)	1.20	1 (0.1)	0.06
Oxygen saturation decreased	0	0	0	0	1 (0.1)	0.06
Prothrombin time prolonged	4 (0.8)	0.78	3 (0.6)	0.80	1 (0.1)	0.06
Pulmonary arterial pressure increased	0	0	0	0	1 (0.1)	0.06
Reticulocyte count increased	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Serum ferritin decreased	0	0	0	0	1 (0.1)	0.06
Smear cervix abnormal	0	0	0	0	1 (0.1)	0.06
Sputum abnormal	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Transferrin saturation decreased	0	0	0	0	1 (0.1)	0.06
Ultrasound biliary tract abnormal	0	0	0	0	1 (0.1)	0.06
Ultrasound liver abnormal	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Urinary sediment present	2 (0.4)	0.39	2 (0.4)	0.60	1 (0.1)	0.13
Urine analysis abnormal	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Vitamin B12 increased	0	0	0	0	1 (0.1)	0.06
pH urine increased	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
Atypical lymphocytes increased	0	0	1 (0.2)	0.40	0	0
Blood albumin increased	0	0	1 (0.2)	0.20	0	0
Blood bicarbonate increased	1 (0.2)	0.19	0	0	0	0
Blood folate decreased	0	0	1 (0.2)	0.20	0	0
Blood immunoglobulin G increased	0	0	1 (0.2)	0.20	0	0

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	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Blood pressure decreased	0	0	2 (0.4)	0.40	0	0
Blood uric acid decreased	1 (0.2)	0.19	0	0	0	0
Burkholderia test positive	0	0	1 (0.2)	0.20	0	0
Cardiac murmur	1 (0.2)	0.19	0	0	0	0
Carotene decreased	0	0	1 (0.2)	0.20	0	0
Coronavirus test positive	0	0	1 (0.2)	0.20	0	0
Electrocardiogram PR prolongation	0	0	1 (0.2)	0.20	0	0
Electrocardiogram QT prolonged	0	0	2 (0.4)	0.40	0	0
Electrocardiogram ST segment depression	1 (0.2)	0.19	0	0	0	0
Enzyme level decreased	1 (0.2)	0.19	0	0	0	0
Escherichia test positive	1 (0.2)	0.19	0	0	0	0
Faecal volume increased	0	0	2 (0.4)	0.40	0	0
Fibrin D dimer increased	1 (0.2)	0.19	0	0	0	0
Giardia test positive	1 (0.2)	0.19	0	0	0	0
Haemoglobin decreased	2 (0.4)	0.39	1 (0.2)	0.20	0	0
Haemophilus test positive	2 (0.4)	0.39	0	0	0	0
Heart rate decreased	0	0	1 (0.2)	0.20	0	0
Heart rate irregular	1 (0.2)	0.19	0	0	0	0
Hormone level abnormal	1 (0.2)	0.19	0	0	0	0
Lipase decreased	0	0	1 (0.2)	0.20	0	0
Lymphocyte count increased	0	0	1 (0.2)	0.40	0	0
Monocyte count increased	0	0	1 (0.2)	0.20	0	0
Mycobacterium test positive	0	0	1 (0.2)	0.20	0	0
Ophthalmological examination abnormal	1 (0.2)	0.19	0	0	0	0

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Protein total increased	0	0	1 (0.2)	0.20	0	0
Protein urine	1 (0.2)	0.19	0	0	0	0
Red blood cell count increased	0	0	1 (0.2)	0.20	0	0
Respiratory rate increased	1 (0.2)	0.19	0	0	0	0
Serratia test positive	1 (0.2)	0.19	0	0	0	0
Urine albumin/creatinine ratio increased	1 (0.2)	0.19	0	0	0	0
Urine output increased	0	0	1 (0.2)	0.20	0	0
Vitamin B12 decreased	0	0	1 (0.2)	0.20	0	0
Vitamin K decreased	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Yersinia test positive	1 (0.2)	0.19	0	0	0	0
General disorders and administration site conditions	119 (24.2)	37.67	142 (29.6)	47.38	259 (31.5)	29.17
Pyrexia	50 (10.2)	13.20	52 (10.8)	13.99	109 (13.3)	9.27
Fatigue	46 (9.4)	11.84	51 (10.6)	12.19	97 (11.8)	8.81
Pain	9 (1.8)	1.94	18 (3.8)	4.20	23 (2.8)	1.69
Influenza like illness	7 (1.4)	1.75	8 (1.7)	2.00	22 (2.7)	1.69
Peripheral swelling	3 (0.6)	0.58	4 (0.8)	1.00	14 (1.7)	1.10
Chills	3 (0.6)	0.58	9 (1.9)	2.00	12 (1.5)	0.91
Asthenia	8 (1.6)	1.75	5 (1.0)	1.20	11 (1.3)	0.78
Malaise	6 (1.2)	1.17	8 (1.7)	1.80	9 (1.1)	0.65
Chest discomfort	3 (0.6)	0.58	6 (1.3)	1.40	7 (0.9)	0.45
Chest pain	3 (0.6)	0.58	6 (1.3)	1.20	7 (0.9)	0.58
Oedema peripheral	5 (1.0)	1.36	4 (0.8)	1.20	5 (0.6)	0.39
Exercise tolerance decreased	1 (0.2)	0.19	0	0	3 (0.4)	0.19

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Feeling cold	2 (0.4)	0.39	1 (0.2)	0.40	3 (0.4)	0.19
General physical health deterioration	0	0	0	0	3 (0.4)	0.19
Adverse drug reaction	0	0	0	0	2 (0.2)	0.19
Application site rash	1 (0.2)	0.19	2 (0.4)	0.40	2 (0.2)	0.13
Chronic fatigue syndrome	0	0	2 (0.4)	0.40	2 (0.2)	0.13
Hyperthermia	1 (0.2)	0.19	0	0	2 (0.2)	0.19
Impaired healing	0	0	0	0	2 (0.2)	0.13
Medical device pain	0	0	2 (0.4)	0.40	2 (0.2)	0.13
Crepitations	0	0	0	0	1 (0.1)	0.06
Cyst	0	0	3 (0.6)	0.60	1 (0.1)	0.06
Drug withdrawal syndrome	0	0	0	0	1 (0.1)	0.06
Dysplasia	0	0	0	0	1 (0.1)	0.06
Face oedema	0	0	0	0	1 (0.1)	0.13
Facial pain	0	0	0	0	1 (0.1)	0.06
Gait disturbance	0	0	0	0	1 (0.1)	0.06
Hernia	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Hunger	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Hyperpyrexia	0	0	0	0	1 (0.1)	0.06
Inflammation	0	0	0	0	1 (0.1)	0.06
Injection site inflammation	0	0	0	0	1 (0.1)	0.13
Injection site pain	0	0	0	0	1 (0.1)	0.06
Injection site rash	0	0	0	0	1 (0.1)	0.06
Maxillofacial pain	0	0	0	0	1 (0.1)	0.06
Sensation of foreign body	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Temperature regulation disorder	0	0	0	0	1 (0.1)	0.06

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Vaccination site discomfort	0	0	0	0	1 (0.1)	0.06
Vaccination site pain	0	0	0	0	1 (0.1)	0.06
Application site reaction	0	0	1 (0.2)	0.20	0	0
Axillary pain	0	0	1 (0.2)	0.20	0	0
Catheter site erythema	0	0	1 (0.2)	0.20	0	0
Device related thrombosis	0	0	1 (0.2)	0.20	0	0
Drug intolerance	0	0	1 (0.2)	0.20	0	0
Ill-defined disorder	0	0	1 (0.2)	0.20	0	0
Implant site pain	0	0	1 (0.2)	0.20	0	0
Mass	1 (0.2)	0.19	0	0	0	0
Medical device site rash	0	0	1 (0.2)	0.20	0	0
Non-cardiac chest pain	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Oedema	0	0	1 (0.2)	0.20	0	0
Soft tissue inflammation	0	0	1 (0.2)	0.20	0	0
Swelling	0	0	1 (0.2)	0.20	0	0
Temperature intolerance	1 (0.2)	0.19	0	0	0	0
Thirst	2 (0.4)	0.39	0	0	0	0
Vascular device occlusion	1 (0.2)	0.19	0	0	0	0
Vessel puncture site pain	0	0	1 (0.2)	0.20	0	0
Nervous system disorders	98 (20.0)	41.36	111 (23.1)	32.59	233 (28.3)	32.15
Headache	63 (12.8)	26.80	76 (15.8)	18.59	153 (18.6)	18.99
Dizziness	16 (3.3)	3.30	13 (2.7)	3.00	29 (3.5)	2.27
Lethargy	2 (0.4)	0.39	7 (1.5)	2.00	20 (2.4)	1.81
Migraine	9 (1.8)	2.33	9 (1.9)	2.00	17 (2.1)	1.23
Syncope	3 (0.6)	0.58	7 (1.5)	2.20	13 (1.6)	0.91

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Paraesthesia	0	0	1 (0.2)	0.20	12 (1.5)	0.91
Brain fog	0	0	1 (0.2)	0.20	10 (1.2)	0.71
Disturbance in attention	3 (0.6)	0.78	0	0	6 (0.7)	0.39
Hypoaesthesia	3 (0.6)	0.78	2 (0.4)	0.40	6 (0.7)	0.58
Carpal tunnel syndrome	1 (0.2)	0.19	0	0	5 (0.6)	0.39
Neuralgia	0	0	0	0	3 (0.4)	0.19
Presyncope	3 (0.6)	0.58	0	0	3 (0.4)	0.32
Amnesia	1 (0.2)	0.39	1 (0.2)	0.20	2 (0.2)	0.13
Dizziness postural	0	0	0	0	2 (0.2)	0.13
Memory impairment	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Migraine with aura	0	0	0	0	2 (0.2)	0.13
Nerve compression	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Neuropathy peripheral	0	0	0	0	2 (0.2)	0.13
Restless legs syndrome	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Sciatica	2 (0.4)	0.39	3 (0.6)	0.60	2 (0.2)	0.13
Seizure	2 (0.4)	0.58	1 (0.2)	0.20	2 (0.2)	0.19
Sensory disturbance	0	0	0	0	2 (0.2)	0.13
Sinus headache	1 (0.2)	0.19	5 (1.0)	1.00	2 (0.2)	0.13
Ageusia	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Alcoholic seizure	0	0	0	0	1 (0.1)	0.13
Anosmia	0	0	2 (0.4)	0.40	1 (0.1)	0.06
Aphantasia	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Aphasia	0	0	0	0	1 (0.1)	0.06
Bell's palsy	0	0	0	0	1 (0.1)	0.06
Dysgeusia	0	0	0	0	1 (0.1)	0.06

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Electric shock sensation	0	0	0	0	1 (0.1)	0.06
Focal dyscognitive seizures	0	0	0	0	1 (0.1)	0.13
Formication	0	0	0	0	1 (0.1)	0.06
Hyperreflexia	0	0	0	0	1 (0.1)	0.06
Hypoglycaemic coma	0	0	0	0	1 (0.1)	0.13
Hypoglycaemic unconsciousness	0	0	0	0	1 (0.1)	0.06
Narcolepsy	0	0	0	0	1 (0.1)	0.06
Ophthalmic migraine	0	0	0	0	1 (0.1)	0.06
Parosmia	0	0	0	0	1 (0.1)	0.06
Radicular pain	0	0	0	0	1 (0.1)	0.06
Radiculopathy	0	0	0	0	1 (0.1)	0.06
Reversible cerebral vasoconstriction syndrome	0	0	0	0	1 (0.1)	0.06
Shift work disorder	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Sleep paralysis	0	0	0	0	1 (0.1)	0.13
Subarachnoid haemorrhage	0	0	0	0	1 (0.1)	0.06
Tension headache	0	0	0	0	1 (0.1)	0.06
Thunderclap headache	0	0	0	0	1 (0.1)	0.06
Tremor	3 (0.6)	0.58	1 (0.2)	0.20	1 (0.1)	0.06
Trigeminal neuralgia	0	0	0	0	1 (0.1)	0.06
Autonomic nervous system imbalance	1 (0.2)	0.19	0	0	0	0
Balance disorder	2 (0.4)	0.39	0	0	0	0
Circadian rhythm sleep disorder	0	0	1 (0.2)	0.40	0	0
Epilepsy	1 (0.2)	0.19	0	0	0	0
Haemorrhage intracranial	0	0	1 (0.2)	0.20	0	0

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

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System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Hyperaesthesia	0	0	1 (0.2)	0.20	0	0
Hyperresponsive to stimuli	1 (0.2)	0.19	0	0	0	0
Hyposmia	1 (0.2)	0.19	0	0	0	0
Loss of consciousness	1 (0.2)	0.19	0	0	0	0
Meralgia paraesthetica	1 (0.2)	0.19	0	0	0	0
Post-traumatic headache	0	0	2 (0.4)	0.40	0	0
Psychomotor hyperactivity	1 (0.2)	0.39	0	0	0	0
Serotonin syndrome	1 (0.2)	0.19	0	0	0	0
Somnolence	1 (0.2)	0.19	0	0	0	0
Musculoskeletal and connective tissue disorders	119 (24.2)	33.40	96 (20.0)	27.39	232 (28.2)	27.16
Arthralgia	36 (7.3)	7.77	24 (5.0)	5.20	70 (8.5)	5.96
Back pain	31 (6.3)	6.41	25 (5.2)	6.20	57 (6.9)	4.08
Myalgia	10 (2.0)	1.94	17 (3.5)	4.00	37 (4.5)	2.79
Pain in extremity	14 (2.9)	2.91	7 (1.5)	1.40	31 (3.8)	2.46
Musculoskeletal chest pain	9 (1.8)	1.94	10 (2.1)	2.20	18 (2.2)	1.36
Osteopenia	2 (0.4)	0.39	1 (0.2)	0.20	11 (1.3)	0.71
Muscle spasms	9 (1.8)	2.33	4 (0.8)	0.80	10 (1.2)	0.78
Neck pain	5 (1.0)	0.97	3 (0.6)	0.60	9 (1.1)	0.65
Musculoskeletal stiffness	1 (0.2)	0.19	1 (0.2)	0.20	8 (1.0)	0.52
Tendonitis	4 (0.8)	0.78	2 (0.4)	0.40	7 (0.9)	0.45
Flank pain	4 (0.8)	0.78	3 (0.6)	0.60	6 (0.7)	0.52
Osteoarthritis	1 (0.2)	0.19	2 (0.4)	0.40	6 (0.7)	0.45
Muscular weakness	2 (0.4)	0.39	0	0	5 (0.6)	0.32
Musculoskeletal pain	1 (0.2)	0.19	1 (0.2)	0.20	5 (0.6)	0.32

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Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Plantar fasciitis	0	0	1 (0.2)	0.20	5 (0.6)	0.32
Joint stiffness	1 (0.2)	0.19	1 (0.2)	0.20	4 (0.5)	0.26
Joint swelling	2 (0.4)	0.39	1 (0.2)	0.20	4 (0.5)	0.26
Osteoporosis	1 (0.2)	0.39	0	0	4 (0.5)	0.26
Periarthritis	2 (0.4)	0.39	1 (0.2)	0.20	4 (0.5)	0.26
Synovial cyst	0	0	0	0	4 (0.5)	0.32
Arthritis	2 (0.4)	0.39	2 (0.4)	0.40	3 (0.4)	0.19
Bursitis	0	0	1 (0.2)	0.20	3 (0.4)	0.19
Muscle tightness	3 (0.6)	0.58	2 (0.4)	0.40	3 (0.4)	0.19
Rotator cuff syndrome	1 (0.2)	0.19	0	0	3 (0.4)	0.19
Bone pain	0	0	0	0	2 (0.2)	0.13
Femoroacetabular impingement	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Intervertebral disc protrusion	2 (0.4)	0.58	1 (0.2)	0.20	2 (0.2)	0.13
Joint range of motion decreased	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Muscle twitching	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Musculoskeletal discomfort	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.19
Pain in jaw	1 (0.2)	0.39	0	0	2 (0.2)	0.13
Patellofemoral pain syndrome	0	0	0	0	2 (0.2)	0.13
Rheumatoid arthritis	0	0	0	0	2 (0.2)	0.13
Tendon disorder	0	0	0	0	2 (0.2)	0.13
Tendon pain	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Tenosynovitis stenosans	1 (0.2)	0.19	2 (0.4)	0.40	2 (0.2)	0.19
Bone cyst	0	0	0	0	1 (0.1)	0.06
Coccydynia	0	0	0	0	1 (0.1)	0.06
Costochondritis	0	0	1 (0.2)	0.20	1 (0.1)	0.06

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	Parent Study Integrated Safety Analysis				OL Study	
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System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Dupuytren's contracture	0	0	0	0	1 (0.1)	0.06
Fibromyalgia	0	0	0	0	1 (0.1)	0.06
Greater trochanteric pain syndrome	0	0	0	0	1 (0.1)	0.06
Groin pain	0	0	0	0	1 (0.1)	0.06
Intervertebral disc degeneration	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Joint effusion	0	0	0	0	1 (0.1)	0.06
Joint hyperextension	0	0	0	0	1 (0.1)	0.06
Joint impingement	0	0	0	0	1 (0.1)	0.06
Muscle contracture	0	0	0	0	1 (0.1)	0.06
Muscle discomfort	0	0	0	0	1 (0.1)	0.06
Muscle fatigue	0	0	0	0	1 (0.1)	0.06
Myosclerosis	0	0	0	0	1 (0.1)	0.06
Osteoporotic fracture	0	0	0	0	1 (0.1)	0.06
Rheumatic disorder	0	0	0	0	1 (0.1)	0.06
Sjogren's syndrome	0	0	0	0	1 (0.1)	0.06
Spinal pain	0	0	0	0	1 (0.1)	0.06
Systemic lupus erythematosus	0	0	1 (0.2)	0.20	1 (0.1)	0.13
Temporomandibular pain and dysfunction syndrome	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Tenosynovitis	0	0	0	0	1 (0.1)	0.06
Trigger finger	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.13
Arthropathy	1 (0.2)	0.58	1 (0.2)	0.20	0	0
Bursa disorder	1 (0.2)	0.19	0	0	0	0
Limb discomfort	1 (0.2)	0.19	0	0	0	0
Myositis	2 (0.4)	0.39	0	0	0	0

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Osteochondrosis	1 (0.2)	0.19	0	0	0	0
Periostitis	0	0	1 (0.2)	0.40	0	0
Polyarthritis	0	0	1 (0.2)	0.20	0	0
Spondylitis	0	0	1 (0.2)	0.20	0	0
Vertebral foraminal stenosis	1 (0.2)	0.19	0	0	0	0
Injury, poisoning and procedural complications	89 (18.1)	25.44	82 (17.1)	26.59	192 (23.4)	21.97
Ligament sprain	6 (1.2)	1.55	8 (1.7)	1.60	23 (2.8)	1.69
Limb injury	3 (0.6)	0.58	6 (1.3)	1.20	19 (2.3)	1.36
Skin laceration	8 (1.6)	1.55	8 (1.7)	2.00	19 (2.3)	1.69
Contusion	4 (0.8)	0.78	8 (1.7)	1.80	17 (2.1)	1.30
Muscle strain	3 (0.6)	0.58	5 (1.0)	1.00	17 (2.1)	1.36
Arthropod bite	6 (1.2)	1.36	4 (0.8)	1.00	9 (1.1)	0.71
Immunisation reaction	5 (1.0)	0.97	9 (1.9)	3.40	9 (1.1)	0.65
Fall	3 (0.6)	0.58	9 (1.9)	2.00	8 (1.0)	0.65
Joint injury	4 (0.8)	1.17	0	0	8 (1.0)	0.52
Procedural pain	7 (1.4)	1.36	3 (0.6)	0.80	8 (1.0)	0.58
Road traffic accident	4 (0.8)	0.78	6 (1.3)	1.20	8 (1.0)	0.52
Skin abrasion	2 (0.4)	0.39	2 (0.4)	0.40	8 (1.0)	0.52
Animal bite	4 (0.8)	0.78	3 (0.6)	0.60	7 (0.9)	0.65
Hand fracture	6 (1.2)	1.36	2 (0.4)	0.40	7 (0.9)	0.58
Thermal burn	4 (0.8)	0.78	2 (0.4)	0.40	7 (0.9)	0.45
Bone contusion	1 (0.2)	0.19	1 (0.2)	0.20	6 (0.7)	0.39
Foot fracture	2 (0.4)	0.39	1 (0.2)	0.20	6 (0.7)	0.45
Concussion	3 (0.6)	0.58	6 (1.3)	1.20	5 (0.6)	0.32

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Ligament rupture	0	0	1 (0.2)	0.20	5 (0.6)	0.32
Chest injury	1 (0.2)	0.19	4 (0.8)	0.80	4 (0.5)	0.26
Ankle fracture	1 (0.2)	0.39	0	0	3 (0.4)	0.19
Back injury	2 (0.4)	0.39	1 (0.2)	0.20	3 (0.4)	0.19
Cartilage injury	0	0	0	0	3 (0.4)	0.19
Muscle injury	0	0	0	0	3 (0.4)	0.19
Muscle rupture	0	0	0	0	3 (0.4)	0.19
Post-traumatic neck syndrome	1 (0.2)	0.19	0	0	3 (0.4)	0.26
Rib fracture	1 (0.2)	0.19	2 (0.4)	0.40	3 (0.4)	0.26
Sunburn	2 (0.4)	0.58	2 (0.4)	0.40	3 (0.4)	0.19
Tooth fracture	2 (0.4)	0.39	0	0	3 (0.4)	0.19
Arthropod sting	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Avulsion fracture	0	0	0	0	2 (0.2)	0.13
Clavicle fracture	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Corneal abrasion	0	0	0	0	2 (0.2)	0.13
Craniofacial fracture	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Epicondylitis	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Face injury	0	0	0	0	2 (0.2)	0.13
Foreign body	0	0	0	0	2 (0.2)	0.13
Head injury	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Heat stroke	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Post procedural haemorrhage	0	0	0	0	2 (0.2)	0.13
Soft tissue injury	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Stress fracture	0	0	0	0	2 (0.2)	0.13
Tendon rupture	0	0	0	0	2 (0.2)	0.13

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Wound	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Accident	0	0	2 (0.4)	0.40	1 (0.1)	0.06
Accidental exposure to product	0	0	0	0	1 (0.1)	0.06
Accidental overdose	0	0	0	0	1 (0.1)	0.06
Alcohol poisoning	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Brain contusion	0	0	0	0	1 (0.1)	0.13
Burns second degree	0	0	0	0	1 (0.1)	0.06
Buttock injury	0	0	0	0	1 (0.1)	0.06
Craniocerebral injury	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Diffuse axonal injury	0	0	0	0	1 (0.1)	0.06
Eye contusion	0	0	0	0	1 (0.1)	0.06
Eye injury	0	0	0	0	1 (0.1)	0.06
Femur fracture	0	0	0	0	1 (0.1)	0.06
Fibula fracture	0	0	0	0	1 (0.1)	0.06
Foreign body in eye	0	0	0	0	1 (0.1)	0.06
Fractured coccyx	0	0	0	0	1 (0.1)	0.06
Heat exhaustion	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Human bite	0	0	0	0	1 (0.1)	0.06
Humerus fracture	0	0	0	0	1 (0.1)	0.06
Incisional hernia	0	0	0	0	1 (0.1)	0.06
Incorrect dose administered	0	0	0	0	1 (0.1)	0.06
Intervertebral disc injury	0	0	0	0	1 (0.1)	0.19
Limb crushing injury	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Limb fracture	0	0	0	0	1 (0.1)	0.06
Meniscus injury	1 (0.2)	0.19	0	0	1 (0.1)	0.06

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Musculoskeletal injury	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Neck injury	2 (0.4)	0.39	2 (0.4)	0.40	1 (0.1)	0.06
Penis injury	0	0	0	0	1 (0.1)	0.06
Periorbital haematoma	0	0	0	0	1 (0.1)	0.06
Poisoning deliberate	0	0	0	0	1 (0.1)	0.06
Post procedural discomfort	0	0	0	0	1 (0.1)	0.06
Post procedural haematuria	0	0	0	0	1 (0.1)	0.06
Postoperative respiratory failure	0	0	0	0	1 (0.1)	0.06
Procedural dizziness	0	0	1 (0.2)	0.20	1 (0.1)	0.13
Radiation pneumonitis	0	0	0	0	1 (0.1)	0.06
Scapula fracture	0	0	0	0	1 (0.1)	0.13
Scratch	0	0	0	0	1 (0.1)	0.06
Skeletal injury	0	0	0	0	1 (0.1)	0.06
Sternal injury	0	0	0	0	1 (0.1)	0.06
Stoma site discomfort	0	0	0	0	1 (0.1)	0.06
Subdural haematoma	0	0	0	0	1 (0.1)	0.06
Superficial injury of eye	0	0	0	0	1 (0.1)	0.06
Torus fracture	0	0	0	0	1 (0.1)	0.06
Venomous sting	0	0	0	0	1 (0.1)	0.06
Wrist fracture	0	0	0	0	1 (0.1)	0.06
Abdominal injury	1 (0.2)	0.19	0	0	0	0
Bone fissure	1 (0.2)	0.19	0	0	0	0
Chillblains	1 (0.2)	0.19	0	0	0	0
Exposure to communicable disease	1 (0.2)	0.19	0	0	0	0
Iliotibial band syndrome	1 (0.2)	0.19	0	0	0	0

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Incision site inflammation	0	0	1 (0.2)	0.20	0	0
Joint dislocation	0	0	1 (0.2)	0.20	0	0
Ligament injury	1 (0.2)	0.19	0	0	0	0
Lumbar vertebral fracture	1 (0.2)	0.19	0	0	0	0
Mouth injury	1 (0.2)	0.19	0	0	0	0
Nail avulsion	1 (0.2)	0.19	0	0	0	0
Nasal injury	1 (0.2)	0.19	0	0	0	0
Post procedural complication	1 (0.2)	0.19	0	0	0	0
Post procedural haematoma	0	0	1 (0.2)	0.20	0	0
Postoperative ileus	1 (0.2)	0.19	0	0	0	0
Procedural complication	1 (0.2)	0.19	0	0	0	0
Radius fracture	0	0	2 (0.4)	0.40	0	0
Respiratory fume inhalation disorder	1 (0.2)	0.39	1 (0.2)	0.20	0	0
Skull fractured base	0	0	1 (0.2)	0.20	0	0
Sports injury	1 (0.2)	0.19	0	0	0	0
Stoma site discharge	2 (0.4)	0.39	1 (0.2)	0.40	0	0
Stoma site erythema	1 (0.2)	0.19	0	0	0	0
Stoma site pain	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Toxicity to various agents	0	0	1 (0.2)	0.20	0	0
Traumatic haematoma	2 (0.4)	0.39	1 (0.2)	0.20	0	0
Traumatic pain	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Ulna fracture	0	0	1 (0.2)	0.20	0	0
Upper limb fracture	0	0	2 (0.4)	0.40	0	0
Skin and subcutaneous tissue disorders	87 (17.7)	22.33	98 (20.4)	27.59	167 (20.3)	15.49
Rash	22 (4.5)	4.85	37 (7.7)	9.20	44 (5.4)	3.31

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Acne	20 (4.1)	4.27	16 (3.3)	3.20	19 (2.3)	1.43
Pruritus	9 (1.8)	2.14	10 (2.1)	2.00	18 (2.2)	1.36
Alopecia	7 (1.4)	1.36	7 (1.5)	1.40	14 (1.7)	0.97
Eczema	4 (0.8)	0.78	5 (1.0)	1.20	13 (1.6)	0.97
Dermatitis	0	0	2 (0.4)	0.40	6 (0.7)	0.45
Urticaria	7 (1.4)	1.36	5 (1.0)	1.60	6 (0.7)	0.97
Dry skin	5 (1.0)	0.97	2 (0.4)	0.40	5 (0.6)	0.39
Night sweats	3 (0.6)	0.58	3 (0.6)	0.60	5 (0.6)	0.32
Rash pruritic	0	0	1 (0.2)	0.20	5 (0.6)	0.32
Acne cystic	0	0	0	0	3 (0.4)	0.19
Dermatitis acneiform	0	0	0	0	3 (0.4)	0.19
Dermatitis contact	3 (0.6)	0.58	3 (0.6)	0.60	3 (0.4)	0.19
Drug eruption	0	0	2 (0.4)	0.40	3 (0.4)	0.19
Ecchymosis	2 (0.4)	0.39	0	0	3 (0.4)	0.19
Miliaria	0	0	1 (0.2)	0.20	3 (0.4)	0.26
Photosensitivity reaction	1 (0.2)	0.19	2 (0.4)	0.40	3 (0.4)	0.19
Rash erythematous	1 (0.2)	0.19	2 (0.4)	0.40	3 (0.4)	0.26
Rash macular	0	0	0	0	3 (0.4)	0.19
Rash maculo-papular	0	0	2 (0.4)	0.40	3 (0.4)	0.19
Actinic keratosis	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Blister	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Dermal cyst	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.19
Dermatitis atopic	0	0	0	0	2 (0.2)	0.13
Hyperhidrosis	1 (0.2)	0.19	4 (0.8)	0.80	2 (0.2)	0.13
Ingrowing nail	0	0	1 (0.2)	0.20	2 (0.2)	0.13

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Mechanical urticaria	0	0	0	0	2 (0.2)	0.13
Nail bed inflammation	0	0	0	0	2 (0.2)	0.13
Rash papular	2 (0.4)	0.39	0	0	2 (0.2)	0.13
Rosacea	0	0	0	0	2 (0.2)	0.19
Seborrhoeic dermatitis	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Skin lesion	0	0	0	0	2 (0.2)	0.13
Cold sweat	1 (0.2)	0.19	0	0	1 (0.1)	0.13
Dandruff	0	0	0	0	1 (0.1)	0.06
Erythema	1 (0.2)	0.19	4 (0.8)	0.80	1 (0.1)	0.06
Granuloma annulare	0	0	0	0	1 (0.1)	0.06
Idiopathic urticaria	0	0	0	0	1 (0.1)	0.06
Macule	0	0	0	0	1 (0.1)	0.06
Milia	0	0	0	0	1 (0.1)	0.06
Onychoclasis	0	0	0	0	1 (0.1)	0.06
Pruritus allergic	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Skin burning sensation	0	0	0	0	1 (0.1)	0.06
Skin fissures	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Skin irritation	0	0	0	0	1 (0.1)	0.06
Skin swelling	0	0	0	0	1 (0.1)	0.06
Skin ulcer	0	0	0	0	1 (0.1)	0.06
Solar dermatitis	0	0	0	0	1 (0.1)	0.06
Solar urticaria	0	0	0	0	1 (0.1)	0.06
Vancomycin infusion reaction	0	0	0	0	1 (0.1)	0.06
Vitiligo	0	0	0	0	1 (0.1)	0.06
Androgenetic alopecia	1 (0.2)	0.19	0	0	0	0

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Blood blister	0	0	1 (0.2)	0.20	0	0
Dermatitis allergic	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Dyshidrotic eczema	1 (0.2)	0.19	0	0	0	0
Ephelides	0	0	1 (0.2)	0.20	0	0
Erythema nodosum	0	0	1 (0.2)	0.20	0	0
Hand dermatitis	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Hangnail	1 (0.2)	0.19	0	0	0	0
Lichen planus	1 (0.2)	0.19	0	0	0	0
Madarosis	0	0	1 (0.2)	0.20	0	0
Neurodermatitis	0	0	1 (0.2)	0.20	0	0
Onycholysis	1 (0.2)	0.19	0	0	0	0
Onychomadesis	0	0	1 (0.2)	0.20	0	0
Palmoplantar keratoderma	1 (0.2)	0.19	0	0	0	0
Perioral dermatitis	1 (0.2)	0.19	0	0	0	0
Pityriasis rosea	0	0	1 (0.2)	0.20	0	0
Psoriasis	1 (0.2)	0.19	0	0	0	0
Rash follicular	0	0	1 (0.2)	0.20	0	0
Rash vesicular	1 (0.2)	0.19	0	0	0	0
Scab	1 (0.2)	0.19	0	0	0	0
Scar pain	1 (0.2)	0.19	0	0	0	0
Sensitive skin	1 (0.2)	0.19	0	0	0	0
Skin discolouration	0	0	1 (0.2)	0.20	0	0
Skin mass	1 (0.2)	0.19	0	0	0	0
Sweat gland disorder	1 (0.2)	0.19	0	0	0	0
Urticaria chronic	0	0	1 (0.2)	0.20	0	0

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- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Psychiatric disorders	70 (14.3)	19.42	60 (12.5)	17.99	136 (16.5)	13.16
Anxiety	10 (2.0)	2.33	21 (4.4)	4.40	35 (4.3)	2.27
Depression	10 (2.0)	1.94	14 (2.9)	3.00	26 (3.2)	1.81
Insomnia	22 (4.5)	4.85	15 (3.1)	3.00	26 (3.2)	1.88
Depressed mood	7 (1.4)	1.36	4 (0.8)	0.80	20 (2.4)	1.56
Attention deficit hyperactivity disorder	4 (0.8)	0.78	1 (0.2)	0.20	10 (1.2)	0.65
Sleep disorder	1 (0.2)	0.19	0	0	9 (1.1)	0.58
Poor quality sleep	5 (1.0)	0.97	3 (0.6)	0.60	5 (0.6)	0.39
Stress	1 (0.2)	0.19	2 (0.4)	0.40	5 (0.6)	0.39
Irritability	2 (0.4)	0.39	1 (0.2)	0.20	4 (0.5)	0.26
Panic attack	3 (0.6)	0.58	1 (0.2)	0.20	4 (0.5)	0.26
Apathy	0	0	0	0	3 (0.4)	0.19
Alcohol use disorder	0	0	0	0	2 (0.2)	0.13
Depressive symptom	3 (0.6)	0.58	0	0	2 (0.2)	0.19
Gender dysphoria	0	0	0	0	2 (0.2)	0.13
Initial insomnia	1 (0.2)	0.19	3 (0.6)	0.60	2 (0.2)	0.13
Libido decreased	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Loss of libido	0	0	0	0	2 (0.2)	0.13
Mood swings	0	0	3 (0.6)	0.60	2 (0.2)	0.13
Suicidal ideation	4 (0.8)	0.78	2 (0.4)	0.40	2 (0.2)	0.13
Abnormal behaviour	0	0	0	0	1 (0.1)	0.06
Adjustment disorder with depressed mood	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Alcohol abuse	0	0	0	0	1 (0.1)	0.06

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Anger	2 (0.4)	0.78	1 (0.2)	0.20	1 (0.1)	0.06
Anhedonia	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Anxiety disorder	0	0	0	0	1 (0.1)	0.19
Burnout syndrome	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Confusional state	0	0	0	0	1 (0.1)	0.06
Dyssomnia	0	0	0	0	1 (0.1)	0.06
Emotional disorder	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Generalised anxiety disorder	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Grief reaction	0	0	0	0	1 (0.1)	0.06
Illusion	0	0	0	0	1 (0.1)	0.06
Listless	0	0	0	0	1 (0.1)	0.06
Major depression	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Mental disorder	0	0	0	0	1 (0.1)	0.06
Mental fatigue	1 (0.2)	0.39	2 (0.4)	0.60	1 (0.1)	0.06
Mental status changes	0	0	0	0	1 (0.1)	0.06
Middle insomnia	1 (0.2)	0.19	2 (0.4)	0.40	1 (0.1)	0.06
Nightmare	0	0	0	0	1 (0.1)	0.06
Premature ejaculation	0	0	0	0	1 (0.1)	0.06
Procedural anxiety	0	0	0	0	1 (0.1)	0.06
Sleep terror	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Social anxiety disorder	0	0	0	0	1 (0.1)	0.06
Substance abuse	0	0	0	0	1 (0.1)	0.06
Tic	0	0	0	0	1 (0.1)	0.06
Abnormal dreams	1 (0.2)	0.19	0	0	0	0
Acute stress disorder	0	0	1 (0.2)	0.20	0	0

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Adjustment disorder	0	0	1 (0.2)	0.20	0	0
Adjustment disorder with anxiety	1 (0.2)	0.19	0	0	0	0
Agitation	0	0	2 (0.4)	0.40	0	0
Alcoholic hangover	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Behaviour disorder	1 (0.2)	0.19	0	0	0	0
Complex tic	1 (0.2)	0.19	0	0	0	0
Depression suicidal	1 (0.2)	0.19	0	0	0	0
Libido increased	0	0	1 (0.2)	0.20	0	0
Mixed anxiety and depressive disorder	1 (0.2)	0.19	0	0	0	0
Mood altered	2 (0.4)	0.39	0	0	0	0
Purging	1 (0.2)	0.19	0	0	0	0
Seasonal affective disorder	0	0	1 (0.2)	0.20	0	0
Somatic symptom disorder	0	0	1 (0.2)	0.20	0	0
Tachyphrenia	1 (0.2)	0.19	0	0	0	0
Metabolism and nutrition disorders	43 (8.8)	10.10	45 (9.4)	10.40	125 (15.2)	11.54
Hypoglycaemia	13 (2.6)	2.91	7 (1.5)	1.40	21 (2.6)	1.56
Decreased appetite	13 (2.6)	2.91	7 (1.5)	1.40	17 (2.1)	1.17
Vitamin D deficiency	2 (0.4)	0.39	2 (0.4)	0.40	15 (1.8)	1.04
Hyperglycaemia	2 (0.4)	0.39	7 (1.5)	1.40	11 (1.3)	0.84
Diabetes mellitus inadequate control	0	0	0	0	9 (1.1)	0.65
Gout	1 (0.2)	0.19	1 (0.2)	0.60	8 (1.0)	0.84
Iron deficiency	4 (0.8)	0.78	4 (0.8)	0.80	8 (1.0)	0.52
Hypokalaemia	1 (0.2)	0.19	3 (0.6)	0.60	7 (0.9)	0.45
Hyponatraemia	2 (0.4)	0.78	2 (0.4)	0.40	7 (0.9)	0.45
Glucose tolerance impaired	1 (0.2)	0.19	3 (0.6)	0.60	6 (0.7)	0.39

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Dehydration	1 (0.2)	0.19	1 (0.2)	0.20	5 (0.6)	0.45
Hypercholesterolaemia	0	0	2 (0.4)	0.40	5 (0.6)	0.32
Abnormal loss of weight	1 (0.2)	0.19	0	0	3 (0.4)	0.19
Hypomagnesaemia	1 (0.2)	0.19	0	0	3 (0.4)	0.19
Increased appetite	0	0	1 (0.2)	0.20	3 (0.4)	0.19
Vitamin A deficiency	0	0	1 (0.2)	0.20	3 (0.4)	0.26
Vitamin B12 deficiency	0	0	0	0	3 (0.4)	0.19
Diabetic ketoacidosis	0	0	0	0	2 (0.2)	0.13
Hypophosphataemia	0	0	0	0	2 (0.2)	0.13
Hypovitaminosis	0	0	0	0	2 (0.2)	0.13
Polydipsia	0	0	0	0	2 (0.2)	0.13
Type 3 diabetes mellitus	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Carbohydrate intolerance	0	0	0	0	1 (0.1)	0.06
Fluid intake reduced	0	0	0	0	1 (0.1)	0.13
Food intolerance	0	0	0	0	1 (0.1)	0.06
Hyperkalaemia	0	0	0	0	1 (0.1)	0.06
Hyperlipidaemia	0	0	0	0	1 (0.1)	0.06
Hyperphagia	0	0	0	0	1 (0.1)	0.06
Hyperphosphatasaemia	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Hypocalcaemia	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Ketosis	0	0	0	0	1 (0.1)	0.06
Lactic acidosis	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Lactose intolerance	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Malnutrition	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Postprandial hypoglycaemia	1 (0.2)	0.19	0	0	1 (0.1)	0.13

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Type 2 diabetes mellitus	0	0	0	0	1 (0.1)	0.06
Vitamin E deficiency	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Vitamin K deficiency	0	0	0	0	1 (0.1)	0.06
Dairy intolerance	0	0	1 (0.2)	0.20	0	0
Dyslipidaemia	0	0	1 (0.2)	0.20	0	0
Hypertriglyceridaemia	0	0	1 (0.2)	0.20	0	0
Insulin resistance	1 (0.2)	0.19	0	0	0	0
Weight gain poor	0	0	1 (0.2)	0.20	0	0
Renal and urinary disorders	31 (6.3)	7.77	15 (3.1)	3.80	84 (10.2)	8.81
Nephrolithiasis	9 (1.8)	2.14	6 (1.3)	1.40	30 (3.6)	2.72
Dysuria	2 (0.4)	0.39	2 (0.4)	0.40	11 (1.3)	0.71
Acute kidney injury	4 (0.8)	0.78	0	0	8 (1.0)	0.65
Glycosuria	2 (0.4)	0.39	0	0	8 (1.0)	0.65
Haematuria	3 (0.6)	0.58	1 (0.2)	0.20	8 (1.0)	0.97
Urine abnormality	2 (0.4)	0.39	0	0	4 (0.5)	0.26
Proteinuria	2 (0.4)	0.39	0	0	3 (0.4)	0.19
Renal cyst	0	0	0	0	3 (0.4)	0.19
Ureterolithiasis	0	0	0	0	3 (0.4)	0.19
Chromaturia	0	0	0	0	2 (0.2)	0.13
Hyperoxaluria	0	0	0	0	2 (0.2)	0.19
Pollakiuria	2 (0.4)	0.39	1 (0.2)	0.20	2 (0.2)	0.13
Polyuria	0	0	0	0	2 (0.2)	0.13
Renal colic	2 (0.4)	0.39	1 (0.2)	0.40	2 (0.2)	0.19
Renal pain	2 (0.4)	0.39	2 (0.4)	0.40	2 (0.2)	0.13
Albuminuria	0	0	0	0	1 (0.1)	0.06

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Calculus bladder	0	0	0	0	1 (0.1)	0.06
Calculus urinary	0	0	0	0	1 (0.1)	0.06
Crystalluria	0	0	0	0	1 (0.1)	0.06
Hydronephrosis	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Hypercalciuria	0	0	0	0	1 (0.1)	0.06
Ketonuria	0	0	0	0	1 (0.1)	0.06
Microalbuminuria	0	0	0	0	1 (0.1)	0.06
Nephrocalcinosis	0	0	0	0	1 (0.1)	0.13
Nocturia	0	0	0	0	1 (0.1)	0.06
Renal failure	0	0	0	0	1 (0.1)	0.06
Renal impairment	0	0	0	0	1 (0.1)	0.06
Renal mass	0	0	0	0	1 (0.1)	0.06
Ureteric obstruction	0	0	0	0	1 (0.1)	0.06
Urethral disorder	0	0	0	0	1 (0.1)	0.06
Urethral pain	0	0	0	0	1 (0.1)	0.06
Urinary hesitation	0	0	0	0	1 (0.1)	0.06
Urinary incontinence	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Urinary tract obstruction	0	0	0	0	1 (0.1)	0.06
Urinary tract pain	0	0	0	0	1 (0.1)	0.06
Alkalinuria	1 (0.2)	0.19	0	0	0	0
Hypersthenuria	1 (0.2)	0.19	0	0	0	0
Micturition urgency	2 (0.4)	0.39	0	0	0	0
Nephropathy toxic	1 (0.2)	0.19	0	0	0	0
Urinary retention	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Urinary tract discomfort	1 (0.2)	0.19	0	0	0	0

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System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Urine flow decreased	1 (0.2)	0.19	0	0	0	0
Urine odour abnormal	0	0	1 (0.2)	0.20	0	0
Eye disorders	27 (5.5)	6.80	24 (5.0)	5.40	67 (8.2)	6.09
Blepharitis	0	0	0	0	6 (0.7)	0.39
Cataract	0	0	2 (0.4)	0.40	6 (0.7)	0.45
Dry eye	10 (2.0)	1.94	3 (0.6)	0.60	6 (0.7)	0.39
Chalazion	3 (0.6)	0.58	1 (0.2)	0.20	4 (0.5)	0.39
Conjunctival haemorrhage	1 (0.2)	0.19	0	0	4 (0.5)	0.26
Diabetic retinopathy	0	0	0	0	4 (0.5)	0.26
Eye discharge	0	0	0	0	4 (0.5)	0.26
Vision blurred	1 (0.2)	0.19	2 (0.4)	0.40	4 (0.5)	0.26
Conjunctivitis allergic	0	0	1 (0.2)	0.20	3 (0.4)	0.26
Eye inflammation	1 (0.2)	0.19	1 (0.2)	0.20	3 (0.4)	0.19
Myopia	0	0	0	0	3 (0.4)	0.19
Astigmatism	0	0	0	0	2 (0.2)	0.13
Blepharospasm	0	0	0	0	2 (0.2)	0.13
Cataract nuclear	0	0	0	0	2 (0.2)	0.13
Eye pain	0	0	0	0	2 (0.2)	0.13
Eye pruritus	1 (0.2)	0.19	2 (0.4)	0.40	2 (0.2)	0.19
Eye swelling	0	0	2 (0.4)	0.40	2 (0.2)	0.13
Lacrimation increased	2 (0.4)	0.39	3 (0.6)	0.60	2 (0.2)	0.13
Ocular hypertension	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Posterior capsule opacification	0	0	0	0	2 (0.2)	0.19
Visual impairment	1 (0.2)	0.19	0	0	2 (0.2)	0.19
Cataract cortical	3 (0.6)	0.58	0	0	1 (0.1)	0.06

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Central serous chorioretinopathy	0	0	0	0	1 (0.1)	0.06
Corneal degeneration	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Corneal lesion	0	0	0	0	1 (0.1)	0.06
Deposit eye	0	0	0	0	1 (0.1)	0.13
Eczema eyelids	0	0	1 (0.2)	0.40	1 (0.1)	0.19
Eye disorder	0	0	0	0	1 (0.1)	0.06
Eye irritation	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Eyelid rash	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Heterophoria	0	0	0	0	1 (0.1)	0.06
Lenticular opacities	0	0	0	0	1 (0.1)	0.06
Periorbital oedema	0	0	0	0	1 (0.1)	0.06
Retinal tear	0	0	0	0	1 (0.1)	0.13
Retinal vein occlusion	0	0	0	0	1 (0.1)	0.06
Retinopathy	0	0	0	0	1 (0.1)	0.06
Strabismus	0	0	0	0	1 (0.1)	0.06
Dacryostenosis acquired	1 (0.2)	0.19	0	0	0	0
Eyelid oedema	0	0	1 (0.2)	0.20	0	0
Glaucoma	0	0	1 (0.2)	0.20	0	0
Keratitis	0	0	1 (0.2)	0.20	0	0
Macular oedema	1 (0.2)	0.19	0	0	0	0
Meibomian gland dysfunction	1 (0.2)	0.19	0	0	0	0
Non-proliferative retinopathy	1 (0.2)	0.19	0	0	0	0
Ocular cyst	1 (0.2)	0.19	0	0	0	0
Periorbital dermatitis	1 (0.2)	0.19	0	0	0	0
Photophobia	0	0	1 (0.2)	0.20	0	0

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Retinal haemorrhage	1 (0.2)	0.39	0	0	0	0
Visual acuity reduced	1 (0.2)	0.19	0	0	0	0
Vitreous haemorrhage	1 (0.2)	0.39	0	0	0	0
Xerophthalmia	0	0	1 (0.2)	0.20	0	0
Reproductive system and breast disorders	34 (6.9)	9.51	17 (3.5)	6.40	58 (7.1)	5.31
Dysmenorrhoea	4 (0.8)	0.78	5 (1.0)	3.00	7 (0.9)	0.91
Heavy menstrual bleeding	2 (0.4)	0.39	3 (0.6)	0.60	5 (0.6)	0.32
Menopausal symptoms	2 (0.4)	0.39	1 (0.2)	0.20	4 (0.5)	0.26
Breast mass	3 (0.6)	0.58	2 (0.4)	0.40	3 (0.4)	0.19
Vulvovaginal dryness	1 (0.2)	0.19	1 (0.2)	0.20	3 (0.4)	0.52
Breast cyst	0	0	0	0	2 (0.2)	0.13
Cervical polyp	0	0	0	0	2 (0.2)	0.13
Intermenstrual bleeding	7 (1.4)	1.75	0	0	2 (0.2)	0.13
Ovarian cyst	2 (0.4)	0.39	0	0	2 (0.2)	0.13
Polymenorrhoea	2 (0.4)	0.39	0	0	2 (0.2)	0.13
Prostatomegaly	0	0	0	0	2 (0.2)	0.13
Testicular cyst	0	0	0	0	2 (0.2)	0.13
Testicular mass	0	0	0	0	2 (0.2)	0.13
Vaginal haemorrhage	2 (0.4)	0.39	2 (0.4)	0.40	2 (0.2)	0.13
Vulvovaginal pruritus	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Abnormal uterine bleeding	0	0	0	0	1 (0.1)	0.06
Adnexa uteri cyst	0	0	0	0	1 (0.1)	0.06
Amenorrhoea	2 (0.4)	0.39	0	0	1 (0.1)	0.06
Azoospermia	0	0	0	0	1 (0.1)	0.06
Benign prostatic hyperplasia	0	0	0	0	1 (0.1)	0.06

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Breast tenderness	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Cervical discharge	0	0	0	0	1 (0.1)	0.06
Dyspareunia	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Epididymal cyst	0	0	0	0	1 (0.1)	0.06
Erectile dysfunction	0	0	0	0	1 (0.1)	0.06
Fallopian tube cyst	0	0	0	0	1 (0.1)	0.13
Genital erythema	0	0	0	0	1 (0.1)	0.06
Gynaecomastia	1 (0.2)	0.39	0	0	1 (0.1)	0.06
Menstruation irregular	2 (0.4)	0.39	1 (0.2)	0.20	1 (0.1)	0.06
Oligomenorrhoea	0	0	0	0	1 (0.1)	0.06
Ovarian cyst ruptured	0	0	0	0	1 (0.1)	0.06
Scrotal pain	0	0	0	0	1 (0.1)	0.06
Seminal vesicular cyst	0	0	0	0	1 (0.1)	0.06
Testicular pain	1 (0.2)	0.39	1 (0.2)	0.20	1 (0.1)	0.06
Testicular retraction	0	0	0	0	1 (0.1)	0.06
Uterine haemorrhage	0	0	0	0	1 (0.1)	0.06
Vaginal discharge	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
Vaginal prolapse	0	0	0	0	1 (0.1)	0.06
Varicocele	0	0	0	0	1 (0.1)	0.06
Vulvovaginal discomfort	0	0	0	0	1 (0.1)	0.13
Vulvovaginal pain	0	0	0	0	1 (0.1)	0.06
Breast discomfort	1 (0.2)	0.19	0	0	0	0
Breast pain	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Cervical dysplasia	0	0	1 (0.2)	0.20	0	0
Endometrial hypertrophy	1 (0.2)	0.19	0	0	0	0

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Endometriosis	1 (0.2)	0.19	0	0	0	0
Galactorrhoea	1 (0.2)	0.19	0	0	0	0
Haematospermia	1 (0.2)	0.39	0	0	0	0
Menometrorrhagia	1 (0.2)	0.19	0	0	0	0
Menstruation delayed	1 (0.2)	0.19	0	0	0	0
Orchitis noninfective	1 (0.2)	0.19	0	0	0	0
Pruritus genital	0	0	1 (0.2)	0.20	0	0
Uterine polyp	1 (0.2)	0.19	0	0	0	0
Vaginal cyst	1 (0.2)	0.19	0	0	0	0
Immune system disorders	10 (2.0)	2.33	16 (3.3)	3.60	45 (5.5)	3.31
Seasonal allergy	7 (1.4)	1.55	10 (2.1)	2.20	32 (3.9)	2.33
Hypersensitivity	0	0	2 (0.4)	0.40	6 (0.7)	0.39
Food allergy	1 (0.2)	0.19	3 (0.6)	0.80	4 (0.5)	0.26
Allergy to animal	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Anaphylactic reaction	0	0	0	0	1 (0.1)	0.06
Contrast media reaction	0	0	0	0	1 (0.1)	0.06
Drug hypersensitivity	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Type IV hypersensitivity reaction	0	0	0	0	1 (0.1)	0.06
Allergy to plants	1 (0.2)	0.39	0	0	0	0
Ear and labyrinth disorders	21 (4.3)	5.24	14 (2.9)	2.80	42 (5.1)	3.56
Ear pain	7 (1.4)	1.55	3 (0.6)	0.60	17 (2.1)	1.17
Vertigo	4 (0.8)	0.78	1 (0.2)	0.20	8 (1.0)	0.52
Tinnitus	3 (0.6)	0.58	2 (0.4)	0.40	6 (0.7)	0.39
Ear discomfort	4 (0.8)	0.78	4 (0.8)	0.80	4 (0.5)	0.26
Middle ear effusion	1 (0.2)	0.19	0	0	3 (0.4)	0.19

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Deafness	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Auditory disorder	0	0	0	0	1 (0.1)	0.06
Cerumen impaction	0	0	0	0	1 (0.1)	0.06
Ear congestion	2 (0.4)	0.39	2 (0.4)	0.40	1 (0.1)	0.06
Ear pruritus	0	0	0	0	1 (0.1)	0.06
Ear swelling	0	0	0	0	1 (0.1)	0.06
Eustachian tube dysfunction	0	0	0	0	1 (0.1)	0.06
Excessive cerumen production	1 (0.2)	0.19	0	0	1 (0.1)	0.06
External ear pain	0	0	0	0	1 (0.1)	0.06
Hypoacusis	0	0	0	0	1 (0.1)	0.06
Motion sickness	0	0	1 (0.2)	0.20	1 (0.1)	0.13
Otorrhoea	0	0	0	0	1 (0.1)	0.06
Vertigo positional	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Vestibular disorder	0	0	0	0	1 (0.1)	0.06
Deafness bilateral	1 (0.2)	0.19	0	0	0	0
Tympanic membrane perforation	2 (0.4)	0.39	0	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	5 (1.0)	0.97	4 (0.8)	0.80	31 (3.8)	2.33
Fibroadenoma of breast	0	0	0	0	4 (0.5)	0.26
Skin papilloma	1 (0.2)	0.19	0	0	4 (0.5)	0.26
Acrochordon	0	0	0	0	3 (0.4)	0.19
Melanocytic naevus	0	0	0	0	3 (0.4)	0.19
Breast cancer	0	0	0	0	2 (0.2)	0.13
Lipoma	0	0	0	0	2 (0.2)	0.13
Neoplasm skin	0	0	0	0	2 (0.2)	0.13

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Adenocarcinoma pancreas	0	0	0	0	1 (0.1)	0.06
Basal cell carcinoma	0	0	0	0	1 (0.1)	0.06
Benign neoplasm of thyroid gland	0	0	0	0	1 (0.1)	0.06
Colorectal adenoma	2 (0.4)	0.39	0	0	1 (0.1)	0.19
Hepatic adenoma	0	0	0	0	1 (0.1)	0.06
Invasive breast carcinoma	0	0	0	0	1 (0.1)	0.06
Lung adenocarcinoma	0	0	0	0	1 (0.1)	0.06
Malignant melanoma stage 0	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Oral fibroma	0	0	0	0	1 (0.1)	0.06
Osteolipoma	0	0	0	0	1 (0.1)	0.06
Renal cell carcinoma	0	0	0	0	1 (0.1)	0.06
Renal perivascular epithelioid cell tumour	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Seborrhoeic keratosis	0	0	0	0	1 (0.1)	0.06
Uterine leiomyoma	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Adenocarcinoma	0	0	1 (0.2)	0.20	0	0
Benign breast neoplasm	0	0	1 (0.2)	0.20	0	0
Intraductal papillary mucinous neoplasm	0	0	1 (0.2)	0.20	0	0
Blood and lymphatic system disorders	14 (2.9)	3.30	3 (0.6)	0.60	30 (3.6)	2.14
Lymphadenopathy	4 (0.8)	0.78	1 (0.2)	0.20	10 (1.2)	0.65
Iron deficiency anaemia	4 (0.8)	0.78	1 (0.2)	0.20	7 (0.9)	0.45
Increased tendency to bruise	1 (0.2)	0.39	0	0	5 (0.6)	0.32
Leukopenia	0	0	0	0	4 (0.5)	0.26
Thrombocytopenia	1 (0.2)	0.19	0	0	3 (0.4)	0.19

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Haemolysis	0	0	0	0	1 (0.1)	0.06
Lymphadenitis	0	0	0	0	1 (0.1)	0.06
Lymphopenia	0	0	0	0	1 (0.1)	0.06
Reticulocytosis	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Anaemia	1 (0.2)	0.19	0	0	0	0
Leukocytosis	1 (0.2)	0.39	0	0	0	0
Neutropenia	1 (0.2)	0.19	0	0	0	0
Neutrophilia	1 (0.2)	0.19	0	0	0	0
Spontaneous haematoma	1 (0.2)	0.19	0	0	0	0
Congenital, familial and genetic disorders	5 (1.0)	0.97	11 (2.3)	2.40	28 (3.4)	1.81
Cystic fibrosis related diabetes	3 (0.6)	0.58	3 (0.6)	0.60	20 (2.4)	1.30
Cystic fibrosis lung	0	0	2 (0.4)	0.40	3 (0.4)	0.19
Cystic fibrosis hepatic disease	0	0	0	0	2 (0.2)	0.13
Atrial septal defect	0	0	0	0	1 (0.1)	0.06
Cystic fibrosis	0	0	0	0	1 (0.1)	0.06
Rathke's cleft cyst	0	0	0	0	1 (0.1)	0.06
Cataract congenital	1 (0.2)	0.19	1 (0.2)	0.40	0	0
Cerebrovascular arteriovenous malformation	0	0	1 (0.2)	0.20	0	0
Congenital cystic kidney disease	0	0	1 (0.2)	0.20	0	0
Congenital vitreous anomaly	0	0	1 (0.2)	0.20	0	0
Cystic fibrosis gastrointestinal disease	0	0	2 (0.4)	0.40	0	0
Naevus anaemicus	1 (0.2)	0.19	0	0	0	0

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Vascular disorders	15 (3.1)	3.69	6 (1.3)	1.40	28 (3.4)	2.01
Hypertension	9 (1.8)	2.52	3 (0.6)	0.60	17 (2.1)	1.10
Hot flush	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Hypotension	1 (0.2)	0.19	0	0	2 (0.2)	0.19
Raynaud's phenomenon	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Deep vein thrombosis	0	0	0	0	1 (0.1)	0.06
Erythromelalgia	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Haematoma	0	0	0	0	1 (0.1)	0.06
Lymphoedema	0	0	0	0	1 (0.1)	0.06
Orthostatic hypotension	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Superficial vein thrombosis	0	0	0	0	1 (0.1)	0.06
Venous thrombosis	0	0	0	0	1 (0.1)	0.06
Cyanosis	0	0	1 (0.2)	0.40	0	0
Essential hypertension	1 (0.2)	0.19	0	0	0	0
Peripheral vein thrombosis	1 (0.2)	0.19	0	0	0	0
Phlebitis	1 (0.2)	0.19	0	0	0	0
Cardiac disorders	7 (1.4)	1.55	11 (2.3)	2.60	24 (2.9)	2.01
Palpitations	2 (0.4)	0.39	2 (0.4)	0.40	11 (1.3)	0.91
Bradycardia	0	0	0	0	2 (0.2)	0.13
Bundle branch block right	0	0	0	0	2 (0.2)	0.13
Atrioventricular block	0	0	0	0	1 (0.1)	0.06
Atrioventricular block first degree	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Cardiac contractility decreased	0	0	0	0	1 (0.1)	0.06
Cardiomegaly	0	0	0	0	1 (0.1)	0.06
Dilated cardiomyopathy	0	0	1 (0.2)	0.20	1 (0.1)	0.06

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Extrasystoles	0	0	0	0	1 (0.1)	0.06
Left ventricular dysfunction	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Right ventricular dilatation	0	0	0	0	1 (0.1)	0.06
Sinus bradycardia	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Supraventricular extrasystoles	0	0	0	0	1 (0.1)	0.06
Supraventricular tachycardia	0	0	0	0	1 (0.1)	0.13
Tachycardia	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Angina pectoris	1 (0.2)	0.19	0	0	0	0
Arrhythmia	0	0	1 (0.2)	0.20	0	0
Arteriospasm coronary	1 (0.2)	0.39	0	0	0	0
Cardiovascular disorder	0	0	2 (0.4)	0.40	0	0
Pericardial calcification	0	0	1 (0.2)	0.20	0	0
Pericardial fibrosis	0	0	1 (0.2)	0.20	0	0
Pericarditis	0	0	1 (0.2)	0.20	0	0
Pericarditis constrictive	0	0	1 (0.2)	0.20	0	0
Right ventricular hypertrophy	1 (0.2)	0.19	0	0	0	0
Ventricular extrasystoles	1 (0.2)	0.19	0	0	0	0
Hepatobiliary disorders	12 (2.4)	3.50	6 (1.3)	1.20	17 (2.1)	1.56
Cholelithiasis	4 (0.8)	0.97	0	0	7 (0.9)	0.45
Hepatic steatosis	0	0	0	0	4 (0.5)	0.26
Alcoholic liver disease	0	0	0	0	1 (0.1)	0.13
Cholangitis sclerosing	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Cholecystitis	1 (0.2)	0.19	0	0	1 (0.1)	0.13
Cholelithiasis migration	0	0	0	0	1 (0.1)	0.06
Hepatic cyst	0	0	0	0	1 (0.1)	0.06

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Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Hepatomegaly	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Hepatotoxicity	0	0	0	0	1 (0.1)	0.06
Hydrocholecystis	0	0	0	0	1 (0.1)	0.06
Jaundice	0	0	0	0	1 (0.1)	0.06
Liver injury	0	0	0	0	1 (0.1)	0.06
Ocular icterus	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Biliary colic	0	0	1 (0.2)	0.20	0	0
Cholangitis	1 (0.2)	0.39	0	0	0	0
Cholecystitis acute	1 (0.2)	0.19	0	0	0	0
Cholestasis	2 (0.4)	0.39	1 (0.2)	0.20	0	0
Fatty liver alcoholic	1 (0.2)	0.19	0	0	0	0
Gallbladder polyp	1 (0.2)	0.19	0	0	0	0
Hepatic cirrhosis	1 (0.2)	0.19	0	0	0	0
Hyperbilirubinaemia	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Hypertransaminasaemia	0	0	2 (0.4)	0.40	0	0
Portal hypertension	1 (0.2)	0.19	0	0	0	0
Endocrine disorders	1 (0.2)	0.19	2 (0.4)	0.40	10 (1.2)	0.65
Hypothyroidism	0	0	1 (0.2)	0.20	4 (0.5)	0.26
Hyperthyroidism	0	0	0	0	2 (0.2)	0.13
Hyperparathyroidism primary	0	0	0	0	1 (0.1)	0.06
Hyperparathyroidism secondary	0	0	0	0	1 (0.1)	0.06
Inappropriate antidiuretic hormone secretion	0	0	0	0	1 (0.1)	0.06
Polycystic ovarian syndrome	0	0	0	0	1 (0.1)	0.06
Adrenal insufficiency	1 (0.2)	0.19	0	0	0	0

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.2a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Thyroid cyst	0	0	1 (0.2)	0.20	0	0
Social circumstances	0	0	1 (0.2)	0.20	5 (0.6)	0.32
Menopause	0	0	0	0	4 (0.5)	0.26
Victim of crime	0	0	0	0	1 (0.1)	0.06
Physical assault	0	0	1 (0.2)	0.20	0	0
Product issues	1 (0.2)	0.19	2 (0.4)	0.60	3 (0.4)	0.26
Device dislocation	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Device malfunction	0	0	0	0	1 (0.1)	0.13
Device physical property issue	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Device leakage	0	0	1 (0.2)	0.40	0	0
Pregnancy, puerperium and perinatal conditions	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Abortion spontaneous	0	0	0	0	1 (0.1)	0.06
Morning sickness	0	0	1 (0.2)	0.20	0	0

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Subjects with any TEAEs	469 (95.5)	459 (95.6)	796 (96.8)
Grade 1/Mild	145 (29.5)	166 (34.6)	194 (23.6)
Grade 2/Moderate	269 (54.8)	239 (49.8)	499 (60.7)
Grade 3/Severe	54 (11.0)	54 (11.3)	98 (11.9)
Grade 4/Life-threatening	1 (0.2)	0	5 (0.6)
Grade 5/Death	0	0	0
Infections and infestations	392 (79.8)	349 (72.7)	703 (85.5)
Grade 1/Mild	161 (32.8)	153 (31.9)	263 (32.0)
Grade 2/Moderate	206 (42.0)	168 (35.0)	382 (46.5)
Grade 3/Severe	24 (4.9)	28 (5.8)	58 (7.1)
Grade 4/Life-threatening	1 (0.2)	0	0
Grade 5/Death	0	0	0
Infective pulmonary exacerbation of cystic fibrosis	158 (32.2)	133 (27.7)	300 (36.5)
Grade 1/Mild	36 (7.3)	38 (7.9)	74 (9.0)
Grade 2/Moderate	105 (21.4)	77 (16.0)	190 (23.1)
Grade 3/Severe	17 (3.5)	18 (3.8)	36 (4.4)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nasopharyngitis	95 (19.3)	102 (21.3)	209 (25.4)
Grade 1/Mild	67 (13.6)	78 (16.3)	156 (19.0)
Grade 2/Moderate	28 (5.7)	24 (5.0)	52 (6.3)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Upper respiratory tract infection	67 (13.6)	72 (15.0)	192 (23.4)
Grade 1/Mild	45 (9.2)	55 (11.5)	133 (16.2)
Grade 2/Moderate	22 (4.5)	17 (3.5)	59 (7.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
COVID-19	127 (25.9)	107 (22.3)	169 (20.6)
Grade 1/Mild	84 (17.1)	71 (14.8)	111 (13.5)
Grade 2/Moderate	42 (8.6)	36 (7.5)	57 (6.9)
Grade 3/Severe	1 (0.2)	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Influenza	26 (5.3)	52 (10.8)	116 (14.1)
Grade 1/Mild	13 (2.6)	20 (4.2)	49 (6.0)
Grade 2/Moderate	11 (2.2)	28 (5.8)	61 (7.4)
Grade 3/Severe	2 (0.4)	4 (0.8)	6 (0.7)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Viral upper respiratory tract infection	35 (7.1)	37 (7.7)	72 (8.8)
Grade 1/Mild	31 (6.3)	28 (5.8)	45 (5.5)
Grade 2/Moderate	4 (0.8)	9 (1.9)	27 (3.3)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Sinusitis	36 (7.3)	19 (4.0)	62 (7.5)
Grade 1/Mild	22 (4.5)	11 (2.3)	35 (4.3)
Grade 2/Moderate	14 (2.9)	8 (1.7)	26 (3.2)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rhinitis	17 (3.5)	16 (3.3)	53 (6.4)
Grade 1/Mild	13 (2.6)	16 (3.3)	40 (4.9)
Grade 2/Moderate	4 (0.8)	0	13 (1.6)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urinary tract infection	16 (3.3)	11 (2.3)	43 (5.2)
Grade 1/Mild	11 (2.2)	7 (1.5)	22 (2.7)
Grade 2/Moderate	5 (1.0)	3 (0.6)	20 (2.4)
Grade 3/Severe	0	1 (0.2)	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pneumonia	10 (2.0)	9 (1.9)	36 (4.4)
Grade 1/Mild	2 (0.4)	3 (0.6)	8 (1.0)
Grade 2/Moderate	5 (1.0)	4 (0.8)	18 (2.2)
Grade 3/Severe	2 (0.4)	2 (0.4)	10 (1.2)
Grade 4/Life-threatening	1 (0.2)	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Respiratory tract infection	16 (3.3)	13 (2.7)	36 (4.4)
Grade 1/Mild	9 (1.8)	6 (1.3)	21 (2.6)
Grade 2/Moderate	7 (1.4)	7 (1.5)	15 (1.8)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastroenteritis	10 (2.0)	10 (2.1)	27 (3.3)
Grade 1/Mild	5 (1.0)	8 (1.7)	22 (2.7)
Grade 2/Moderate	5 (1.0)	2 (0.4)	5 (0.6)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lower respiratory tract infection	10 (2.0)	8 (1.7)	27 (3.3)
Grade 1/Mild	7 (1.4)	0	13 (1.6)
Grade 2/Moderate	3 (0.6)	8 (1.7)	13 (1.6)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vulvovaginal mycotic infection	9 (1.8)	6 (1.3)	25 (3.0)
Grade 1/Mild	4 (0.8)	3 (0.6)	17 (2.1)
Grade 2/Moderate	5 (1.0)	3 (0.6)	8 (1.0)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Conjunctivitis	12 (2.4)	6 (1.3)	23 (2.8)
Grade 1/Mild	5 (1.0)	5 (1.0)	20 (2.4)
Grade 2/Moderate	7 (1.4)	1 (0.2)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bronchitis	9 (1.8)	8 (1.7)	20 (2.4)
Grade 1/Mild	3 (0.6)	3 (0.6)	10 (1.2)
Grade 2/Moderate	6 (1.2)	5 (1.0)	10 (1.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Respiratory tract infection viral	5 (1.0)	6 (1.3)	19 (2.3)
Grade 1/Mild	5 (1.0)	3 (0.6)	13 (1.6)
Grade 2/Moderate	0	3 (0.6)	6 (0.7)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastroenteritis viral	4 (0.8)	4 (0.8)	16 (1.9)
Grade 1/Mild	4 (0.8)	3 (0.6)	12 (1.5)
Grade 2/Moderate	0	1 (0.2)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pharyngitis	8 (1.6)	8 (1.7)	15 (1.8)
Grade 1/Mild	5 (1.0)	5 (1.0)	9 (1.1)
Grade 2/Moderate	3 (0.6)	3 (0.6)	6 (0.7)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tonsillitis	6 (1.2)	6 (1.3)	15 (1.8)
Grade 1/Mild	5 (1.0)	4 (0.8)	10 (1.2)
Grade 2/Moderate	1 (0.2)	2 (0.4)	5 (0.6)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oral herpes	7 (1.4)	4 (0.8)	14 (1.7)
Grade 1/Mild	5 (1.0)	3 (0.6)	10 (1.2)
Grade 2/Moderate	2 (0.4)	1 (0.2)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ear infection	5 (1.0)	6 (1.3)	13 (1.6)
Grade 1/Mild	1 (0.2)	4 (0.8)	9 (1.1)
Grade 2/Moderate	4 (0.8)	2 (0.4)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pharyngitis streptococcal	4 (0.8)	3 (0.6)	13 (1.6)
Grade 1/Mild	3 (0.6)	3 (0.6)	6 (0.7)
Grade 2/Moderate	1 (0.2)	0	7 (0.9)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Viral infection	6 (1.2)	3 (0.6)	12 (1.5)
Grade 1/Mild	5 (1.0)	2 (0.4)	9 (1.1)
Grade 2/Moderate	1 (0.2)	1 (0.2)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oral candidiasis	7 (1.4)	7 (1.5)	11 (1.3)
Grade 1/Mild	6 (1.2)	4 (0.8)	8 (1.0)
Grade 2/Moderate	1 (0.2)	3 (0.6)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Chronic sinusitis	6 (1.2)	2 (0.4)	10 (1.2)
Grade 1/Mild	2 (0.4)	0	3 (0.4)
Grade 2/Moderate	4 (0.8)	2 (0.4)	6 (0.7)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Laryngitis	6 (1.2)	1 (0.2)	10 (1.2)
Grade 1/Mild	3 (0.6)	1 (0.2)	8 (1.0)
Grade 2/Moderate	3 (0.6)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hordeolum	8 (1.6)	1 (0.2)	9 (1.1)
Grade 1/Mild	8 (1.6)	0	8 (1.0)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Fungal skin infection	1 (0.2)	0	8 (1.0)
Grade 1/Mild	1 (0.2)	0	5 (0.6)
Grade 2/Moderate	0	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tooth infection	4 (0.8)	3 (0.6)	8 (1.0)
Grade 1/Mild	2 (0.4)	2 (0.4)	3 (0.4)
Grade 2/Moderate	2 (0.4)	0	5 (0.6)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Acute sinusitis	4 (0.8)	3 (0.6)	7 (0.9)
Grade 1/Mild	3 (0.6)	3 (0.6)	4 (0.5)
Grade 2/Moderate	1 (0.2)	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bacterial disease carrier	2 (0.4)	1 (0.2)	7 (0.9)
Grade 1/Mild	2 (0.4)	0	5 (0.6)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cystitis	3 (0.6)	7 (1.5)	7 (0.9)
Grade 1/Mild	2 (0.4)	3 (0.6)	4 (0.5)
Grade 2/Moderate	1 (0.2)	4 (0.8)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Suspected COVID-19	0	0	7 (0.9)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	5 (0.6)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Vulvovaginal candidiasis	10 (2.0)	3 (0.6)	7 (0.9)
Grade 1/Mild	7 (1.4)	2 (0.4)	5 (0.6)
Grade 2/Moderate	3 (0.6)	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Herpes zoster	5 (1.0)	4 (0.8)	6 (0.7)
Grade 1/Mild	2 (0.4)	1 (0.2)	2 (0.2)
Grade 2/Moderate	3 (0.6)	3 (0.6)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Otitis media	6 (1.2)	6 (1.3)	6 (0.7)
Grade 1/Mild	3 (0.6)	4 (0.8)	3 (0.4)
Grade 2/Moderate	3 (0.6)	2 (0.4)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pulpitis dental	0	1 (0.2)	6 (0.7)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Bacterial vaginosis	0	1 (0.2)	5 (0.6)
Grade 1/Mild	0	1 (0.2)	4 (0.5)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cellulitis	2 (0.4)	1 (0.2)	5 (0.6)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	3 (0.4)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Respiratory tract infection bacterial	1 (0.2)	5 (1.0)	5 (0.6)
Grade 1/Mild	0	4 (0.8)	2 (0.2)
Grade 2/Moderate	1 (0.2)	1 (0.2)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tinea pedis	1 (0.2)	1 (0.2)	5 (0.6)
Grade 1/Mild	0	1 (0.2)	4 (0.5)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Bronchopulmonary aspergillosis allergic	1 (0.2)	0	4 (0.5)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Localised infection	2 (0.4)	1 (0.2)	4 (0.5)
Grade 1/Mild	2 (0.4)	0	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oral fungal infection	2 (0.4)	2 (0.4)	4 (0.5)
Grade 1/Mild	1 (0.2)	1 (0.2)	2 (0.2)
Grade 2/Moderate	1 (0.2)	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Respiratory syncytial virus infection	0	3 (0.6)	4 (0.5)
Grade 1/Mild	0	3 (0.6)	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Tooth abscess	1 (0.2)	2 (0.4)	4 (0.5)
Grade 1/Mild	0	1 (0.2)	3 (0.4)
Grade 2/Moderate	1 (0.2)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Upper respiratory tract infection bacterial	1 (0.2)	1 (0.2)	4 (0.5)
Grade 1/Mild	1 (0.2)	0	3 (0.4)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Atypical mycobacterial pneumonia	1 (0.2)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bacteriuria	0	0	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Bronchitis viral	0	0	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Folliculitis	2 (0.4)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastroenteritis norovirus	0	0	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastrointestinal viral infection	1 (0.2)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Genital infection fungal	1 (0.2)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hand-foot-and-mouth disease	1 (0.2)	1 (0.2)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Infective exacerbation of bronchiectasis	3 (0.6)	2 (0.4)	3 (0.4)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	2 (0.4)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	1 (0.2)	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Onychomycosis	1 (0.2)	1 (0.2)	3 (0.4)
Grade 1/Mild	1 (0.2)	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Otitis media acute	1 (0.2)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pneumonia staphylococcal	0	1 (0.2)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pyelonephritis	1 (0.2)	1 (0.2)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rhinovirus infection	3 (0.6)	2 (0.4)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	3 (0.6)	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Tinea versicolour	0	0	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Viral rhinitis	1 (0.2)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Wound infection	1 (0.2)	1 (0.2)	3 (0.4)
Grade 1/Mild	1 (0.2)	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bacterial vulvovaginitis	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

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Escherichia urinary tract infection	0	2 (0.4)	2 (0.2)
Grade 1/Mild	0	2 (0.4)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Fungal infection	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastric infection	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Genital herpes	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	1 (0.2)	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Gingivitis	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Impetigo	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Laryngopharyngitis	1 (0.2)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lower respiratory tract infection bacterial	2 (0.4)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Mycobacterial disease carrier	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Norovirus infection	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Otitis externa	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Paronychia	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pharyngotonsillitis	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	1 (0.2)	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pilonidal disease	1 (0.2)	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pneumonia pseudomonal	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Post procedural infection	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Postoperative abscess	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sepsis	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skin infection	3 (0.6)	0	2 (0.2)
Grade 1/Mild	2 (0.4)	0	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tinea infection	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Tongue fungal infection	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tracheitis	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urinary tract candidiasis	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vaginal infection	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Viral pharyngitis	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abscess limb	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Adenoviral conjunctivitis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Anorectal cellulitis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Appendicitis	1 (0.2)	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	1 (0.2)	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Aspergilloma	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bacterial rhinitis	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Body tinea	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Bronchopulmonary aspergillosis	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
COVID-19 pneumonia	1 (0.2)	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Campylobacter gastroenteritis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Conjunctivitis bacterial	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Conjunctivitis viral	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Croup infectious	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Diarrhoea infectious	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ear, nose and throat infection	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Enterobiasis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Epididymitis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eye infection	1 (0.2)	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Fungal disease carrier	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Fungal foot infection	1 (0.2)	1 (0.2)	1 (0.1)
Grade 1/Mild	1 (0.2)	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Furuncle	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastroenteritis clostridial	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastrointestinal infection	3 (0.6)	1 (0.2)	1 (0.1)
Grade 1/Mild	2 (0.4)	1 (0.2)	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Gastrointestinal microorganism overgrowth	1 (0.2)	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Giardiasis	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hepatitis A	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Herpangina	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Herpes simplex	1 (0.2)	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Herpes virus infection	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Infectious mononucleosis	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Kidney infection	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Klebsiella urinary tract infection	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Laryngitis viral	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lower respiratory tract infection viral	1 (0.2)	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lung abscess	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Nail bed infection	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oesophageal candidiasis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oral infection	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oropharyngeal candidiasis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pelvic infection	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Periorbital cellulitis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Perirectal abscess	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pertussis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pharyngeal pustule	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pneumonia aspiration	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pneumonia bordetella	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pneumonia haemophilus	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pneumonia parainfluenzae viral	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pneumonia serratia	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pseudomonas infection	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pyuria	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Scabies	1 (0.2)	1 (0.2)	1 (0.1)
Grade 1/Mild	1 (0.2)	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sialoadenitis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sinusitis bacterial	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skin bacterial infection	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Sputum purulent	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urinary tract infection enterococcal	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Viral labyrinthitis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Viral sinusitis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Vulvovaginitis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abscess neck	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Adenoviral upper respiratory infection	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Asymptomatic bacteriuria	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Balanitis candida	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Clostridium difficile colitis	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dermatophytosis	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Diverticulitis	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Erysipelas	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Erythema migrans	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eye infection bacterial	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eye infection staphylococcal	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Gastritis viral	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Genital candidiasis	1 (0.2)	2 (0.4)	0
Grade 1/Mild	1 (0.2)	1 (0.2)	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Genital herpes simplex	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Genital infection	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Gingival abscess	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Herpes dermatitis	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Infected bite	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Mastoiditis	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Meningitis aseptic	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Metapneumovirus infection	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Metapneumovirus pneumonia	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nasal vestibulitis	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Ocular demodicosis	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Omphalitis	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pelvic inflammatory disease	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pneumonia moraxella	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pneumonia respiratory syncytial viral	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pneumonia viral	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pulmonary nocardiosis	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rash pustular	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Retinitis	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sexually transmitted disease	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Staphylococcal skin infection	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Streptococcal infection	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Subcutaneous abscess	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Superinfection bacterial	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tinea faciei	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tonsillitis bacterial	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Urinary tract infection bacterial	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urinary tract infection fungal	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urogenital infection fungal	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vascular device infection	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Viral myocarditis	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Viral tonsillitis	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Respiratory, thoracic and mediastinal disorders	251 (51.1)	239 (49.8)	488 (59.4)
Grade 1/Mild	175 (35.6)	171 (35.6)	317 (38.6)
Grade 2/Moderate	72 (14.7)	62 (12.9)	164 (20.0)
Grade 3/Severe	4 (0.8)	6 (1.3)	6 (0.7)
Grade 4/Life-threatening	0	0	1 (0.1)
Grade 5/Death	0	0	0
Cough	101 (20.6)	108 (22.5)	240 (29.2)
Grade 1/Mild	77 (15.7)	87 (18.1)	178 (21.7)
Grade 2/Moderate	23 (4.7)	21 (4.4)	61 (7.4)
Grade 3/Severe	1 (0.2)	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Oropharyngeal pain	60 (12.2)	69 (14.4)	154 (18.7)
Grade 1/Mild	46 (9.4)	53 (11.0)	130 (15.8)
Grade 2/Moderate	14 (2.9)	16 (3.3)	24 (2.9)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sputum increased	50 (10.2)	45 (9.4)	127 (15.5)
Grade 1/Mild	37 (7.5)	30 (6.3)	99 (12.0)
Grade 2/Moderate	13 (2.6)	15 (3.1)	28 (3.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nasal congestion	47 (9.6)	48 (10.0)	108 (13.1)
Grade 1/Mild	41 (8.4)	43 (9.0)	87 (10.6)
Grade 2/Moderate	6 (1.2)	4 (0.8)	21 (2.6)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rhinorrhoea	36 (7.3)	35 (7.3)	88 (10.7)
Grade 1/Mild	33 (6.7)	28 (5.8)	77 (9.4)
Grade 2/Moderate	3 (0.6)	7 (1.5)	11 (1.3)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Productive cough	24 (4.9)	28 (5.8)	85 (10.3)
Grade 1/Mild	18 (3.7)	21 (4.4)	61 (7.4)
Grade 2/Moderate	5 (1.0)	7 (1.5)	24 (2.9)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dyspnoea	28 (5.7)	18 (3.8)	63 (7.7)
Grade 1/Mild	18 (3.7)	11 (2.3)	46 (5.6)
Grade 2/Moderate	10 (2.0)	7 (1.5)	17 (2.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Haemoptysis	33 (6.7)	30 (6.3)	60 (7.3)
Grade 1/Mild	18 (3.7)	19 (4.0)	31 (3.8)
Grade 2/Moderate	14 (2.9)	8 (1.7)	25 (3.0)
Grade 3/Severe	1 (0.2)	3 (0.6)	3 (0.4)
Grade 4/Life-threatening	0	0	1 (0.1)
Grade 5/Death	0	0	0
Sinus congestion	15 (3.1)	32 (6.7)	51 (6.2)
Grade 1/Mild	13 (2.6)	28 (5.8)	39 (4.7)
Grade 2/Moderate	2 (0.4)	4 (0.8)	12 (1.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Lower respiratory tract congestion	8 (1.6)	14 (2.9)	37 (4.5)
Grade 1/Mild	5 (1.0)	12 (2.5)	25 (3.0)
Grade 2/Moderate	2 (0.4)	2 (0.4)	12 (1.5)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Wheezing	11 (2.2)	13 (2.7)	32 (3.9)
Grade 1/Mild	8 (1.6)	8 (1.7)	21 (2.6)
Grade 2/Moderate	3 (0.6)	5 (1.0)	11 (1.3)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Respiration abnormal	12 (2.4)	17 (3.5)	30 (3.6)
Grade 1/Mild	7 (1.4)	13 (2.7)	21 (2.6)
Grade 2/Moderate	5 (1.0)	4 (0.8)	9 (1.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rhinitis allergic	4 (0.8)	2 (0.4)	18 (2.2)
Grade 1/Mild	1 (0.2)	1 (0.2)	13 (1.6)
Grade 2/Moderate	3 (0.6)	1 (0.2)	5 (0.6)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Upper-airway cough syndrome	8 (1.6)	5 (1.0)	17 (2.1)
Grade 1/Mild	8 (1.6)	4 (0.8)	9 (1.1)
Grade 2/Moderate	0	1 (0.2)	8 (1.0)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Paranasal sinus discomfort	4 (0.8)	4 (0.8)	16 (1.9)
Grade 1/Mild	3 (0.6)	3 (0.6)	10 (1.2)
Grade 2/Moderate	1 (0.2)	1 (0.2)	6 (0.7)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Epistaxis	5 (1.0)	7 (1.5)	15 (1.8)
Grade 1/Mild	4 (0.8)	6 (1.3)	8 (1.0)
Grade 2/Moderate	1 (0.2)	1 (0.2)	7 (0.9)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Throat irritation	4 (0.8)	2 (0.4)	15 (1.8)
Grade 1/Mild	4 (0.8)	2 (0.4)	14 (1.7)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Dyspnoea exertional	0	10 (2.1)	12 (1.5)
Grade 1/Mild	0	9 (1.9)	10 (1.2)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dysphonia	4 (0.8)	6 (1.3)	11 (1.3)
Grade 1/Mild	3 (0.6)	4 (0.8)	11 (1.3)
Grade 2/Moderate	1 (0.2)	1 (0.2)	0
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pleuritic pain	3 (0.6)	7 (1.5)	11 (1.3)
Grade 1/Mild	1 (0.2)	5 (1.0)	5 (0.6)
Grade 2/Moderate	2 (0.4)	2 (0.4)	6 (0.7)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sneezing	5 (1.0)	1 (0.2)	11 (1.3)
Grade 1/Mild	5 (1.0)	1 (0.2)	10 (1.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Bronchospasm	3 (0.6)	0	10 (1.2)
Grade 1/Mild	3 (0.6)	0	7 (0.9)
Grade 2/Moderate	0	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Paranasal sinus hypersecretion	6 (1.2)	7 (1.5)	10 (1.2)
Grade 1/Mild	6 (1.2)	7 (1.5)	8 (1.0)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sputum discoloured	7 (1.4)	9 (1.9)	10 (1.2)
Grade 1/Mild	5 (1.0)	4 (0.8)	7 (0.9)
Grade 2/Moderate	2 (0.4)	5 (1.0)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Asthma	5 (1.0)	6 (1.3)	9 (1.1)
Grade 1/Mild	2 (0.4)	4 (0.8)	3 (0.4)
Grade 2/Moderate	3 (0.6)	2 (0.4)	6 (0.7)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pulmonary congestion	2 (0.4)	1 (0.2)	9 (1.1)
Grade 1/Mild	1 (0.2)	1 (0.2)	7 (0.9)
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sinus pain	2 (0.4)	5 (1.0)	8 (1.0)
Grade 1/Mild	1 (0.2)	4 (0.8)	4 (0.5)
Grade 2/Moderate	1 (0.2)	1 (0.2)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rales	6 (1.2)	3 (0.6)	7 (0.9)
Grade 1/Mild	6 (1.2)	2 (0.4)	5 (0.6)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nasal obstruction	1 (0.2)	4 (0.8)	6 (0.7)
Grade 1/Mild	1 (0.2)	4 (0.8)	5 (0.6)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Nasal polyps	2 (0.4)	0	6 (0.7)
Grade 1/Mild	2 (0.4)	0	6 (0.7)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Painful respiration	5 (1.0)	3 (0.6)	6 (0.7)
Grade 1/Mild	5 (1.0)	3 (0.6)	3 (0.4)
Grade 2/Moderate	0	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Respiratory symptom	0	2 (0.4)	5 (0.6)
Grade 1/Mild	0	2 (0.4)	4 (0.5)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Upper respiratory tract inflammation	0	0	5 (0.6)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Increased viscosity of bronchial secretion	2 (0.4)	2 (0.4)	4 (0.5)
Grade 1/Mild	2 (0.4)	2 (0.4)	3 (0.4)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Obstructive airways disorder	0	1 (0.2)	4 (0.5)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Upper respiratory tract congestion	3 (0.6)	3 (0.6)	4 (0.5)
Grade 1/Mild	3 (0.6)	3 (0.6)	2 (0.2)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Aphonia	3 (0.6)	4 (0.8)	3 (0.4)
Grade 1/Mild	3 (0.6)	3 (0.6)	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Dry throat	0	1 (0.2)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nasal discomfort	0	0	3 (0.4)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Obstructive sleep apnoea syndrome	0	0	3 (0.4)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pleurisy	0	1 (0.2)	3 (0.4)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pulmonary pain	2 (0.4)	3 (0.6)	3 (0.4)
Grade 1/Mild	2 (0.4)	2 (0.4)	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bronchial secretion retention	1 (0.2)	2 (0.4)	2 (0.2)
Grade 1/Mild	1 (0.2)	2 (0.4)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypoxia	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nasal septum deviation	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Respiratory tract congestion	2 (0.4)	2 (0.4)	2 (0.2)
Grade 1/Mild	1 (0.2)	2 (0.4)	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rhonchi	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sputum retention	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tonsillar hypertrophy	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

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Tonsillolith	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Allergic cough	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bronchial artery hypertrophy	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bronchial disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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Zusatzanalysen zur Studie VX20-121-104

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Bronchial hyperreactivity	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bronchial obstruction	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bronchial wall thickening	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Catarrh	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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Zusatzanalysen zur Studie VX20-121-104

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Hiccups	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Increased bronchial secretion	0	2 (0.4)	1 (0.1)
Grade 1/Mild	0	2 (0.4)	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lung infiltration	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nasal crusting	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Nasal discharge discolouration	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nasal dryness	2 (0.4)	1 (0.2)	1 (0.1)
Grade 1/Mild	2 (0.4)	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nasal oedema	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oropharyngeal plaque	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Paranasal sinus inflammation	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pneumonitis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pneumothorax	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pulmonary cavitation	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	1 (0.2)	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pulmonary hypertension	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pulmonary mass	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Reflux laryngitis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sinonasal obstruction	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Sinus disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Throat tightness	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bronchiectasis	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bronchopulmonary disease	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Diaphragmatic paralysis	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Increased upper airway secretion	3 (0.6)	1 (0.2)	0
Grade 1/Mild	3 (0.6)	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lung opacity	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pharyngeal disorder	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pleural thickening	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Respiratory tract irritation	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Throat clearing	2 (0.4)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	1 (0.2)	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastrointestinal disorders	179 (36.5)	178 (37.1)	376 (45.7)
Grade 1/Mild	107 (21.8)	115 (24.0)	230 (28.0)
Grade 2/Moderate	67 (13.6)	57 (11.9)	133 (16.2)
Grade 3/Severe	5 (1.0)	6 (1.3)	13 (1.6)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Diarrhoea	59 (12.0)	58 (12.1)	140 (17.0)
Grade 1/Mild	46 (9.4)	48 (10.0)	106 (12.9)
Grade 2/Moderate	12 (2.4)	10 (2.1)	32 (3.9)
Grade 3/Severe	1 (0.2)	0	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abdominal pain	37 (7.5)	25 (5.2)	72 (8.8)
Grade 1/Mild	21 (4.3)	16 (3.3)	45 (5.5)
Grade 2/Moderate	15 (3.1)	8 (1.7)	25 (3.0)
Grade 3/Severe	1 (0.2)	1 (0.2)	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nausea	30 (6.1)	29 (6.0)	71 (8.6)
Grade 1/Mild	26 (5.3)	23 (4.8)	51 (6.2)
Grade 2/Moderate	4 (0.8)	6 (1.3)	18 (2.2)
Grade 3/Severe	0	0	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abdominal pain upper	19 (3.9)	26 (5.4)	57 (6.9)
Grade 1/Mild	13 (2.6)	16 (3.3)	37 (4.5)
Grade 2/Moderate	6 (1.2)	8 (1.7)	20 (2.4)
Grade 3/Severe	0	2 (0.4)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Constipation	30 (6.1)	22 (4.6)	55 (6.7)
Grade 1/Mild	15 (3.1)	13 (2.7)	31 (3.8)
Grade 2/Moderate	14 (2.9)	8 (1.7)	23 (2.8)
Grade 3/Severe	1 (0.2)	1 (0.2)	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vomiting	27 (5.5)	15 (3.1)	53 (6.4)
Grade 1/Mild	17 (3.5)	12 (2.5)	41 (5.0)
Grade 2/Moderate	10 (2.0)	3 (0.6)	10 (1.2)
Grade 3/Severe	0	0	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abdominal distension	15 (3.1)	11 (2.3)	31 (3.8)
Grade 1/Mild	10 (2.0)	10 (2.1)	22 (2.7)
Grade 2/Moderate	5 (1.0)	1 (0.2)	9 (1.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Flatulence	15 (3.1)	8 (1.7)	23 (2.8)
Grade 1/Mild	12 (2.4)	8 (1.7)	19 (2.3)
Grade 2/Moderate	3 (0.6)	0	3 (0.4)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Gastrooesophageal reflux disease	10 (2.0)	8 (1.7)	20 (2.4)
Grade 1/Mild	7 (1.4)	5 (1.0)	13 (1.6)
Grade 2/Moderate	2 (0.4)	3 (0.6)	6 (0.7)
Grade 3/Severe	1 (0.2)	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Toothache	5 (1.0)	8 (1.7)	20 (2.4)
Grade 1/Mild	3 (0.6)	4 (0.8)	14 (1.7)
Grade 2/Moderate	2 (0.4)	4 (0.8)	6 (0.7)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abdominal discomfort	2 (0.4)	2 (0.4)	12 (1.5)
Grade 1/Mild	2 (0.4)	2 (0.4)	11 (1.3)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Distal intestinal obstruction syndrome	6 (1.2)	2 (0.4)	11 (1.3)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	6 (1.2)	0	8 (1.0)
Grade 3/Severe	0	2 (0.4)	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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Zusatzanalysen zur Studie VX20-121-104

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Dental caries	1 (0.2)	3 (0.6)	9 (1.1)
Grade 1/Mild	0	2 (0.4)	0
Grade 2/Moderate	0	1 (0.2)	9 (1.1)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastritis	6 (1.2)	2 (0.4)	9 (1.1)
Grade 1/Mild	3 (0.6)	1 (0.2)	4 (0.5)
Grade 2/Moderate	3 (0.6)	1 (0.2)	5 (0.6)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dyspepsia	2 (0.4)	4 (0.8)	8 (1.0)
Grade 1/Mild	2 (0.4)	4 (0.8)	2 (0.2)
Grade 2/Moderate	0	0	6 (0.7)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Haemorrhoids	1 (0.2)	2 (0.4)	8 (1.0)
Grade 1/Mild	1 (0.2)	1 (0.2)	7 (0.9)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Haematochezia	2 (0.4)	2 (0.4)	7 (0.9)
Grade 1/Mild	0	2 (0.4)	4 (0.5)
Grade 2/Moderate	2 (0.4)	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Large intestine polyp	2 (0.4)	0	7 (0.9)
Grade 1/Mild	0	0	5 (0.6)
Grade 2/Moderate	2 (0.4)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Intestinal obstruction	0	0	6 (0.7)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	3 (0.4)
Grade 3/Severe	0	0	3 (0.4)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Odynophagia	1 (0.2)	2 (0.4)	6 (0.7)
Grade 1/Mild	1 (0.2)	2 (0.4)	6 (0.7)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Rectal haemorrhage	0	3 (0.6)	6 (0.7)
Grade 1/Mild	0	2 (0.4)	6 (0.7)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abdominal pain lower	1 (0.2)	1 (0.2)	5 (0.6)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Food poisoning	6 (1.2)	4 (0.8)	5 (0.6)
Grade 1/Mild	3 (0.6)	1 (0.2)	2 (0.2)
Grade 2/Moderate	3 (0.6)	2 (0.4)	3 (0.4)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hiatus hernia	1 (0.2)	0	5 (0.6)
Grade 1/Mild	1 (0.2)	0	4 (0.5)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Steatorrhoea	0	5 (1.0)	5 (0.6)
Grade 1/Mild	0	3 (0.6)	4 (0.5)
Grade 2/Moderate	0	2 (0.4)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Anal fissure	0	0	3 (0.4)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gingival pain	1 (0.2)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Inguinal hernia	1 (0.2)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Stomatitis	0	0	3 (0.4)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abdominal hernia	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Aphthous ulcer	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dysphagia	4 (0.8)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	3 (0.6)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Epigastric discomfort	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Faecaloma	5 (1.0)	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	5 (1.0)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Faeces pale	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Faeces soft	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	1 (0.2)	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Gingival bleeding	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lip swelling	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Malabsorption	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Mouth ulceration	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Oral mucosal blistering	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Proctalgia	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Small intestinal obstruction	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abnormal faeces	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Aerophagia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Angular cheilitis	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Anorectal polyp	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Barrett's oesophagus	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Bowel movement irregularity	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Colitis	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Colitis ischaemic	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Duodenitis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Eructation	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Faeces discoloured	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Frequent bowel movements	0	4 (0.8)	1 (0.1)
Grade 1/Mild	0	4 (0.8)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastritis erosive	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Gastrointestinal inflammation	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastrointestinal motility disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastrointestinal tract irritation	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gingival swelling	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Haemorrhoids thrombosed	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperaesthesia teeth	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Intestinal metaplasia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Irritable bowel syndrome	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Lip pain	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Loose tooth	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Malpositioned teeth	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Mucous stools	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Oral discomfort	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oral disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oral pain	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Palatal disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pancreatic steatosis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pancreatitis	2 (0.4)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Proctitis ulcerative	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rectal prolapse	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Salivary hypersecretion	1 (0.2)	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tongue blistering	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tongue coated	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tongue discomfort	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Tongue geographic	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tooth disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tooth impacted	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Umbilical hernia	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Change of bowel habit	2 (0.4)	0	0
Grade 1/Mild	2 (0.4)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Chronic gastritis	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Coeliac disease	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Colitis ulcerative	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Dental discomfort	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dental plaque	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Diverticulum intestinal	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dry mouth	2 (0.4)	1 (0.2)	0
Grade 1/Mild	2 (0.4)	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Faeces hard	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gastrointestinal pain	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Glossitis	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Haemorrhoidal haemorrhage	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hyperchlorhydria	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Intestinal prolapse	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Mechanical ileus	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Melaena	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pancreatic cyst	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Post-tussive vomiting	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Subileus	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Varices oesophageal	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Investigations	166 (33.8)	176 (36.7)	338 (41.1)
Grade 1/Mild	96 (19.6)	111 (23.1)	202 (24.6)
Grade 2/Moderate	62 (12.6)	58 (12.1)	126 (15.3)
Grade 3/Severe	8 (1.6)	7 (1.5)	10 (1.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood creatine phosphokinase increased	41 (8.4)	43 (9.0)	68 (8.3)
Grade 1/Mild	28 (5.7)	30 (6.3)	41 (5.0)
Grade 2/Moderate	11 (2.2)	12 (2.5)	23 (2.8)
Grade 3/Severe	2 (0.4)	1 (0.2)	4 (0.5)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Alanine aminotransferase increased	29 (5.9)	38 (7.9)	56 (6.8)
Grade 1/Mild	15 (3.1)	22 (4.6)	32 (3.9)
Grade 2/Moderate	13 (2.6)	12 (2.5)	23 (2.8)
Grade 3/Severe	1 (0.2)	4 (0.8)	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Aspartate aminotransferase increased	27 (5.5)	33 (6.9)	56 (6.8)
Grade 1/Mild	17 (3.5)	17 (3.5)	29 (3.5)
Grade 2/Moderate	9 (1.8)	14 (2.9)	25 (3.0)
Grade 3/Severe	1 (0.2)	2 (0.4)	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Weight decreased	6 (1.2)	15 (3.1)	35 (4.3)
Grade 1/Mild	5 (1.0)	11 (2.3)	26 (3.2)
Grade 2/Moderate	1 (0.2)	4 (0.8)	9 (1.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bacterial test positive	19 (3.9)	14 (2.9)	31 (3.8)
Grade 1/Mild	15 (3.1)	11 (2.3)	24 (2.9)
Grade 2/Moderate	4 (0.8)	3 (0.6)	7 (0.9)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood glucose increased	8 (1.6)	8 (1.7)	30 (3.6)
Grade 1/Mild	6 (1.2)	5 (1.0)	22 (2.7)
Grade 2/Moderate	2 (0.4)	3 (0.6)	7 (0.9)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Forced expiratory volume decreased	4 (0.8)	9 (1.9)	24 (2.9)
Grade 1/Mild	2 (0.4)	5 (1.0)	12 (1.5)
Grade 2/Moderate	2 (0.4)	4 (0.8)	12 (1.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Gamma-glutamyltransferase increased	13 (2.6)	9 (1.9)	23 (2.8)
Grade 1/Mild	7 (1.4)	3 (0.6)	10 (1.2)
Grade 2/Moderate	4 (0.8)	4 (0.8)	12 (1.5)
Grade 3/Severe	2 (0.4)	2 (0.4)	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Glycosylated haemoglobin increased	8 (1.6)	3 (0.6)	21 (2.6)
Grade 1/Mild	4 (0.8)	2 (0.4)	17 (2.1)
Grade 2/Moderate	3 (0.6)	1 (0.2)	4 (0.5)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
SARS-CoV-2 test positive	11 (2.2)	14 (2.9)	20 (2.4)
Grade 1/Mild	8 (1.6)	11 (2.3)	10 (1.2)
Grade 2/Moderate	3 (0.6)	3 (0.6)	10 (1.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pulmonary function test decreased	11 (2.2)	7 (1.5)	18 (2.2)
Grade 1/Mild	6 (1.2)	5 (1.0)	12 (1.5)
Grade 2/Moderate	5 (1.0)	2 (0.4)	6 (0.7)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Blood alkaline phosphatase increased	9 (1.8)	9 (1.9)	14 (1.7)
Grade 1/Mild	4 (0.8)	0	9 (1.1)
Grade 2/Moderate	3 (0.6)	7 (1.5)	4 (0.5)
Grade 3/Severe	2 (0.4)	2 (0.4)	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood creatinine increased	2 (0.4)	2 (0.4)	13 (1.6)
Grade 1/Mild	1 (0.2)	2 (0.4)	7 (0.9)
Grade 2/Moderate	1 (0.2)	0	6 (0.7)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Crystal urine present	7 (1.4)	9 (1.9)	13 (1.6)
Grade 1/Mild	6 (1.2)	9 (1.9)	11 (1.3)
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood lactate dehydrogenase increased	3 (0.6)	3 (0.6)	12 (1.5)
Grade 1/Mild	2 (0.4)	2 (0.4)	9 (1.1)
Grade 2/Moderate	1 (0.2)	1 (0.2)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Glucose urine present	6 (1.2)	6 (1.3)	12 (1.5)
Grade 1/Mild	5 (1.0)	6 (1.3)	12 (1.5)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Weight increased	2 (0.4)	4 (0.8)	12 (1.5)
Grade 1/Mild	1 (0.2)	4 (0.8)	12 (1.5)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
White blood cells urine positive	8 (1.6)	5 (1.0)	10 (1.2)
Grade 1/Mild	7 (1.4)	5 (1.0)	10 (1.2)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood bilirubin increased	17 (3.5)	9 (1.9)	8 (1.0)
Grade 1/Mild	9 (1.8)	5 (1.0)	4 (0.5)
Grade 2/Moderate	7 (1.4)	2 (0.4)	4 (0.5)
Grade 3/Severe	1 (0.2)	2 (0.4)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Blood cholesterol increased	1 (0.2)	1 (0.2)	7 (0.9)
Grade 1/Mild	1 (0.2)	1 (0.2)	5 (0.6)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood urea increased	1 (0.2)	1 (0.2)	6 (0.7)
Grade 1/Mild	1 (0.2)	1 (0.2)	6 (0.7)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Protein urine present	1 (0.2)	2 (0.4)	6 (0.7)
Grade 1/Mild	1 (0.2)	2 (0.4)	6 (0.7)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vitamin D decreased	2 (0.4)	1 (0.2)	6 (0.7)
Grade 1/Mild	1 (0.2)	1 (0.2)	5 (0.6)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Blood glucose decreased	6 (1.2)	1 (0.2)	5 (0.6)
Grade 1/Mild	3 (0.6)	1 (0.2)	5 (0.6)
Grade 2/Moderate	3 (0.6)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood glucose fluctuation	0	5 (1.0)	5 (0.6)
Grade 1/Mild	0	3 (0.6)	3 (0.4)
Grade 2/Moderate	0	2 (0.4)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood pressure increased	4 (0.8)	2 (0.4)	5 (0.6)
Grade 1/Mild	3 (0.6)	1 (0.2)	5 (0.6)
Grade 2/Moderate	1 (0.2)	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Body temperature increased	2 (0.4)	2 (0.4)	5 (0.6)
Grade 1/Mild	2 (0.4)	1 (0.2)	4 (0.5)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
International normalised ratio increased	6 (1.2)	6 (1.3)	5 (0.6)
Grade 1/Mild	4 (0.8)	3 (0.6)	5 (0.6)
Grade 2/Moderate	2 (0.4)	3 (0.6)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Specific gravity urine increased	0	2 (0.4)	5 (0.6)
Grade 1/Mild	0	2 (0.4)	5 (0.6)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Activated partial thromboplastin time prolonged	2 (0.4)	2 (0.4)	4 (0.5)
Grade 1/Mild	0	2 (0.4)	4 (0.5)
Grade 2/Moderate	2 (0.4)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood bilirubin unconjugated increased	7 (1.4)	5 (1.0)	4 (0.5)
Grade 1/Mild	4 (0.8)	2 (0.4)	4 (0.5)
Grade 2/Moderate	2 (0.4)	2 (0.4)	0
Grade 3/Severe	1 (0.2)	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Eosinophil count increased	1 (0.2)	1 (0.2)	4 (0.5)
Grade 1/Mild	1 (0.2)	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Fungal test positive	0	3 (0.6)	4 (0.5)
Grade 1/Mild	0	2 (0.4)	4 (0.5)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Human rhinovirus test positive	2 (0.4)	1 (0.2)	4 (0.5)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	2 (0.4)	1 (0.2)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Influenza A virus test positive	4 (0.8)	1 (0.2)	4 (0.5)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	3 (0.6)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Staphylococcus test positive	1 (0.2)	0	4 (0.5)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urine bilirubin increased	0	0	4 (0.5)
Grade 1/Mild	0	0	4 (0.5)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urine ketone body present	3 (0.6)	2 (0.4)	4 (0.5)
Grade 1/Mild	3 (0.6)	2 (0.4)	4 (0.5)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Viral test positive	0	0	4 (0.5)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
White blood cell count decreased	1 (0.2)	2 (0.4)	4 (0.5)
Grade 1/Mild	1 (0.2)	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Amylase increased	0	1 (0.2)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood iron decreased	0	0	3 (0.4)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood sodium decreased	0	0	3 (0.4)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Blood urine present	2 (0.4)	1 (0.2)	3 (0.4)
Grade 1/Mild	2 (0.4)	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
C-reactive protein increased	1 (0.2)	1 (0.2)	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	1 (0.2)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Glucose tolerance test abnormal	0	0	3 (0.4)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lymphocyte count decreased	2 (0.4)	1 (0.2)	3 (0.4)
Grade 1/Mild	2 (0.4)	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Neutrophil count decreased	1 (0.2)	3 (0.6)	3 (0.4)
Grade 1/Mild	1 (0.2)	2 (0.4)	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pseudomonas test positive	2 (0.4)	2 (0.4)	3 (0.4)
Grade 1/Mild	2 (0.4)	2 (0.4)	1 (0.1)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Red blood cells urine positive	3 (0.6)	1 (0.2)	3 (0.4)
Grade 1/Mild	3 (0.6)	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Respiratory syncytial virus test positive	1 (0.2)	1 (0.2)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Stenotrophomonas test positive	1 (0.2)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Streptococcus test positive	2 (0.4)	1 (0.2)	3 (0.4)
Grade 1/Mild	1 (0.2)	1 (0.2)	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urinary squamous epithelial cells increased	1 (0.2)	1 (0.2)	3 (0.4)
Grade 1/Mild	1 (0.2)	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vitamin E decreased	0	0	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Atypical mycobacterium test positive	1 (0.2)	2 (0.4)	2 (0.2)
Grade 1/Mild	1 (0.2)	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bilirubin conjugated increased	5 (1.0)	1 (0.2)	2 (0.2)
Grade 1/Mild	4 (0.8)	1 (0.2)	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bilirubin urine present	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood bicarbonate decreased	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Blood potassium decreased	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood potassium increased	0	3 (0.6)	2 (0.2)
Grade 1/Mild	0	2 (0.4)	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Breath sounds abnormal	1 (0.2)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Clostridium test positive	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Electrocardiogram QT shortened	1 (0.2)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Glomerular filtration rate decreased	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Haemoglobin increased	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Heart rate increased	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Lipase increased	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nitrite urine present	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Platelet count decreased	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	1 (0.2)	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Spirometry abnormal	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Urinary casts	0	2 (0.4)	2 (0.2)
Grade 1/Mild	0	2 (0.4)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
White blood cell count increased	5 (1.0)	2 (0.4)	2 (0.2)
Grade 1/Mild	5 (1.0)	2 (0.4)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Acinetobacter test positive	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Aspergillus test positive	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Biopsy thyroid gland abnormal	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bleeding time prolonged	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood calcium increased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood chloride increased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Blood immunoglobulin E increased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood magnesium decreased	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood phosphorus increased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood pressure diastolic increased	2 (0.4)	2 (0.4)	1 (0.1)
Grade 1/Mild	2 (0.4)	2 (0.4)	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

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Blood sodium increased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood testosterone decreased	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood thyroid stimulating hormone increased	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood triglycerides increased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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Zusatzanalysen zur Studie VX20-121-104

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Blood urine	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Citric acid urine decreased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eosinophil percentage increased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Faecal occult blood positive	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Gastric pH decreased	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Glucose urine	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Influenza B virus test positive	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Influenza virus test positive	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Lymphocyte percentage decreased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Moraxella test positive	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Neutrophil count increased	3 (0.6)	3 (0.6)	1 (0.1)
Grade 1/Mild	3 (0.6)	3 (0.6)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oxygen saturation decreased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Prothrombin time prolonged	4 (0.8)	3 (0.6)	1 (0.1)
Grade 1/Mild	2 (0.4)	2 (0.4)	1 (0.1)
Grade 2/Moderate	2 (0.4)	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pulmonary arterial pressure increased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Reticulocyte count increased	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Serum ferritin decreased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Smear cervix abnormal	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sputum abnormal	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Transferrin saturation decreased	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ultrasound biliary tract abnormal	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Ultrasound liver abnormal	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urinary sediment present	2 (0.4)	2 (0.4)	1 (0.1)
Grade 1/Mild	2 (0.4)	2 (0.4)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urine analysis abnormal	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vitamin B12 increased	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
pH urine increased	1 (0.2)	1 (0.2)	1 (0.1)
Grade 1/Mild	1 (0.2)	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Atypical lymphocytes increased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood albumin increased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood bicarbonate increased	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Blood folate decreased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood immunoglobulin G increased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood pressure decreased	0	2 (0.4)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood uric acid decreased	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Burkholderia test positive	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cardiac murmur	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Carotene decreased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Coronavirus test positive	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Electrocardiogram PR prolongation	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Electrocardiogram QT prolonged	0	2 (0.4)	0
Grade 1/Mild	0	2 (0.4)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Electrocardiogram ST segment depression	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Enzyme level decreased	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Escherichia test positive	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Faecal volume increased	0	2 (0.4)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Fibrin D dimer increased	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Giardia test positive	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Haemoglobin decreased	2 (0.4)	1 (0.2)	0
Grade 1/Mild	2 (0.4)	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Haemophilus test positive	2 (0.4)	0	0
Grade 1/Mild	2 (0.4)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Heart rate decreased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Heart rate irregular	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hormone level abnormal	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lipase decreased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lymphocyte count increased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Monocyte count increased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Mycobacterium test positive	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ophthalmological examination abnormal	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Protein total increased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Protein urine	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Red blood cell count increased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Respiratory rate increased	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Serratia test positive	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urine albumin/creatinine ratio increased	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Urine output increased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vitamin B12 decreased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vitamin K decreased	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Yersinia test positive	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
General disorders and administration site conditions	119 (24.2)	142 (29.6)	259 (31.5)
Grade 1/Mild	91 (18.5)	102 (21.3)	185 (22.5)
Grade 2/Moderate	28 (5.7)	37 (7.7)	72 (8.8)
Grade 3/Severe	0	3 (0.6)	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pyrexia	50 (10.2)	52 (10.8)	109 (13.3)
Grade 1/Mild	35 (7.1)	37 (7.7)	85 (10.3)
Grade 2/Moderate	15 (3.1)	15 (3.1)	22 (2.7)
Grade 3/Severe	0	0	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Fatigue	46 (9.4)	51 (10.6)	97 (11.8)
Grade 1/Mild	37 (7.5)	38 (7.9)	73 (8.9)
Grade 2/Moderate	9 (1.8)	11 (2.3)	24 (2.9)
Grade 3/Severe	0	2 (0.4)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pain	9 (1.8)	18 (3.8)	23 (2.8)
Grade 1/Mild	7 (1.4)	12 (2.5)	15 (1.8)
Grade 2/Moderate	2 (0.4)	6 (1.3)	8 (1.0)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Influenza like illness	7 (1.4)	8 (1.7)	22 (2.7)
Grade 1/Mild	4 (0.8)	2 (0.4)	14 (1.7)
Grade 2/Moderate	3 (0.6)	5 (1.0)	8 (1.0)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Peripheral swelling	3 (0.6)	4 (0.8)	14 (1.7)
Grade 1/Mild	3 (0.6)	3 (0.6)	11 (1.3)
Grade 2/Moderate	0	1 (0.2)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Chills	3 (0.6)	9 (1.9)	12 (1.5)
Grade 1/Mild	2 (0.4)	7 (1.5)	8 (1.0)
Grade 2/Moderate	1 (0.2)	2 (0.4)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Asthenia	8 (1.6)	5 (1.0)	11 (1.3)
Grade 1/Mild	6 (1.2)	4 (0.8)	7 (0.9)
Grade 2/Moderate	2 (0.4)	1 (0.2)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Malaise	6 (1.2)	8 (1.7)	9 (1.1)
Grade 1/Mild	6 (1.2)	7 (1.5)	7 (0.9)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Chest discomfort	3 (0.6)	6 (1.3)	7 (0.9)
Grade 1/Mild	3 (0.6)	6 (1.3)	6 (0.7)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Chest pain	3 (0.6)	6 (1.3)	7 (0.9)
Grade 1/Mild	3 (0.6)	3 (0.6)	5 (0.6)
Grade 2/Moderate	0	3 (0.6)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oedema peripheral	5 (1.0)	4 (0.8)	5 (0.6)
Grade 1/Mild	3 (0.6)	3 (0.6)	4 (0.5)
Grade 2/Moderate	2 (0.4)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Exercise tolerance decreased	1 (0.2)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Feeling cold	2 (0.4)	1 (0.2)	3 (0.4)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	1 (0.2)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
General physical health deterioration	0	0	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Adverse drug reaction	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Application site rash	1 (0.2)	2 (0.4)	2 (0.2)
Grade 1/Mild	1 (0.2)	2 (0.4)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Chronic fatigue syndrome	0	2 (0.4)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperthermia	1 (0.2)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Impaired healing	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Medical device pain	0	2 (0.4)	2 (0.2)
Grade 1/Mild	0	2 (0.4)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Crepitations	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cyst	0	3 (0.6)	1 (0.1)
Grade 1/Mild	0	3 (0.6)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Drug withdrawal syndrome	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Dysplasia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Face oedema	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Facial pain	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gait disturbance	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hernia	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hunger	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperpyrexia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Inflammation	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Injection site inflammation	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Injection site pain	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Injection site rash	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Maxillofacial pain	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Sensation of foreign body	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Temperature regulation disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vaccination site discomfort	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vaccination site pain	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Application site reaction	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Axillary pain	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Catheter site erythema	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Device related thrombosis	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Drug intolerance	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ill-defined disorder	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Implant site pain	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Mass	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Medical device site rash	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Non-cardiac chest pain	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oedema	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Soft tissue inflammation	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Swelling	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Temperature intolerance	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Thirst	2 (0.4)	0	0
Grade 1/Mild	2 (0.4)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vascular device occlusion	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Vessel puncture site pain	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nervous system disorders	98 (20.0)	111 (23.1)	233 (28.3)
Grade 1/Mild	65 (13.2)	74 (15.4)	161 (19.6)
Grade 2/Moderate	28 (5.7)	30 (6.3)	67 (8.2)
Grade 3/Severe	5 (1.0)	7 (1.5)	4 (0.5)
Grade 4/Life-threatening	0	0	1 (0.1)
Grade 5/Death	0	0	0
Headache	63 (12.8)	76 (15.8)	153 (18.6)
Grade 1/Mild	45 (9.2)	55 (11.5)	115 (14.0)
Grade 2/Moderate	15 (3.1)	19 (4.0)	36 (4.4)
Grade 3/Severe	3 (0.6)	2 (0.4)	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dizziness	16 (3.3)	13 (2.7)	29 (3.5)
Grade 1/Mild	12 (2.4)	11 (2.3)	25 (3.0)
Grade 2/Moderate	4 (0.8)	2 (0.4)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Lethargy	2 (0.4)	7 (1.5)	20 (2.4)
Grade 1/Mild	1 (0.2)	6 (1.3)	18 (2.2)
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Migraine	9 (1.8)	9 (1.9)	17 (2.1)
Grade 1/Mild	5 (1.0)	4 (0.8)	7 (0.9)
Grade 2/Moderate	4 (0.8)	2 (0.4)	10 (1.2)
Grade 3/Severe	0	3 (0.6)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Syncope	3 (0.6)	7 (1.5)	13 (1.6)
Grade 1/Mild	1 (0.2)	4 (0.8)	10 (1.2)
Grade 2/Moderate	2 (0.4)	2 (0.4)	3 (0.4)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Paraesthesia	0	1 (0.2)	12 (1.5)
Grade 1/Mild	0	1 (0.2)	10 (1.2)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Brain fog	0	1 (0.2)	10 (1.2)
Grade 1/Mild	0	0	7 (0.9)
Grade 2/Moderate	0	1 (0.2)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Disturbance in attention	3 (0.6)	0	6 (0.7)
Grade 1/Mild	1 (0.2)	0	4 (0.5)
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypoaesthesia	3 (0.6)	2 (0.4)	6 (0.7)
Grade 1/Mild	3 (0.6)	1 (0.2)	5 (0.6)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Carpal tunnel syndrome	1 (0.2)	0	5 (0.6)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Neuralgia	0	0	3 (0.4)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Presyncope	3 (0.6)	0	3 (0.4)
Grade 1/Mild	3 (0.6)	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Amnesia	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	1 (0.2)	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dizziness postural	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Memory impairment	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Migraine with aura	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nerve compression	1 (0.2)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Neuropathy peripheral	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Restless legs syndrome	1 (0.2)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sciatica	2 (0.4)	3 (0.6)	2 (0.2)
Grade 1/Mild	1 (0.2)	2 (0.4)	2 (0.2)
Grade 2/Moderate	1 (0.2)	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Seizure	2 (0.4)	1 (0.2)	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	1 (0.2)	1 (0.2)	1 (0.1)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sensory disturbance	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Sinus headache	1 (0.2)	5 (1.0)	2 (0.2)
Grade 1/Mild	1 (0.2)	3 (0.6)	2 (0.2)
Grade 2/Moderate	0	2 (0.4)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ageusia	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Alcoholic seizure	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Anosmia	0	2 (0.4)	1 (0.1)
Grade 1/Mild	0	2 (0.4)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Aphantasia	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Aphasia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bell's palsy	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dysgeusia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Electric shock sensation	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Focal dyscognitive seizures	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Formication	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperreflexia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hypoglycaemic coma	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	1 (0.1)
Grade 5/Death	0	0	0
Hypoglycaemic unconsciousness	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Narcolepsy	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ophthalmic migraine	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Parosmia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Radicular pain	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Radiculopathy	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Reversible cerebral vasoconstriction syndrome	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Shift work disorder	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sleep paralysis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Subarachnoid haemorrhage	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tension headache	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Thunderclap headache	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tremor	3 (0.6)	1 (0.2)	1 (0.1)
Grade 1/Mild	3 (0.6)	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Trigeminal neuralgia	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Autonomic nervous system imbalance	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Balance disorder	2 (0.4)	0	0
Grade 1/Mild	2 (0.4)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Circadian rhythm sleep disorder	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Epilepsy	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Haemorrhage intracranial	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hyperaesthesia	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperresponsive to stimuli	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyposmia	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Loss of consciousness	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Meralgia paraesthetica	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Post-traumatic headache	0	2 (0.4)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Psychomotor hyperactivity	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Serotonin syndrome	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Somnolence	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Musculoskeletal and connective tissue disorders	119 (24.2)	96 (20.0)	232 (28.2)
Grade 1/Mild	69 (14.1)	65 (13.5)	154 (18.7)
Grade 2/Moderate	50 (10.2)	29 (6.0)	77 (9.4)
Grade 3/Severe	0	2 (0.4)	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Arthralgia	36 (7.3)	24 (5.0)	70 (8.5)
Grade 1/Mild	23 (4.7)	16 (3.3)	46 (5.6)
Grade 2/Moderate	13 (2.6)	7 (1.5)	24 (2.9)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Back pain	31 (6.3)	25 (5.2)	57 (6.9)
Grade 1/Mild	18 (3.7)	18 (3.8)	36 (4.4)
Grade 2/Moderate	13 (2.6)	6 (1.3)	21 (2.6)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Myalgia	10 (2.0)	17 (3.5)	37 (4.5)
Grade 1/Mild	8 (1.6)	14 (2.9)	28 (3.4)
Grade 2/Moderate	2 (0.4)	3 (0.6)	9 (1.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pain in extremity	14 (2.9)	7 (1.5)	31 (3.8)
Grade 1/Mild	10 (2.0)	6 (1.3)	24 (2.9)
Grade 2/Moderate	4 (0.8)	1 (0.2)	7 (0.9)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Musculoskeletal chest pain	9 (1.8)	10 (2.1)	18 (2.2)
Grade 1/Mild	7 (1.4)	10 (2.1)	14 (1.7)
Grade 2/Moderate	2 (0.4)	0	3 (0.4)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Osteopenia	2 (0.4)	1 (0.2)	11 (1.3)
Grade 1/Mild	1 (0.2)	1 (0.2)	9 (1.1)
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Muscle spasms	9 (1.8)	4 (0.8)	10 (1.2)
Grade 1/Mild	8 (1.6)	2 (0.4)	7 (0.9)
Grade 2/Moderate	1 (0.2)	2 (0.4)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Neck pain	5 (1.0)	3 (0.6)	9 (1.1)
Grade 1/Mild	2 (0.4)	1 (0.2)	5 (0.6)
Grade 2/Moderate	3 (0.6)	2 (0.4)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Musculoskeletal stiffness	1 (0.2)	1 (0.2)	8 (1.0)
Grade 1/Mild	1 (0.2)	0	6 (0.7)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tendonitis	4 (0.8)	2 (0.4)	7 (0.9)
Grade 1/Mild	1 (0.2)	2 (0.4)	3 (0.4)
Grade 2/Moderate	3 (0.6)	0	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Flank pain	4 (0.8)	3 (0.6)	6 (0.7)
Grade 1/Mild	3 (0.6)	2 (0.4)	4 (0.5)
Grade 2/Moderate	1 (0.2)	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Osteoarthritis	1 (0.2)	2 (0.4)	6 (0.7)
Grade 1/Mild	0	0	5 (0.6)
Grade 2/Moderate	1 (0.2)	2 (0.4)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Muscular weakness	2 (0.4)	0	5 (0.6)
Grade 1/Mild	1 (0.2)	0	5 (0.6)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Musculoskeletal pain	1 (0.2)	1 (0.2)	5 (0.6)
Grade 1/Mild	0	1 (0.2)	3 (0.4)
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Plantar fasciitis	0	1 (0.2)	5 (0.6)
Grade 1/Mild	0	1 (0.2)	4 (0.5)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Joint stiffness	1 (0.2)	1 (0.2)	4 (0.5)
Grade 1/Mild	0	1 (0.2)	3 (0.4)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Joint swelling	2 (0.4)	1 (0.2)	4 (0.5)
Grade 1/Mild	1 (0.2)	1 (0.2)	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Osteoporosis	1 (0.2)	0	4 (0.5)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Periarthritis	2 (0.4)	1 (0.2)	4 (0.5)
Grade 1/Mild	1 (0.2)	1 (0.2)	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Synovial cyst	0	0	4 (0.5)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Arthritis	2 (0.4)	2 (0.4)	3 (0.4)
Grade 1/Mild	2 (0.4)	0	2 (0.2)
Grade 2/Moderate	0	2 (0.4)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bursitis	0	1 (0.2)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Muscle tightness	3 (0.6)	2 (0.4)	3 (0.4)
Grade 1/Mild	2 (0.4)	1 (0.2)	3 (0.4)
Grade 2/Moderate	1 (0.2)	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rotator cuff syndrome	1 (0.2)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bone pain	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Femoroacetabular impingement	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Intervertebral disc protrusion	2 (0.4)	1 (0.2)	2 (0.2)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	1 (0.2)	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Joint range of motion decreased	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Muscle twitching	1 (0.2)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Musculoskeletal discomfort	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	1 (0.2)	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pain in jaw	1 (0.2)	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Patellofemoral pain syndrome	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rheumatoid arthritis	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tendon disorder	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Tendon pain	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tenosynovitis stenosans	1 (0.2)	2 (0.4)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	1 (0.2)	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bone cyst	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Coccydynia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

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Costochondritis	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dupuytren's contracture	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Fibromyalgia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Greater trochanteric pain syndrome	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Groin pain	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Intervertebral disc degeneration	1 (0.2)	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Joint effusion	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Joint hyperextension	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Joint impingement	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Muscle contracture	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Muscle discomfort	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Muscle fatigue	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Myosclerosis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Osteoporotic fracture	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rheumatic disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sjogren's syndrome	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Spinal pain	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Systemic lupus erythematosus	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Temporomandibular pain and dysfunction syndrome	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tenosynovitis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Trigger finger	1 (0.2)	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Arthropathy	1 (0.2)	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bursa disorder	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Limb discomfort	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Myositis	2 (0.4)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	2 (0.4)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Osteochondrosis	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Periostitis	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Polyarthritis	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Spondylitis	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vertebral foraminal stenosis	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Injury, poisoning and procedural complications	89 (18.1)	82 (17.1)	192 (23.4)
Grade 1/Mild	53 (10.8)	47 (9.8)	100 (12.2)
Grade 2/Moderate	32 (6.5)	34 (7.1)	83 (10.1)
Grade 3/Severe	4 (0.8)	1 (0.2)	8 (1.0)
Grade 4/Life-threatening	0	0	1 (0.1)
Grade 5/Death	0	0	0
Ligament sprain	6 (1.2)	8 (1.7)	23 (2.8)
Grade 1/Mild	3 (0.6)	5 (1.0)	17 (2.1)
Grade 2/Moderate	3 (0.6)	3 (0.6)	5 (0.6)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Limb injury	3 (0.6)	6 (1.3)	19 (2.3)
Grade 1/Mild	3 (0.6)	4 (0.8)	16 (1.9)
Grade 2/Moderate	0	2 (0.4)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skin laceration	8 (1.6)	8 (1.7)	19 (2.3)
Grade 1/Mild	5 (1.0)	3 (0.6)	11 (1.3)
Grade 2/Moderate	3 (0.6)	5 (1.0)	8 (1.0)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Contusion	4 (0.8)	8 (1.7)	17 (2.1)
Grade 1/Mild	3 (0.6)	6 (1.3)	12 (1.5)
Grade 2/Moderate	1 (0.2)	2 (0.4)	5 (0.6)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Muscle strain	3 (0.6)	5 (1.0)	17 (2.1)
Grade 1/Mild	3 (0.6)	4 (0.8)	13 (1.6)
Grade 2/Moderate	0	1 (0.2)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Arthropod bite	6 (1.2)	4 (0.8)	9 (1.1)
Grade 1/Mild	5 (1.0)	2 (0.4)	5 (0.6)
Grade 2/Moderate	1 (0.2)	2 (0.4)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Immunisation reaction	5 (1.0)	9 (1.9)	9 (1.1)
Grade 1/Mild	4 (0.8)	7 (1.5)	5 (0.6)
Grade 2/Moderate	1 (0.2)	2 (0.4)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Fall	3 (0.6)	9 (1.9)	8 (1.0)
Grade 1/Mild	2 (0.4)	4 (0.8)	4 (0.5)
Grade 2/Moderate	1 (0.2)	4 (0.8)	4 (0.5)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Joint injury	4 (0.8)	0	8 (1.0)
Grade 1/Mild	3 (0.6)	0	5 (0.6)
Grade 2/Moderate	1 (0.2)	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Procedural pain	7 (1.4)	3 (0.6)	8 (1.0)
Grade 1/Mild	3 (0.6)	3 (0.6)	6 (0.7)
Grade 2/Moderate	4 (0.8)	0	1 (0.1)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Road traffic accident	4 (0.8)	6 (1.3)	8 (1.0)
Grade 1/Mild	3 (0.6)	2 (0.4)	6 (0.7)
Grade 2/Moderate	1 (0.2)	4 (0.8)	1 (0.1)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skin abrasion	2 (0.4)	2 (0.4)	8 (1.0)
Grade 1/Mild	2 (0.4)	2 (0.4)	4 (0.5)
Grade 2/Moderate	0	0	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Animal bite	4 (0.8)	3 (0.6)	7 (0.9)
Grade 1/Mild	2 (0.4)	2 (0.4)	5 (0.6)
Grade 2/Moderate	2 (0.4)	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hand fracture	6 (1.2)	2 (0.4)	7 (0.9)
Grade 1/Mild	3 (0.6)	1 (0.2)	1 (0.1)
Grade 2/Moderate	3 (0.6)	1 (0.2)	5 (0.6)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Thermal burn	4 (0.8)	2 (0.4)	7 (0.9)
Grade 1/Mild	4 (0.8)	2 (0.4)	3 (0.4)
Grade 2/Moderate	0	0	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bone contusion	1 (0.2)	1 (0.2)	6 (0.7)
Grade 1/Mild	1 (0.2)	0	5 (0.6)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Foot fracture	2 (0.4)	1 (0.2)	6 (0.7)
Grade 1/Mild	0	0	4 (0.5)
Grade 2/Moderate	2 (0.4)	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Concussion	3 (0.6)	6 (1.3)	5 (0.6)
Grade 1/Mild	2 (0.4)	3 (0.6)	2 (0.2)
Grade 2/Moderate	1 (0.2)	3 (0.6)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ligament rupture	0	1 (0.2)	5 (0.6)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Chest injury	1 (0.2)	4 (0.8)	4 (0.5)
Grade 1/Mild	1 (0.2)	3 (0.6)	4 (0.5)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ankle fracture	1 (0.2)	0	3 (0.4)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Back injury	2 (0.4)	1 (0.2)	3 (0.4)
Grade 1/Mild	1 (0.2)	1 (0.2)	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cartilage injury	0	0	3 (0.4)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Muscle injury	0	0	3 (0.4)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Muscle rupture	0	0	3 (0.4)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Post-traumatic neck syndrome	1 (0.2)	0	3 (0.4)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rib fracture	1 (0.2)	2 (0.4)	3 (0.4)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	2 (0.4)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sunburn	2 (0.4)	2 (0.4)	3 (0.4)
Grade 1/Mild	2 (0.4)	2 (0.4)	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tooth fracture	2 (0.4)	0	3 (0.4)
Grade 1/Mild	2 (0.4)	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Arthropod sting	1 (0.2)	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Avulsion fracture	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Clavicle fracture	1 (0.2)	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Corneal abrasion	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Craniofacial fracture	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Epicondylitis	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Face injury	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Foreign body	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Head injury	1 (0.2)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Heat stroke	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Post procedural haemorrhage	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Soft tissue injury	1 (0.2)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Stress fracture	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tendon rupture	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Wound	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Accident	0	2 (0.4)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Accidental exposure to product	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Accidental overdose	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Alcohol poisoning	1 (0.2)	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Brain contusion	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Burns second degree	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Buttock injury	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Craniocerebral injury	1 (0.2)	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Diffuse axonal injury	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Eye contusion	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eye injury	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Femur fracture	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Fibula fracture	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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Zusatzanalysen zur Studie VX20-121-104

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Foreign body in eye	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Fractured coccyx	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Heat exhaustion	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Human bite	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Humerus fracture	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Incisional hernia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Incorrect dose administered	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Intervertebral disc injury	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Limb crushing injury	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Limb fracture	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Meniscus injury	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Musculoskeletal injury	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Neck injury	2 (0.4)	2 (0.4)	1 (0.1)
Grade 1/Mild	2 (0.4)	2 (0.4)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Penis injury	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Periorbital haematoma	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Poisoning deliberate	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	1 (0.1)
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Post procedural discomfort	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Post procedural haematuria	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Postoperative respiratory failure	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Procedural dizziness	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Radiation pneumonitis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Scapula fracture	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Scratch	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skeletal injury	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Sternal injury	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Stoma site discomfort	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Subdural haematoma	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Superficial injury of eye	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Torus fracture	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Venomous sting	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Wrist fracture	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abdominal injury	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Bone fissure	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Chillblains	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Exposure to communicable disease	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Iliotibial band syndrome	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Incision site inflammation	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Joint dislocation	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ligament injury	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lumbar vertebral fracture	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Mouth injury	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nail avulsion	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nasal injury	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Post procedural complication	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Post procedural haematoma	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Postoperative ileus	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Procedural complication	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Radius fracture	0	2 (0.4)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Respiratory fume inhalation disorder	1 (0.2)	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skull fractured base	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sports injury	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Stoma site discharge	2 (0.4)	1 (0.2)	0
Grade 1/Mild	2 (0.4)	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Stoma site erythema	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Stoma site pain	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Toxicity to various agents	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Traumatic haematoma	2 (0.4)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	1 (0.2)	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Traumatic pain	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ulna fracture	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Upper limb fracture	0	2 (0.4)	0
Grade 1/Mild	0	2 (0.4)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skin and subcutaneous tissue disorders	87 (17.7)	98 (20.4)	167 (20.3)
Grade 1/Mild	68 (13.8)	68 (14.2)	120 (14.6)
Grade 2/Moderate	19 (3.9)	29 (6.0)	44 (5.4)
Grade 3/Severe	0	1 (0.2)	3 (0.4)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Rash	22 (4.5)	37 (7.7)	44 (5.4)
Grade 1/Mild	13 (2.6)	27 (5.6)	32 (3.9)
Grade 2/Moderate	9 (1.8)	9 (1.9)	11 (1.3)
Grade 3/Severe	0	1 (0.2)	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Acne	20 (4.1)	16 (3.3)	19 (2.3)
Grade 1/Mild	18 (3.7)	12 (2.5)	11 (1.3)
Grade 2/Moderate	2 (0.4)	4 (0.8)	8 (1.0)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pruritus	9 (1.8)	10 (2.1)	18 (2.2)
Grade 1/Mild	7 (1.4)	7 (1.5)	13 (1.6)
Grade 2/Moderate	2 (0.4)	3 (0.6)	5 (0.6)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Alopecia	7 (1.4)	7 (1.5)	14 (1.7)
Grade 1/Mild	7 (1.4)	5 (1.0)	11 (1.3)
Grade 2/Moderate	0	2 (0.4)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Eczema	4 (0.8)	5 (1.0)	13 (1.6)
Grade 1/Mild	2 (0.4)	4 (0.8)	9 (1.1)
Grade 2/Moderate	2 (0.4)	1 (0.2)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dermatitis	0	2 (0.4)	6 (0.7)
Grade 1/Mild	0	1 (0.2)	4 (0.5)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urticaria	7 (1.4)	5 (1.0)	6 (0.7)
Grade 1/Mild	6 (1.2)	5 (1.0)	5 (0.6)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dry skin	5 (1.0)	2 (0.4)	5 (0.6)
Grade 1/Mild	5 (1.0)	2 (0.4)	3 (0.4)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Night sweats	3 (0.6)	3 (0.6)	5 (0.6)
Grade 1/Mild	3 (0.6)	2 (0.4)	4 (0.5)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rash pruritic	0	1 (0.2)	5 (0.6)
Grade 1/Mild	0	0	4 (0.5)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Acne cystic	0	0	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dermatitis acneiform	0	0	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Dermatitis contact	3 (0.6)	3 (0.6)	3 (0.4)
Grade 1/Mild	2 (0.4)	2 (0.4)	1 (0.1)
Grade 2/Moderate	1 (0.2)	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Drug eruption	0	2 (0.4)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ecchymosis	2 (0.4)	0	3 (0.4)
Grade 1/Mild	2 (0.4)	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Miliaria	0	1 (0.2)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Photosensitivity reaction	1 (0.2)	2 (0.4)	3 (0.4)
Grade 1/Mild	1 (0.2)	2 (0.4)	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rash erythematous	1 (0.2)	2 (0.4)	3 (0.4)
Grade 1/Mild	1 (0.2)	2 (0.4)	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rash macular	0	0	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rash maculo-papular	0	2 (0.4)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Actinic keratosis	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blister	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dermal cyst	1 (0.2)	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dermatitis atopic	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hyperhidrosis	1 (0.2)	4 (0.8)	2 (0.2)
Grade 1/Mild	0	2 (0.4)	2 (0.2)
Grade 2/Moderate	1 (0.2)	2 (0.4)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ingrowing nail	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Mechanical urticaria	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nail bed inflammation	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Rash papular	2 (0.4)	0	2 (0.2)
Grade 1/Mild	2 (0.4)	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rosacea	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Seborrhoeic dermatitis	1 (0.2)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skin lesion	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Cold sweat	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dandruff	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Erythema	1 (0.2)	4 (0.8)	1 (0.1)
Grade 1/Mild	1 (0.2)	3 (0.6)	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Granuloma annulare	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

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Idiopathic urticaria	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Macule	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Milia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Onychoclasis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pruritus allergic	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skin burning sensation	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skin fissures	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skin irritation	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Skin swelling	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skin ulcer	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Solar dermatitis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Solar urticaria	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Vancomycin infusion reaction	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vitiligo	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Androgenetic alopecia	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood blister	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Dermatitis allergic	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dyshidrotic eczema	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ephelides	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Erythema nodosum	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hand dermatitis	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hangnail	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lichen planus	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Madarosis	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Neurodermatitis	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Onycholysis	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Onychomadesis	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Palmoplantar keratoderma	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Perioral dermatitis	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pityriasis rosea	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Psoriasis	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Rash follicular	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Rash vesicular	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Scab	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Scar pain	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sensitive skin	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Skin discolouration	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Skin mass	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sweat gland disorder	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urticaria chronic	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Psychiatric disorders	70 (14.3)	60 (12.5)	136 (16.5)
Grade 1/Mild	34 (6.9)	33 (6.9)	69 (8.4)
Grade 2/Moderate	31 (6.3)	23 (4.8)	61 (7.4)
Grade 3/Severe	5 (1.0)	4 (0.8)	5 (0.6)
Grade 4/Life-threatening	0	0	1 (0.1)
Grade 5/Death	0	0	0
Anxiety	10 (2.0)	21 (4.4)	35 (4.3)
Grade 1/Mild	5 (1.0)	11 (2.3)	15 (1.8)
Grade 2/Moderate	4 (0.8)	9 (1.9)	17 (2.1)
Grade 3/Severe	1 (0.2)	1 (0.2)	3 (0.4)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Depression	10 (2.0)	14 (2.9)	26 (3.2)
Grade 1/Mild	6 (1.2)	6 (1.3)	11 (1.3)
Grade 2/Moderate	4 (0.8)	6 (1.3)	15 (1.8)
Grade 3/Severe	0	2 (0.4)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Insomnia	22 (4.5)	15 (3.1)	26 (3.2)
Grade 1/Mild	12 (2.4)	10 (2.1)	11 (1.3)
Grade 2/Moderate	10 (2.0)	4 (0.8)	15 (1.8)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Depressed mood	7 (1.4)	4 (0.8)	20 (2.4)
Grade 1/Mild	2 (0.4)	2 (0.4)	11 (1.3)
Grade 2/Moderate	5 (1.0)	2 (0.4)	9 (1.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Attention deficit hyperactivity disorder	4 (0.8)	1 (0.2)	10 (1.2)
Grade 1/Mild	2 (0.4)	1 (0.2)	5 (0.6)
Grade 2/Moderate	2 (0.4)	0	5 (0.6)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sleep disorder	1 (0.2)	0	9 (1.1)
Grade 1/Mild	1 (0.2)	0	6 (0.7)
Grade 2/Moderate	0	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Poor quality sleep	5 (1.0)	3 (0.6)	5 (0.6)
Grade 1/Mild	2 (0.4)	3 (0.6)	5 (0.6)
Grade 2/Moderate	3 (0.6)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Stress	1 (0.2)	2 (0.4)	5 (0.6)
Grade 1/Mild	1 (0.2)	1 (0.2)	5 (0.6)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Irritability	2 (0.4)	1 (0.2)	4 (0.5)
Grade 1/Mild	1 (0.2)	1 (0.2)	3 (0.4)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Panic attack	3 (0.6)	1 (0.2)	4 (0.5)
Grade 1/Mild	1 (0.2)	0	3 (0.4)
Grade 2/Moderate	2 (0.4)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Apathy	0	0	3 (0.4)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Alcohol use disorder	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Depressive symptom	3 (0.6)	0	2 (0.2)
Grade 1/Mild	3 (0.6)	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gender dysphoria	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Initial insomnia	1 (0.2)	3 (0.6)	2 (0.2)
Grade 1/Mild	1 (0.2)	3 (0.6)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Libido decreased	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Loss of libido	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Mood swings	0	3 (0.6)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	2 (0.4)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Suicidal ideation	4 (0.8)	2 (0.4)	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	2 (0.4)	0	1 (0.1)
Grade 3/Severe	2 (0.4)	2 (0.4)	0
Grade 4/Life-threatening	0	0	1 (0.1)
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Abnormal behaviour	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Adjustment disorder with depressed mood	1 (0.2)	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Alcohol abuse	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Anger	2 (0.4)	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	2 (0.4)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Anhedonia	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Anxiety disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Burnout syndrome	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Confusional state	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Dyssomnia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Emotional disorder	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Generalised anxiety disorder	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Grief reaction	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Illusion	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Listless	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Major depression	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Mental disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Mental fatigue	1 (0.2)	2 (0.4)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Mental status changes	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Middle insomnia	1 (0.2)	2 (0.4)	1 (0.1)
Grade 1/Mild	1 (0.2)	2 (0.4)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nightmare	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Premature ejaculation	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Procedural anxiety	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sleep terror	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Social anxiety disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Substance abuse	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tic	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abnormal dreams	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Acute stress disorder	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Adjustment disorder	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Adjustment disorder with anxiety	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Agitation	0	2 (0.4)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Alcoholic hangover	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Behaviour disorder	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Complex tic	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Depression suicidal	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Libido increased	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Mixed anxiety and depressive disorder	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Mood altered	2 (0.4)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Purging	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Seasonal affective disorder	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Somatic symptom disorder	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tachyphrenia	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Metabolism and nutrition disorders	43 (8.8)	45 (9.4)	125 (15.2)
Grade 1/Mild	30 (6.1)	33 (6.9)	72 (8.8)
Grade 2/Moderate	12 (2.4)	11 (2.3)	47 (5.7)
Grade 3/Severe	1 (0.2)	1 (0.2)	6 (0.7)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypoglycaemia	13 (2.6)	7 (1.5)	21 (2.6)
Grade 1/Mild	6 (1.2)	4 (0.8)	13 (1.6)
Grade 2/Moderate	7 (1.4)	2 (0.4)	8 (1.0)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Decreased appetite	13 (2.6)	7 (1.5)	17 (2.1)
Grade 1/Mild	12 (2.4)	6 (1.3)	16 (1.9)
Grade 2/Moderate	1 (0.2)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vitamin D deficiency	2 (0.4)	2 (0.4)	15 (1.8)
Grade 1/Mild	2 (0.4)	2 (0.4)	10 (1.2)
Grade 2/Moderate	0	0	5 (0.6)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperglycaemia	2 (0.4)	7 (1.5)	11 (1.3)
Grade 1/Mild	1 (0.2)	6 (1.3)	9 (1.1)
Grade 2/Moderate	1 (0.2)	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Diabetes mellitus inadequate control	0	0	9 (1.1)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	6 (0.7)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Gout	1 (0.2)	1 (0.2)	8 (1.0)
Grade 1/Mild	1 (0.2)	0	4 (0.5)
Grade 2/Moderate	0	1 (0.2)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Iron deficiency	4 (0.8)	4 (0.8)	8 (1.0)
Grade 1/Mild	4 (0.8)	3 (0.6)	6 (0.7)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypokalaemia	1 (0.2)	3 (0.6)	7 (0.9)
Grade 1/Mild	0	3 (0.6)	3 (0.4)
Grade 2/Moderate	1 (0.2)	0	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyponatraemia	2 (0.4)	2 (0.4)	7 (0.9)
Grade 1/Mild	1 (0.2)	2 (0.4)	4 (0.5)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Glucose tolerance impaired	1 (0.2)	3 (0.6)	6 (0.7)
Grade 1/Mild	1 (0.2)	2 (0.4)	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dehydration	1 (0.2)	1 (0.2)	5 (0.6)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	2 (0.2)
Grade 3/Severe	0	0	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypercholesterolaemia	0	2 (0.4)	5 (0.6)
Grade 1/Mild	0	2 (0.4)	3 (0.4)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abnormal loss of weight	1 (0.2)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hypomagnesaemia	1 (0.2)	0	3 (0.4)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Increased appetite	0	1 (0.2)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vitamin A deficiency	0	1 (0.2)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vitamin B12 deficiency	0	0	3 (0.4)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Diabetic ketoacidosis	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypophosphataemia	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypovitaminosis	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Polydipsia	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Type 3 diabetes mellitus	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Carbohydrate intolerance	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Fluid intake reduced	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Food intolerance	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hyperkalaemia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperlipidaemia	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperphagia	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperphosphatasaemia	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hypocalcaemia	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ketosis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lactic acidosis	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lactose intolerance	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Malnutrition	1 (0.2)	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Postprandial hypoglycaemia	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Type 2 diabetes mellitus	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vitamin E deficiency	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Vitamin K deficiency	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dairy intolerance	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dyslipidaemia	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypertriglyceridaemia	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Insulin resistance	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Weight gain poor	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Renal and urinary disorders	31 (6.3)	15 (3.1)	84 (10.2)
Grade 1/Mild	16 (3.3)	9 (1.9)	50 (6.1)
Grade 2/Moderate	14 (2.9)	5 (1.0)	28 (3.4)
Grade 3/Severe	1 (0.2)	1 (0.2)	6 (0.7)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nephrolithiasis	9 (1.8)	6 (1.3)	30 (3.6)
Grade 1/Mild	3 (0.6)	3 (0.6)	15 (1.8)
Grade 2/Moderate	5 (1.0)	2 (0.4)	11 (1.3)
Grade 3/Severe	1 (0.2)	1 (0.2)	4 (0.5)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Dysuria	2 (0.4)	2 (0.4)	11 (1.3)
Grade 1/Mild	2 (0.4)	1 (0.2)	9 (1.1)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Acute kidney injury	4 (0.8)	0	8 (1.0)
Grade 1/Mild	1 (0.2)	0	3 (0.4)
Grade 2/Moderate	3 (0.6)	0	4 (0.5)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Glycosuria	2 (0.4)	0	8 (1.0)
Grade 1/Mild	2 (0.4)	0	8 (1.0)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Haematuria	3 (0.6)	1 (0.2)	8 (1.0)
Grade 1/Mild	1 (0.2)	1 (0.2)	5 (0.6)
Grade 2/Moderate	2 (0.4)	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Urine abnormality	2 (0.4)	0	4 (0.5)
Grade 1/Mild	2 (0.4)	0	3 (0.4)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Proteinuria	2 (0.4)	0	3 (0.4)
Grade 1/Mild	2 (0.4)	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Renal cyst	0	0	3 (0.4)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ureterolithiasis	0	0	3 (0.4)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Chromaturia	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperoxaluria	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pollakiuria	2 (0.4)	1 (0.2)	2 (0.2)
Grade 1/Mild	1 (0.2)	1 (0.2)	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Polyuria	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Renal colic	2 (0.4)	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	2 (0.4)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Renal pain	2 (0.4)	2 (0.4)	2 (0.2)
Grade 1/Mild	2 (0.4)	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Albuminuria	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Calculus bladder	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Calculus urinary	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Crystalluria	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hydronephrosis	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypercalciuria	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Ketonuria	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Microalbuminuria	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nephrocalcinosis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nocturia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Renal failure	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Renal impairment	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Renal mass	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ureteric obstruction	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Urethral disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urethral pain	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urinary hesitation	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urinary incontinence	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Urinary tract obstruction	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urinary tract pain	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Alkalinuria	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypersthenuria	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Micturition urgency	2 (0.4)	0	0
Grade 1/Mild	2 (0.4)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Nephropathy toxic	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urinary retention	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urinary tract discomfort	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Urine flow decreased	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Urine odour abnormal	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eye disorders	27 (5.5)	24 (5.0)	67 (8.2)
Grade 1/Mild	21 (4.3)	16 (3.3)	42 (5.1)
Grade 2/Moderate	6 (1.2)	8 (1.7)	25 (3.0)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blepharitis	0	0	6 (0.7)
Grade 1/Mild	0	0	6 (0.7)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Cataract	0	2 (0.4)	6 (0.7)
Grade 1/Mild	0	1 (0.2)	4 (0.5)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dry eye	10 (2.0)	3 (0.6)	6 (0.7)
Grade 1/Mild	9 (1.8)	2 (0.4)	5 (0.6)
Grade 2/Moderate	1 (0.2)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Chalazion	3 (0.6)	1 (0.2)	4 (0.5)
Grade 1/Mild	3 (0.6)	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Conjunctival haemorrhage	1 (0.2)	0	4 (0.5)
Grade 1/Mild	1 (0.2)	0	4 (0.5)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Diabetic retinopathy	0	0	4 (0.5)
Grade 1/Mild	0	0	4 (0.5)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eye discharge	0	0	4 (0.5)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vision blurred	1 (0.2)	2 (0.4)	4 (0.5)
Grade 1/Mild	1 (0.2)	0	3 (0.4)
Grade 2/Moderate	0	2 (0.4)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Conjunctivitis allergic	0	1 (0.2)	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Eye inflammation	1 (0.2)	1 (0.2)	3 (0.4)
Grade 1/Mild	1 (0.2)	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Myopia	0	0	3 (0.4)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Astigmatism	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blepharospasm	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Cataract nuclear	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eye pain	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eye pruritus	1 (0.2)	2 (0.4)	2 (0.2)
Grade 1/Mild	1 (0.2)	2 (0.4)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eye swelling	0	2 (0.4)	2 (0.2)
Grade 1/Mild	0	2 (0.4)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Lacrimation increased	2 (0.4)	3 (0.6)	2 (0.2)
Grade 1/Mild	1 (0.2)	2 (0.4)	2 (0.2)
Grade 2/Moderate	1 (0.2)	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ocular hypertension	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Posterior capsule opacification	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Visual impairment	1 (0.2)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Cataract cortical	3 (0.6)	0	1 (0.1)
Grade 1/Mild	3 (0.6)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Central serous chorioretinopathy	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Corneal degeneration	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Corneal lesion	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Deposit eye	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eczema eyelids	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eye disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eye irritation	1 (0.2)	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Eyelid rash	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Heterophoria	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lenticular opacities	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Periorbital oedema	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Retinal tear	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Retinal vein occlusion	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Retinopathy	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Strabismus	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Dacryostenosis acquired	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eyelid oedema	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Glaucoma	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Keratitis	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Macular oedema	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Meibomian gland dysfunction	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Non-proliferative retinopathy	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ocular cyst	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Periorbital dermatitis	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Photophobia	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Retinal haemorrhage	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Visual acuity reduced	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Vitreous haemorrhage	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Xerophthalmia	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Reproductive system and breast disorders	34 (6.9)	17 (3.5)	58 (7.1)
Grade 1/Mild	22 (4.5)	9 (1.9)	38 (4.6)
Grade 2/Moderate	11 (2.2)	8 (1.7)	20 (2.4)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dysmenorrhoea	4 (0.8)	5 (1.0)	7 (0.9)
Grade 1/Mild	2 (0.4)	3 (0.6)	4 (0.5)
Grade 2/Moderate	1 (0.2)	2 (0.4)	3 (0.4)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Heavy menstrual bleeding	2 (0.4)	3 (0.6)	5 (0.6)
Grade 1/Mild	2 (0.4)	2 (0.4)	3 (0.4)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Menopausal symptoms	2 (0.4)	1 (0.2)	4 (0.5)
Grade 1/Mild	1 (0.2)	0	3 (0.4)
Grade 2/Moderate	1 (0.2)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Breast mass	3 (0.6)	2 (0.4)	3 (0.4)
Grade 1/Mild	3 (0.6)	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vulvovaginal dryness	1 (0.2)	1 (0.2)	3 (0.4)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	1 (0.2)	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Breast cyst	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cervical polyp	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Intermenstrual bleeding	7 (1.4)	0	2 (0.2)
Grade 1/Mild	5 (1.0)	0	1 (0.1)
Grade 2/Moderate	2 (0.4)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ovarian cyst	2 (0.4)	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	2 (0.4)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Polymenorrhoea	2 (0.4)	0	2 (0.2)
Grade 1/Mild	2 (0.4)	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Prostatomegaly	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Testicular cyst	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Testicular mass	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Vaginal haemorrhage	2 (0.4)	2 (0.4)	2 (0.2)
Grade 1/Mild	2 (0.4)	0	2 (0.2)
Grade 2/Moderate	0	2 (0.4)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vulvovaginal pruritus	1 (0.2)	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Abnormal uterine bleeding	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Adnexa uteri cyst	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Amenorrhoea	2 (0.4)	0	1 (0.1)
Grade 1/Mild	2 (0.4)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Azoospermia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Benign prostatic hyperplasia	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Breast tenderness	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Cervical discharge	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dyspareunia	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Epididymal cyst	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Erectile dysfunction	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Fallopian tube cyst	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Genital erythema	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Gynaecomastia	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Menstruation irregular	2 (0.4)	1 (0.2)	1 (0.1)
Grade 1/Mild	2 (0.4)	0	1 (0.1)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Oligomenorrhoea	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ovarian cyst ruptured	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Scrotal pain	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Seminal vesicular cyst	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Testicular pain	1 (0.2)	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Testicular retraction	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Uterine haemorrhage	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vaginal discharge	1 (0.2)	1 (0.2)	1 (0.1)
Grade 1/Mild	1 (0.2)	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Vaginal prolapse	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Varicocele	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vulvovaginal discomfort	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vulvovaginal pain	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Breast discomfort	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Breast pain	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cervical dysplasia	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Endometrial hypertrophy	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Endometriosis	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Galactorrhoea	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Haematospermia	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Menometrorrhagia	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Menstruation delayed	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Orchitis noninfective	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pruritus genital	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Uterine polyp	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Vaginal cyst	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Immune system disorders	10 (2.0)	16 (3.3)	45 (5.5)
Grade 1/Mild	8 (1.6)	9 (1.9)	33 (4.0)
Grade 2/Moderate	2 (0.4)	4 (0.8)	10 (1.2)
Grade 3/Severe	0	3 (0.6)	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Seasonal allergy	7 (1.4)	10 (2.1)	32 (3.9)
Grade 1/Mild	7 (1.4)	7 (1.5)	25 (3.0)
Grade 2/Moderate	0	2 (0.4)	7 (0.9)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypersensitivity	0	2 (0.4)	6 (0.7)
Grade 1/Mild	0	1 (0.2)	3 (0.4)
Grade 2/Moderate	0	1 (0.2)	3 (0.4)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Food allergy	1 (0.2)	3 (0.6)	4 (0.5)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	1 (0.2)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	2 (0.4)	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Allergy to animal	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Anaphylactic reaction	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Contrast media reaction	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Drug hypersensitivity	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Type IV hypersensitivity reaction	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Allergy to plants	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ear and labyrinth disorders	21 (4.3)	14 (2.9)	42 (5.1)
Grade 1/Mild	18 (3.7)	14 (2.9)	33 (4.0)
Grade 2/Moderate	3 (0.6)	0	9 (1.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Ear pain	7 (1.4)	3 (0.6)	17 (2.1)
Grade 1/Mild	6 (1.2)	3 (0.6)	12 (1.5)
Grade 2/Moderate	1 (0.2)	0	5 (0.6)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vertigo	4 (0.8)	1 (0.2)	8 (1.0)
Grade 1/Mild	4 (0.8)	1 (0.2)	8 (1.0)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tinnitus	3 (0.6)	2 (0.4)	6 (0.7)
Grade 1/Mild	2 (0.4)	2 (0.4)	6 (0.7)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ear discomfort	4 (0.8)	4 (0.8)	4 (0.5)
Grade 1/Mild	2 (0.4)	4 (0.8)	4 (0.5)
Grade 2/Moderate	2 (0.4)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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Zusatzanalysen zur Studie VX20-121-104

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Middle ear effusion	1 (0.2)	0	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Deafness	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Auditory disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cerumen impaction	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
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Zusatzanalysen zur Studie VX20-121-104

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Ear congestion	2 (0.4)	2 (0.4)	1 (0.1)
Grade 1/Mild	2 (0.4)	2 (0.4)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ear pruritus	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ear swelling	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Eustachian tube dysfunction	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

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- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Zusatzanalysen zur Studie VX20-121-104

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Excessive cerumen production	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
External ear pain	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypoacusis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Motion sickness	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Otorrhoea	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vertigo positional	1 (0.2)	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vestibular disorder	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Deafness bilateral	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis		OL Study
System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	Any VNZ/TEZ/D-IVA N = 822 n (%)
Tympanic membrane perforation	2 (0.4)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	5 (1.0)	4 (0.8)	31 (3.8)
Grade 1/Mild	5 (1.0)	1 (0.2)	17 (2.1)
Grade 2/Moderate	0	3 (0.6)	11 (1.3)
Grade 3/Severe	0	0	2 (0.2)
Grade 4/Life-threatening	0	0	1 (0.1)
Grade 5/Death	0	0	0
Fibroadenoma of breast	0	0	4 (0.5)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Skin papilloma	1 (0.2)	0	4 (0.5)
Grade 1/Mild	1 (0.2)	0	3 (0.4)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Acrochordon	0	0	3 (0.4)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Melanocytic naevus	0	0	3 (0.4)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Breast cancer	0	0	2 (0.2)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Lipoma	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Neoplasm skin	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Adenocarcinoma pancreas	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	1 (0.1)
Grade 5/Death	0	0	0
Basal cell carcinoma	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Benign neoplasm of thyroid gland	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Colorectal adenoma	2 (0.4)	0	1 (0.1)
Grade 1/Mild	2 (0.4)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hepatic adenoma	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Invasive breast carcinoma	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Lung adenocarcinoma	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Malignant melanoma stage 0	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Oral fibroma	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Osteolipoma	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Renal cell carcinoma	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Renal perivascular epithelioid cell tumour	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Seborrhoeic keratosis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Uterine leiomyoma	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Adenocarcinoma	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Benign breast neoplasm	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Intraductal papillary mucinous neoplasm	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Blood and lymphatic system disorders	14 (2.9)	3 (0.6)	30 (3.6)
Grade 1/Mild	6 (1.2)	3 (0.6)	19 (2.3)
Grade 2/Moderate	7 (1.4)	0	10 (1.2)
Grade 3/Severe	1 (0.2)	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Lymphadenopathy	4 (0.8)	1 (0.2)	10 (1.2)
Grade 1/Mild	4 (0.8)	1 (0.2)	7 (0.9)
Grade 2/Moderate	0	0	2 (0.2)
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Iron deficiency anaemia	4 (0.8)	1 (0.2)	7 (0.9)
Grade 1/Mild	1 (0.2)	1 (0.2)	3 (0.4)
Grade 2/Moderate	3 (0.6)	0	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Increased tendency to bruise	1 (0.2)	0	5 (0.6)
Grade 1/Mild	0	0	5 (0.6)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Leukopenia	0	0	4 (0.5)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Thrombocytopenia	1 (0.2)	0	3 (0.4)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Haemolysis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lymphadenitis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lymphopenia	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Reticulocytosis	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Anaemia	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Leukocytosis	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Neutropenia	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Neutrophilia	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Spontaneous haematoma	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Congenital, familial and genetic disorders	5 (1.0)	11 (2.3)	28 (3.4)
Grade 1/Mild	5 (1.0)	8 (1.7)	18 (2.2)
Grade 2/Moderate	0	2 (0.4)	10 (1.2)
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cystic fibrosis related diabetes	3 (0.6)	3 (0.6)	20 (2.4)
Grade 1/Mild	3 (0.6)	1 (0.2)	12 (1.5)
Grade 2/Moderate	0	2 (0.4)	8 (1.0)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Cystic fibrosis lung	0	2 (0.4)	3 (0.4)
Grade 1/Mild	0	2 (0.4)	2 (0.2)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cystic fibrosis hepatic disease	0	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Atrial septal defect	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cystic fibrosis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Rathke's cleft cyst	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cataract congenital	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cerebrovascular arteriovenous malformation	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Congenital cystic kidney disease	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Congenital vitreous anomaly	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cystic fibrosis gastrointestinal disease	0	2 (0.4)	0
Grade 1/Mild	0	2 (0.4)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Naevus anaemicus	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Vascular disorders	15 (3.1)	6 (1.3)	28 (3.4)
Grade 1/Mild	12 (2.4)	6 (1.3)	20 (2.4)
Grade 2/Moderate	3 (0.6)	0	8 (1.0)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hypertension	9 (1.8)	3 (0.6)	17 (2.1)
Grade 1/Mild	8 (1.6)	3 (0.6)	13 (1.6)
Grade 2/Moderate	1 (0.2)	0	4 (0.5)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hot flush	1 (0.2)	0	2 (0.2)
Grade 1/Mild	1 (0.2)	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypotension	1 (0.2)	0	2 (0.2)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Raynaud's phenomenon	0	1 (0.2)	2 (0.2)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Deep vein thrombosis	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Erythromelalgia	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Haematoma	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Lymphoedema	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
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Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Orthostatic hypotension	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Superficial vein thrombosis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Venous thrombosis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cyanosis	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Essential hypertension	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Peripheral vein thrombosis	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Phlebitis	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cardiac disorders	7 (1.4)	11 (2.3)	24 (2.9)
Grade 1/Mild	6 (1.2)	8 (1.7)	19 (2.3)
Grade 2/Moderate	0	3 (0.6)	5 (0.6)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Palpitations	2 (0.4)	2 (0.4)	11 (1.3)
Grade 1/Mild	2 (0.4)	1 (0.2)	9 (1.1)
Grade 2/Moderate	0	1 (0.2)	2 (0.2)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bradycardia	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Bundle branch block right	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Atrioventricular block	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Atrioventricular block first degree	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cardiac contractility decreased	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cardiomegaly	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Dilated cardiomyopathy	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Extrasystoles	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Left ventricular dysfunction	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Right ventricular dilatation	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Sinus bradycardia	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Supraventricular extrasystoles	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Supraventricular tachycardia	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Tachycardia	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Angina pectoris	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Arrhythmia	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Arteriospasm coronary	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cardiovascular disorder	0	2 (0.4)	0
Grade 1/Mild	0	2 (0.4)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pericardial calcification	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Pericardial fibrosis	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pericarditis	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pericarditis constrictive	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Right ventricular hypertrophy	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Ventricular extrasystoles	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hepatobiliary disorders	12 (2.4)	6 (1.3)	17 (2.1)
Grade 1/Mild	6 (1.2)	3 (0.6)	8 (1.0)
Grade 2/Moderate	1 (0.2)	3 (0.6)	6 (0.7)
Grade 3/Severe	5 (1.0)	0	2 (0.2)
Grade 4/Life-threatening	0	0	1 (0.1)
Grade 5/Death	0	0	0
Cholelithiasis	4 (0.8)	0	7 (0.9)
Grade 1/Mild	1 (0.2)	0	5 (0.6)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	3 (0.6)	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hepatic steatosis	0	0	4 (0.5)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Alcoholic liver disease	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cholangitis sclerosing	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cholecystitis	1 (0.2)	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cholelithiasis migration	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hepatic cyst	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hepatomegaly	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hepatotoxicity	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	1 (0.1)
Grade 5/Death	0	0	0
Hydrocholecystis	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Jaundice	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Liver injury	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Ocular icterus	1 (0.2)	0	1 (0.1)
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Biliary colic	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Cholangitis	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cholecystitis acute	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Cholestasis	2 (0.4)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	1 (0.2)	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Fatty liver alcoholic	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Gallbladder polyp	1 (0.2)	0	0
Grade 1/Mild	1 (0.2)	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hepatic cirrhosis	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperbilirubinaemia	1 (0.2)	1 (0.2)	0
Grade 1/Mild	1 (0.2)	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypertransaminasaemia	0	2 (0.4)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Portal hypertension	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	1 (0.2)	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Endocrine disorders	1 (0.2)	2 (0.4)	10 (1.2)
Grade 1/Mild	0	1 (0.2)	7 (0.9)
Grade 2/Moderate	1 (0.2)	1 (0.2)	1 (0.1)
Grade 3/Severe	0	0	2 (0.2)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hypothyroidism	0	1 (0.2)	4 (0.5)
Grade 1/Mild	0	0	4 (0.5)
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperthyroidism	0	0	2 (0.2)
Grade 1/Mild	0	0	2 (0.2)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Hyperparathyroidism primary	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Hyperparathyroidism secondary	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Inappropriate antidiuretic hormone secretion	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Polycystic ovarian syndrome	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Adrenal insufficiency	1 (0.2)	0	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Thyroid cyst	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Social circumstances	0	1 (0.2)	5 (0.6)
Grade 1/Mild	0	1 (0.2)	4 (0.5)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Menopause	0	0	4 (0.5)
Grade 1/Mild	0	0	3 (0.4)
Grade 2/Moderate	0	0	1 (0.1)
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Victim of crime	0	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Physical assault	0	1 (0.2)	0
Grade 1/Mild	0	1 (0.2)	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Product issues	1 (0.2)	2 (0.4)	3 (0.4)
Grade 1/Mild	0	1 (0.2)	2 (0.2)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	1 (0.2)	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Device dislocation	1 (0.2)	0	1 (0.1)
Grade 1/Mild	0	0	1 (0.1)
Grade 2/Moderate	1 (0.2)	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

System Organ Class Preferred Term Maximum Severity	Parent Study Integrated Safety Analysis ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	Parent Study Integrated Safety Analysis VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	OL Study Any VNZ/TEZ/D-IVA N = 822 n (%)
Device malfunction	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Device physical property issue	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	1 (0.2)	1 (0.1)
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Device leakage	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	1 (0.2)	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Pregnancy, puerperium and perinatal conditions	0	1 (0.2)	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.1.5a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis		OL Study
System Organ Class Preferred Term Maximum Severity	ELX/TEZ/IVA in 121-102 or 121-103 N = 491 n (%)	VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480 n (%)	Any VNZ/TEZ/D-IVA N = 822 n (%)
Abortion spontaneous	0	0	1 (0.1)
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	0	0
Grade 3/Severe	0	0	1 (0.1)
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0
Morning sickness	0	1 (0.2)	0
Grade 1/Mild	0	0	0
Grade 2/Moderate	0	1 (0.2)	0
Grade 3/Severe	0	0	0
Grade 4/Life-threatening	0	0	0
Grade 5/Death	0	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once with the maximum severity in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX20-121-104

Table 14.3.2.1a
Treatment-Emergent Adverse Events Leading to Death by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY

No data met the criteria for this table.

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.2a
Serious TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Total duration of safety analysis period in 100 PY	--	5.15	--	5.00	--	15.43
Subjects with any serious TEAEs	81 (16.5)	22.33	68 (14.2)	20.39	164 (20.0)	18.21
Infections and infestations	50 (10.2)	11.65	46 (9.6)	11.60	113 (13.7)	10.31
Infective pulmonary exacerbation of cystic fibrosis	35 (7.1)	7.77	29 (6.0)	7.40	80 (9.7)	6.68
Pneumonia	6 (1.2)	1.36	4 (0.8)	0.80	18 (2.2)	1.23
Influenza	3 (0.6)	0.58	7 (1.5)	1.40	10 (1.2)	0.65
COVID-19	4 (0.8)	0.78	2 (0.4)	0.40	2 (0.2)	0.13
Infective exacerbation of bronchiectasis	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Sinusitis	0	0	0	0	2 (0.2)	0.13
Tonsillitis	0	0	0	0	2 (0.2)	0.13
Anorectal cellulitis	0	0	0	0	1 (0.1)	0.06
Appendicitis	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
Bronchopulmonary aspergillosis allergic	0	0	0	0	1 (0.1)	0.06
Campylobacter gastroenteritis	0	0	0	0	1 (0.1)	0.06
Chronic sinusitis	0	0	0	0	1 (0.1)	0.06
Gastroenteritis	0	0	0	0	1 (0.1)	0.06
Gastroenteritis clostridial	0	0	0	0	1 (0.1)	0.06
Gastroenteritis viral	0	0	0	0	1 (0.1)	0.06

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.2a
Serious TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Giardiasis	0	0	0	0	1 (0.1)	0.06
Lower respiratory tract infection bacterial	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Lung abscess	0	0	0	0	1 (0.1)	0.06
Perirectal abscess	0	0	0	0	1 (0.1)	0.06
Pilonidal disease	0	0	0	0	1 (0.1)	0.06
Pneumonia parainfluenzae viral	0	0	0	0	1 (0.1)	0.06
Postoperative abscess	0	0	0	0	1 (0.1)	0.06
Pseudomonas infection	0	0	0	0	1 (0.1)	0.06
Pyelonephritis	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Respiratory syncytial virus infection	0	0	0	0	1 (0.1)	0.06
Upper respiratory tract infection bacterial	0	0	0	0	1 (0.1)	0.06
Cellulitis	0	0	1 (0.2)	0.20	0	0
Diverticulitis	0	0	1 (0.2)	0.20	0	0
Erysipelas	0	0	1 (0.2)	0.20	0	0
Meningitis aseptic	1 (0.2)	0.19	0	0	0	0
Metapneumovirus pneumonia	1 (0.2)	0.19	0	0	0	0
Respiratory tract infection viral	0	0	1 (0.2)	0.20	0	0
Urinary tract infection	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Viral myocarditis	0	0	1 (0.2)	0.20	0	0
Gastrointestinal disorders	12 (2.4)	2.72	6 (1.3)	1.60	16 (1.9)	1.69
Distal intestinal obstruction syndrome	3 (0.6)	0.58	2 (0.4)	0.80	4 (0.5)	0.32
Intestinal obstruction	0	0	0	0	3 (0.4)	0.19

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.2a
Serious TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Constipation	3 (0.6)	0.58	0	0	2 (0.2)	0.26
Small intestinal obstruction	0	0	1 (0.2)	0.20	2 (0.2)	0.26
Abdominal pain upper	0	0	0	0	1 (0.1)	0.06
Barrett's oesophagus	0	0	0	0	1 (0.1)	0.06
Colitis ischaemic	0	0	0	0	1 (0.1)	0.06
Diarrhoea	0	0	0	0	1 (0.1)	0.06
Flatulence	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Gastritis	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Gastrooesophageal reflux disease	0	0	0	0	1 (0.1)	0.06
Rectal prolapse	0	0	0	0	1 (0.1)	0.13
Vomiting	0	0	0	0	1 (0.1)	0.06
Abdominal pain	1 (0.2)	0.39	0	0	0	0
Dysphagia	1 (0.2)	0.19	0	0	0	0
Faecaloma	1 (0.2)	0.19	0	0	0	0
Mechanical ileus	0	0	1 (0.2)	0.20	0	0
Melaena	0	0	1 (0.2)	0.20	0	0
Pancreatic cyst	0	0	1 (0.2)	0.20	0	0
Pancreatitis	1 (0.2)	0.19	0	0	0	0
Subileus	1 (0.2)	0.19	0	0	0	0
Respiratory, thoracic and mediastinal disorders	4 (0.8)	0.78	3 (0.6)	0.60	15 (1.8)	1.17
Haemoptysis	3 (0.6)	0.58	3 (0.6)	0.60	11 (1.3)	0.84
Bronchial artery hypertrophy	0	0	0	0	1 (0.1)	0.06
Pneumothorax	0	0	0	0	1 (0.1)	0.06

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.2a
Serious TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Productive cough	0	0	0	0	1 (0.1)	0.06
Pulmonary cavitation	0	0	0	0	1 (0.1)	0.06
Reflux laryngitis	0	0	0	0	1 (0.1)	0.06
Nasal polyps	1 (0.2)	0.19	0	0	0	0
Injury, poisoning and procedural complications	5 (1.0)	0.97	2 (0.4)	0.80	10 (1.2)	0.65
Alcohol poisoning	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Concussion	0	0	0	0	1 (0.1)	0.06
Hand fracture	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Incisional hernia	0	0	0	0	1 (0.1)	0.06
Ligament sprain	0	0	0	0	1 (0.1)	0.06
Poisoning deliberate	0	0	0	0	1 (0.1)	0.06
Postoperative respiratory failure	0	0	0	0	1 (0.1)	0.06
Procedural pain	0	0	0	0	1 (0.1)	0.06
Scapula fracture	0	0	0	0	1 (0.1)	0.06
Wrist fracture	0	0	0	0	1 (0.1)	0.06
Ankle fracture	1 (0.2)	0.19	0	0	0	0
Craniocerebral injury	1 (0.2)	0.19	0	0	0	0
Fall	0	0	1 (0.2)	0.20	0	0
Post procedural haematoma	0	0	1 (0.2)	0.20	0	0
Postoperative ileus	1 (0.2)	0.19	0	0	0	0
Skin laceration	0	0	1 (0.2)	0.20	0	0
Skull fractured base	0	0	1 (0.2)	0.20	0	0
Metabolism and nutrition disorders	1 (0.2)	0.19	2 (0.4)	0.40	9 (1.1)	0.58

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.2a
Serious TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Diabetes mellitus inadequate control	0	0	0	0	3 (0.4)	0.19
Diabetic ketoacidosis	0	0	0	0	2 (0.2)	0.13
Dehydration	0	0	0	0	1 (0.1)	0.06
Hyperglycaemia	0	0	0	0	1 (0.1)	0.06
Hyponatraemia	0	0	0	0	1 (0.1)	0.06
Malnutrition	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Hyperphosphatasaemia	0	0	1 (0.2)	0.20	0	0
Type 3 diabetes mellitus	0	0	1 (0.2)	0.20	0	0
Renal and urinary disorders	2 (0.4)	0.39	0	0	8 (1.0)	0.78
Nephrolithiasis	2 (0.4)	0.39	0	0	5 (0.6)	0.39
Acute kidney injury	0	0	0	0	1 (0.1)	0.13
Calculus urinary	0	0	0	0	1 (0.1)	0.06
Ureteric obstruction	0	0	0	0	1 (0.1)	0.06
Ureterolithiasis	0	0	0	0	1 (0.1)	0.06
Urinary tract obstruction	0	0	0	0	1 (0.1)	0.06
Investigations	5 (1.0)	1.36	4 (0.8)	1.80	7 (0.9)	0.65
Blood creatine phosphokinase increased	1 (0.2)	0.19	1 (0.2)	0.20	2 (0.2)	0.13
Alanine aminotransferase increased	2 (0.4)	0.39	2 (0.4)	0.40	1 (0.1)	0.06
Blood alkaline phosphatase increased	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Blood bilirubin unconjugated increased	0	0	0	0	1 (0.1)	0.06
Blood creatinine increased	0	0	0	0	1 (0.1)	0.06
Blood glucose increased	0	0	0	0	1 (0.1)	0.06
Gamma-glutamyltransferase increased	1 (0.2)	0.19	2 (0.4)	0.40	1 (0.1)	0.06
Influenza A virus test positive	0	0	0	0	1 (0.1)	0.06

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.2a
Serious TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
SARS-CoV-2 test positive	0	0	0	0	1 (0.1)	0.06
Aspartate aminotransferase increased	1 (0.2)	0.19	2 (0.4)	0.40	0	0
Blood bilirubin increased	0	0	1 (0.2)	0.20	0	0
Glycosylated haemoglobin increased	1 (0.2)	0.19	0	0	0	0
Pulmonary function test decreased	1 (0.2)	0.19	0	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	0	1 (0.2)	0.20	6 (0.7)	0.39
Adenocarcinoma pancreas	0	0	0	0	1 (0.1)	0.06
Breast cancer	0	0	0	0	1 (0.1)	0.06
Invasive breast carcinoma	0	0	0	0	1 (0.1)	0.06
Osteolipoma	0	0	0	0	1 (0.1)	0.06
Renal cell carcinoma	0	0	0	0	1 (0.1)	0.06
Uterine leiomyoma	0	0	0	0	1 (0.1)	0.06
Adenocarcinoma	0	0	1 (0.2)	0.20	0	0
Nervous system disorders	4 (0.8)	1.17	5 (1.0)	1.20	6 (0.7)	0.52
Alcoholic seizure	0	0	0	0	1 (0.1)	0.13
Dizziness	0	0	0	0	1 (0.1)	0.06
Focal dyscognitive seizures	0	0	0	0	1 (0.1)	0.06
Hypoglycaemic coma	0	0	0	0	1 (0.1)	0.13
Seizure	1 (0.2)	0.39	1 (0.2)	0.20	1 (0.1)	0.06
Subarachnoid haemorrhage	0	0	0	0	1 (0.1)	0.06
Disturbance in attention	1 (0.2)	0.19	0	0	0	0
Epilepsy	1 (0.2)	0.19	0	0	0	0
Haemorrhage intracranial	0	0	1 (0.2)	0.20	0	0

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.2a
Serious TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Headache	0	0	1 (0.2)	0.20	0	0
Post-traumatic headache	0	0	1 (0.2)	0.20	0	0
Psychomotor hyperactivity	1 (0.2)	0.19	0	0	0	0
Serotonin syndrome	1 (0.2)	0.19	0	0	0	0
Syncope	0	0	2 (0.4)	0.40	0	0
Psychiatric disorders	3 (0.6)	0.97	5 (1.0)	1.00	4 (0.5)	0.32
Depression	0	0	2 (0.4)	0.40	2 (0.2)	0.13
Suicidal ideation	2 (0.4)	0.39	2 (0.4)	0.40	2 (0.2)	0.13
Mental disorder	0	0	0	0	1 (0.1)	0.06
Acute stress disorder	0	0	1 (0.2)	0.20	0	0
Behaviour disorder	1 (0.2)	0.19	0	0	0	0
Depression suicidal	1 (0.2)	0.19	0	0	0	0
Mixed anxiety and depressive disorder	1 (0.2)	0.19	0	0	0	0
General disorders and administration site conditions	0	0	1 (0.2)	0.20	3 (0.4)	0.19
Adverse drug reaction	0	0	0	0	1 (0.1)	0.06
General physical health deterioration	0	0	0	0	1 (0.1)	0.06
Pyrexia	0	0	0	0	1 (0.1)	0.06
Chest pain	0	0	1 (0.2)	0.20	0	0
Congenital, familial and genetic disorders	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Cystic fibrosis lung	0	0	0	0	1 (0.1)	0.06
Cystic fibrosis related diabetes	0	0	0	0	1 (0.1)	0.06

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.2a
Serious TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Cerebrovascular arteriovenous malformation	0	0	1 (0.2)	0.20	0	0
Hepatobiliary disorders	4 (0.8)	1.17	1 (0.2)	0.20	2 (0.2)	0.13
Cholecystitis	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Cholelithiasis	3 (0.6)	0.58	0	0	1 (0.1)	0.06
Cholangitis	1 (0.2)	0.19	0	0	0	0
Cholestasis	0	0	1 (0.2)	0.20	0	0
Fatty liver alcoholic	1 (0.2)	0.19	0	0	0	0
Musculoskeletal and connective tissue disorders	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Musculoskeletal chest pain	0	0	0	0	1 (0.1)	0.06
Periarthritis	0	0	0	0	1 (0.1)	0.06
Osteoarthritis	1 (0.2)	0.19	0	0	0	0
Blood and lymphatic system disorders	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Lymphadenopathy	0	0	0	0	1 (0.1)	0.06
Leukocytosis	1 (0.2)	0.19	0	0	0	0
Cardiac disorders	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Palpitations	0	0	0	0	1 (0.1)	0.06
Arteriospasm coronary	1 (0.2)	0.19	0	0	0	0
Eye disorders	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Cataract cortical	0	0	0	0	1 (0.1)	0.06
Vision blurred	0	0	1 (0.2)	0.20	0	0
Immune system disorders	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Anaphylactic reaction	0	0	0	0	1 (0.1)	0.06

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.2a
Serious TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Hypersensitivity	0	0	1 (0.2)	0.20	0	0
Pregnancy, puerperium and perinatal conditions	0	0	0	0	1 (0.1)	0.06
Abortion spontaneous	0	0	0	0	1 (0.1)	0.06
Product issues	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Device dislocation	0	0	0	0	1 (0.1)	0.06
Device leakage	0	0	1 (0.2)	0.20	0	0
Reproductive system and breast disorders	2 (0.4)	0.39	0	0	1 (0.1)	0.13
Fallopian tube cyst	0	0	0	0	1 (0.1)	0.06
Ovarian cyst	0	0	0	0	1 (0.1)	0.06
Intermenstrual bleeding	1 (0.2)	0.19	0	0	0	0
Vaginal cyst	1 (0.2)	0.19	0	0	0	0
Skin and subcutaneous tissue disorders	0	0	0	0	1 (0.1)	0.06
Drug eruption	0	0	0	0	1 (0.1)	0.06

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.5a
Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Total duration of safety analysis period in 100 PY	--	5.15	--	5.00	--	15.43
Subjects with TEAEs leading to treatment discontinuation	18 (3.7)	5.24	18 (3.8)	9.00	27 (3.3)	2.46
Investigations	6 (1.2)	2.14	9 (1.9)	4.40	6 (0.7)	0.65
Alanine aminotransferase increased	3 (0.6)	0.58	7 (1.5)	1.40	2 (0.2)	0.13
Aspartate aminotransferase increased	3 (0.6)	0.58	6 (1.3)	1.20	2 (0.2)	0.13
Blood alkaline phosphatase increased	1 (0.2)	0.19	2 (0.4)	0.40	1 (0.1)	0.06
Blood bilirubin increased	0	0	2 (0.4)	0.40	1 (0.1)	0.06
Blood creatine phosphokinase increased	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
Blood glucose increased	0	0	0	0	1 (0.1)	0.06
Gamma-glutamyltransferase increased	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
Weight decreased	0	0	0	0	1 (0.1)	0.06
Blood bilirubin unconjugated increased	0	0	2 (0.4)	0.40	0	0
Pulmonary function test decreased	2 (0.4)	0.39	0	0	0	0
Sputum abnormal	0	0	1 (0.2)	0.20	0	0
Respiratory, thoracic and mediastinal disorders	2 (0.4)	0.39	4 (0.8)	1.20	6 (0.7)	0.58
Dyspnoea	0	0	0	0	4 (0.5)	0.26
Cough	1 (0.2)	0.19	2 (0.4)	0.40	2 (0.2)	0.13
Pulmonary cavitation	0	0	0	0	1 (0.1)	0.13
Sputum increased	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.5a
Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Dysphonia	0	0	2 (0.4)	0.40	0	0
Sputum discoloured	0	0	1 (0.2)	0.20	0	0
Infections and infestations	2 (0.4)	0.39	1 (0.2)	0.20	5 (0.6)	0.32
Infective pulmonary exacerbation of cystic fibrosis	0	0	0	0	2 (0.2)	0.13
Aspergilloma	0	0	0	0	1 (0.1)	0.06
Bronchitis	0	0	0	0	1 (0.1)	0.06
Bronchopulmonary aspergillosis allergic	0	0	0	0	1 (0.1)	0.06
Appendicitis	1 (0.2)	0.19	0	0	0	0
Giardiasis	0	0	1 (0.2)	0.20	0	0
Meningitis aseptic	1 (0.2)	0.19	0	0	0	0
Psychiatric disorders	2 (0.4)	0.39	3 (0.6)	1.60	4 (0.5)	0.39
Alcohol use disorder	0	0	0	0	1 (0.1)	0.06
Anxiety	0	0	2 (0.4)	0.40	1 (0.1)	0.06
Depression	0	0	2 (0.4)	0.40	1 (0.1)	0.06
Insomnia	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Mental disorder	0	0	0	0	1 (0.1)	0.06
Suicidal ideation	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Agitation	0	0	1 (0.2)	0.20	0	0
Mental fatigue	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Stress	0	0	1 (0.2)	0.20	0	0
Gastrointestinal disorders	4 (0.8)	0.97	0	0	2 (0.2)	0.13
Diarrhoea	0	0	0	0	2 (0.2)	0.13

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.5a
Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Abdominal pain	1 (0.2)	0.19	0	0	0	0
Constipation	1 (0.2)	0.19	0	0	0	0
Distal intestinal obstruction syndrome	1 (0.2)	0.19	0	0	0	0
Gastritis	1 (0.2)	0.19	0	0	0	0
Pancreatitis	1 (0.2)	0.19	0	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	0	0	0	2 (0.2)	0.13
Breast cancer	0	0	0	0	1 (0.1)	0.06
Invasive breast carcinoma	0	0	0	0	1 (0.1)	0.06
Nervous system disorders	1 (0.2)	0.19	2 (0.4)	0.40	2 (0.2)	0.13
Brain fog	0	0	0	0	1 (0.1)	0.06
Focal dyscognitive seizures	0	0	0	0	1 (0.1)	0.06
Amnesia	0	0	1 (0.2)	0.20	0	0
Hyperresponsive to stimuli	1 (0.2)	0.19	0	0	0	0
Lethargy	0	0	1 (0.2)	0.20	0	0
General disorders and administration site conditions	2 (0.4)	0.39	3 (0.6)	0.60	1 (0.1)	0.06
Asthenia	0	0	0	0	1 (0.1)	0.06
Fatigue	2 (0.4)	0.39	3 (0.6)	0.60	0	0
Hepatobiliary disorders	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Cholangitis sclerosing	0	0	0	0	1 (0.1)	0.06
Cholangitis	1 (0.2)	0.19	0	0	0	0
Immune system disorders	0	0	1 (0.2)	0.20	0	0
Hypersensitivity	0	0	1 (0.2)	0.20	0	0

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.5a
Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Metabolism and nutrition disorders	1 (0.2)	0.19	0	0	0	0
Malnutrition	1 (0.2)	0.19	0	0	0	0
Reproductive system and breast disorders	0	0	1 (0.2)	0.20	0	0
Heavy menstrual bleeding	0	0	1 (0.2)	0.20	0	0
Skin and subcutaneous tissue disorders	0	0	1 (0.2)	0.20	0	0
Rash maculo-papular	0	0	1 (0.2)	0.20	0	0

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.

Table 14.3.2.7a
Grade 3+ TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Total duration of safety analysis period in 100 PY	--	5.15	--	5.00	--	15.43
Subjects with any Grade 3+ TEAEs	55 (11.2)	17.48	54 (11.3)	20.19	103 (12.5)	12.12
Infections and infestations	25 (5.1)	6.21	28 (5.8)	7.20	58 (7.1)	4.99
Infective pulmonary exacerbation of cystic fibrosis	17 (3.5)	4.27	18 (3.8)	4.40	36 (4.4)	2.66
Pneumonia	3 (0.6)	0.58	2 (0.4)	0.60	10 (1.2)	0.65
Influenza	2 (0.4)	0.39	4 (0.8)	0.80	6 (0.7)	0.45
Infective exacerbation of bronchiectasis	0	0	1 (0.2)	0.20	2 (0.2)	0.13
Anorectal cellulitis	0	0	0	0	1 (0.1)	0.06
Appendicitis	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
COVID-19	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Chronic sinusitis	0	0	0	0	1 (0.1)	0.06
Genital herpes	0	0	0	0	1 (0.1)	0.06
Lower respiratory tract infection	0	0	0	0	1 (0.1)	0.06
Nasopharyngitis	0	0	0	0	1 (0.1)	0.06
Perirectal abscess	0	0	0	0	1 (0.1)	0.13
Pilonidal disease	0	0	0	0	1 (0.1)	0.06
Pneumonia aspiration	0	0	0	0	1 (0.1)	0.06
Postoperative abscess	0	0	0	0	1 (0.1)	0.06

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.
- Subjects with Grade 3+ TEAEs include the 'Severe', 'Life-threatening' and 'Death' categories.

Table 14.3.2.7a
Grade 3+ TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Pyelonephritis	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Respiratory syncytial virus infection	0	0	0	0	1 (0.1)	0.06
Sinusitis	0	0	0	0	1 (0.1)	0.06
Urinary tract infection	0	0	1 (0.2)	0.20	1 (0.1)	0.13
Cellulitis	0	0	1 (0.2)	0.20	0	0
Lower respiratory tract infection bacterial	1 (0.2)	0.19	0	0	0	0
Mastoiditis	0	0	1 (0.2)	0.20	0	0
Meningitis aseptic	1 (0.2)	0.19	0	0	0	0
Tooth infection	0	0	1 (0.2)	0.20	0	0
Viral myocarditis	0	0	1 (0.2)	0.20	0	0
Gastrointestinal disorders	5 (1.0)	1.55	6 (1.3)	2.20	13 (1.6)	1.36
Intestinal obstruction	0	0	0	0	3 (0.4)	0.19
Abdominal pain	1 (0.2)	0.78	1 (0.2)	0.20	2 (0.2)	0.13
Diarrhoea	1 (0.2)	0.19	0	0	2 (0.2)	0.13
Distal intestinal obstruction syndrome	0	0	2 (0.4)	0.80	2 (0.2)	0.13
Nausea	0	0	0	0	2 (0.2)	0.13
Small intestinal obstruction	0	0	0	0	2 (0.2)	0.19
Vomiting	0	0	0	0	2 (0.2)	0.13
Abdominal pain lower	0	0	0	0	1 (0.1)	0.06
Colitis ischaemic	0	0	0	0	1 (0.1)	0.06
Constipation	1 (0.2)	0.19	1 (0.2)	0.20	1 (0.1)	0.06
Flatulence	0	0	0	0	1 (0.1)	0.06

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.
- Subjects with Grade 3+ TEAEs include the 'Severe', 'Life-threatening' and 'Death' categories.

Table 14.3.2.7a
Grade 3+ TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Gastrooesophageal reflux disease	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Abdominal pain upper	0	0	2 (0.4)	0.40	0	0
Dental caries	1 (0.2)	0.19	0	0	0	0
Food poisoning	0	0	1 (0.2)	0.20	0	0
Pancreatic cyst	0	0	1 (0.2)	0.40	0	0
Investigations	8 (1.6)	2.14	7 (1.5)	2.80	10 (1.2)	0.78
Blood creatine phosphokinase increased	2 (0.4)	0.39	1 (0.2)	0.20	4 (0.5)	0.26
Aspartate aminotransferase increased	1 (0.2)	0.19	2 (0.4)	0.40	2 (0.2)	0.13
Alanine aminotransferase increased	1 (0.2)	0.19	4 (0.8)	0.80	1 (0.1)	0.06
Blood alkaline phosphatase increased	2 (0.4)	0.39	2 (0.4)	0.40	1 (0.1)	0.06
Blood glucose increased	0	0	0	0	1 (0.1)	0.06
Blood sodium decreased	0	0	0	0	1 (0.1)	0.06
Gamma-glutamyltransferase increased	2 (0.4)	0.39	2 (0.4)	0.40	1 (0.1)	0.06
Influenza A virus test positive	0	0	0	0	1 (0.1)	0.06
Blood bilirubin increased	1 (0.2)	0.19	2 (0.4)	0.40	0	0
Blood bilirubin unconjugated increased	1 (0.2)	0.19	1 (0.2)	0.20	0	0
Glycosylated haemoglobin increased	1 (0.2)	0.19	0	0	0	0
Injury, poisoning and procedural complications	4 (0.8)	0.97	1 (0.2)	0.40	9 (1.1)	0.84
Alcohol poisoning	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Hand fracture	0	0	0	0	1 (0.1)	0.06
Intervertebral disc injury	0	0	0	0	1 (0.1)	0.19
Ligament sprain	0	0	0	0	1 (0.1)	0.13

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.
- Subjects with Grade 3+ TEAEs include the 'Severe', 'Life-threatening' and 'Death' categories.

Table 14.3.2.7a
Grade 3+ TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Poisoning deliberate	0	0	0	0	1 (0.1)	0.06
Postoperative respiratory failure	0	0	0	0	1 (0.1)	0.06
Procedural pain	0	0	0	0	1 (0.1)	0.06
Road traffic accident	0	0	0	0	1 (0.1)	0.06
Torus fracture	0	0	0	0	1 (0.1)	0.06
Wrist fracture	0	0	0	0	1 (0.1)	0.06
Ankle fracture	1 (0.2)	0.39	0	0	0	0
Craniocerebral injury	1 (0.2)	0.19	0	0	0	0
Fall	0	0	1 (0.2)	0.20	0	0
Postoperative ileus	1 (0.2)	0.19	0	0	0	0
Skull fractured base	0	0	1 (0.2)	0.20	0	0
Respiratory, thoracic and mediastinal disorders	4 (0.8)	0.78	6 (1.3)	1.40	7 (0.9)	0.58
Haemoptysis	1 (0.2)	0.19	3 (0.6)	0.60	4 (0.5)	0.32
Bronchial artery hypertrophy	0	0	0	0	1 (0.1)	0.06
Cough	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Pulmonary cavitation	0	0	1 (0.2)	0.20	1 (0.1)	0.13
Dysphonia	0	0	1 (0.2)	0.20	0	0
Lower respiratory tract congestion	1 (0.2)	0.19	0	0	0	0
Nasal congestion	0	0	1 (0.2)	0.20	0	0
Productive cough	1 (0.2)	0.19	0	0	0	0
Pulmonary pain	0	0	1 (0.2)	0.20	0	0
Metabolism and nutrition disorders	1 (0.2)	0.19	1 (0.2)	0.20	6 (0.7)	0.58

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
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- Subjects with Grade 3+ TEAEs include the 'Severe', 'Life-threatening' and 'Death' categories.

Table 14.3.2.7a
Grade 3+ TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Dehydration	0	0	0	0	2 (0.2)	0.19
Diabetic ketoacidosis	0	0	0	0	2 (0.2)	0.13
Hyponatraemia	0	0	0	0	2 (0.2)	0.13
Ketosis	0	0	0	0	1 (0.1)	0.06
Malnutrition	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Hypoglycaemia	0	0	1 (0.2)	0.20	0	0
Psychiatric disorders	5 (1.0)	1.55	4 (0.8)	1.60	6 (0.7)	0.39
Anxiety	1 (0.2)	0.39	1 (0.2)	0.20	3 (0.4)	0.19
Alcohol use disorder	0	0	0	0	1 (0.1)	0.06
Mental disorder	0	0	0	0	1 (0.1)	0.06
Suicidal ideation	2 (0.4)	0.39	2 (0.4)	0.40	1 (0.1)	0.06
Agitation	0	0	1 (0.2)	0.20	0	0
Behaviour disorder	1 (0.2)	0.19	0	0	0	0
Depression	0	0	2 (0.4)	0.40	0	0
Depression suicidal	1 (0.2)	0.19	0	0	0	0
Insomnia	0	0	1 (0.2)	0.20	0	0
Mental fatigue	1 (0.2)	0.19	0	0	0	0
Mixed anxiety and depressive disorder	1 (0.2)	0.19	0	0	0	0
Stress	0	0	1 (0.2)	0.20	0	0
Renal and urinary disorders	1 (0.2)	0.19	1 (0.2)	0.20	6 (0.7)	0.84
Nephrolithiasis	1 (0.2)	0.19	1 (0.2)	0.20	4 (0.5)	0.45
Acute kidney injury	0	0	0	0	1 (0.1)	0.13
Calculus urinary	0	0	0	0	1 (0.1)	0.06

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
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Table 14.3.2.7a
Grade 3+ TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Renal failure	0	0	0	0	1 (0.1)	0.06
Ureterolithiasis	0	0	0	0	1 (0.1)	0.06
Urinary tract obstruction	0	0	0	0	1 (0.1)	0.06
Nervous system disorders	5 (1.0)	1.75	7 (1.5)	2.00	5 (0.6)	0.52
Headache	3 (0.6)	0.58	2 (0.4)	0.60	2 (0.2)	0.13
Alcoholic seizure	0	0	0	0	1 (0.1)	0.13
Hypoglycaemic coma	0	0	0	0	1 (0.1)	0.13
Hypoglycaemic unconsciousness	0	0	0	0	1 (0.1)	0.06
Subarachnoid haemorrhage	0	0	0	0	1 (0.1)	0.06
Disturbance in attention	1 (0.2)	0.19	0	0	0	0
Epilepsy	1 (0.2)	0.19	0	0	0	0
Haemorrhage intracranial	0	0	1 (0.2)	0.20	0	0
Hyperresponsive to stimuli	1 (0.2)	0.19	0	0	0	0
Lethargy	0	0	1 (0.2)	0.20	0	0
Migraine	0	0	3 (0.6)	0.60	0	0
Post-traumatic headache	0	0	1 (0.2)	0.20	0	0
Psychomotor hyperactivity	1 (0.2)	0.19	0	0	0	0
Seizure	1 (0.2)	0.39	0	0	0	0
Syncope	0	0	1 (0.2)	0.20	0	0
Hepatobiliary disorders	5 (1.0)	1.55	0	0	3 (0.4)	0.19
Alcoholic liver disease	0	0	0	0	1 (0.1)	0.06
Cholelithiasis	3 (0.6)	0.58	0	0	1 (0.1)	0.06
Hepatotoxicity	0	0	0	0	1 (0.1)	0.06

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
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Table 14.3.2.7a
Grade 3+ TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Cholangitis	1 (0.2)	0.19	0	0	0	0
Cholecystitis	1 (0.2)	0.19	0	0	0	0
Fatty liver alcoholic	1 (0.2)	0.19	0	0	0	0
Hepatic cirrhosis	1 (0.2)	0.19	0	0	0	0
Portal hypertension	1 (0.2)	0.19	0	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	0	0	0	3 (0.4)	0.19
Adenocarcinoma pancreas	0	0	0	0	1 (0.1)	0.06
Breast cancer	0	0	0	0	1 (0.1)	0.06
Renal cell carcinoma	0	0	0	0	1 (0.1)	0.06
Skin and subcutaneous tissue disorders	0	0	1 (0.2)	0.20	3 (0.4)	0.19
Drug eruption	0	0	0	0	1 (0.1)	0.06
Rash	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Rash maculo-papular	0	0	0	0	1 (0.1)	0.06
Endocrine disorders	0	0	0	0	2 (0.2)	0.13
Hyperparathyroidism primary	0	0	0	0	1 (0.1)	0.06
Inappropriate antidiuretic hormone secretion	0	0	0	0	1 (0.1)	0.06
General disorders and administration site conditions	0	0	3 (0.6)	0.60	2 (0.2)	0.13
Pyrexia	0	0	0	0	2 (0.2)	0.13
Fatigue	0	0	2 (0.4)	0.40	0	0
Influenza like illness	0	0	1 (0.2)	0.20	0	0

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the Any VNZ/TEZ/D-IVA column by SOC, and by PT within each SOC.
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Table 14.3.2.7a
Grade 3+ TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Immune system disorders	0	0	3 (0.6)	0.60	2 (0.2)	0.13
Anaphylactic reaction	0	0	0	0	1 (0.1)	0.06
Food allergy	0	0	2 (0.4)	0.40	1 (0.1)	0.06
Seasonal allergy	0	0	1 (0.2)	0.20	0	0
Blood and lymphatic system disorders	1 (0.2)	0.19	0	0	1 (0.1)	0.06
Lymphadenopathy	0	0	0	0	1 (0.1)	0.06
Thrombocytopenia	1 (0.2)	0.19	0	0	0	0
Musculoskeletal and connective tissue disorders	0	0	2 (0.4)	0.40	1 (0.1)	0.06
Musculoskeletal chest pain	0	0	0	0	1 (0.1)	0.06
Arthralgia	0	0	1 (0.2)	0.20	0	0
Back pain	0	0	1 (0.2)	0.20	0	0
Pregnancy, puerperium and perinatal conditions	0	0	0	0	1 (0.1)	0.06
Abortion spontaneous	0	0	0	0	1 (0.1)	0.06
Product issues	0	0	1 (0.2)	0.20	1 (0.1)	0.06
Device malfunction	0	0	0	0	1 (0.1)	0.06
Device leakage	0	0	1 (0.2)	0.20	0	0
Cardiac disorders	1 (0.2)	0.19	0	0	0	0
Arteriospasm coronary	1 (0.2)	0.19	0	0	0	0
Congenital, familial and genetic disorders	0	0	1 (0.2)	0.20	0	0

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
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Table 14.3.2.7a
Grade 3+ TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Pooled Safety Set and OL Safety Set

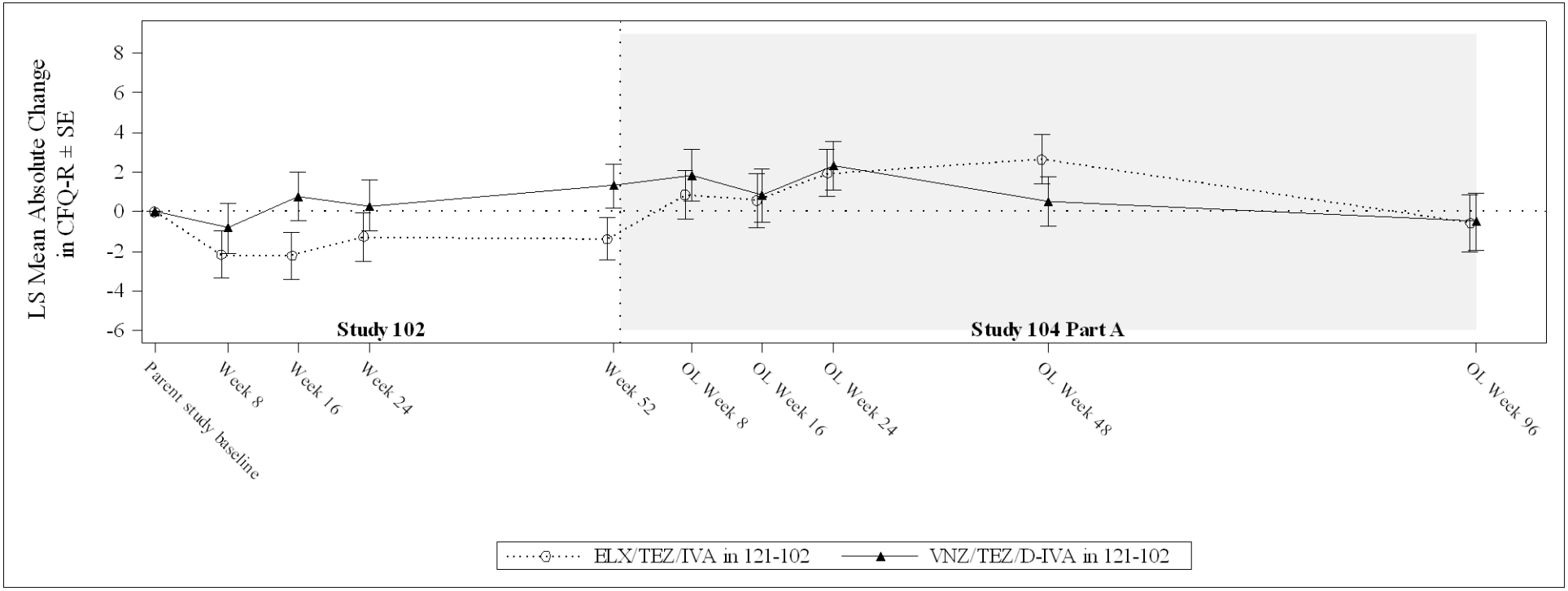
	Parent Study Integrated Safety Analysis				OL Study	
	ELX/TEZ/IVA in 121-102 or 121-103 N = 491		VNZ/TEZ/D-IVA in 121-102 or 121-103 N = 480		Any VNZ/TEZ/D-IVA N = 822	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY	n (%)	Events/100PY
Cerebrovascular arteriovenous malformation	0	0	1 (0.2)	0.20	0	0
Reproductive system and breast disorders	1 (0.2)	0.19	0	0	0	0
Dysmenorrhoea	1 (0.2)	0.19	0	0	0	0

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
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Zusatzanalysen zur Studie VX20-121-104

Figure 14.2.6.4.1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

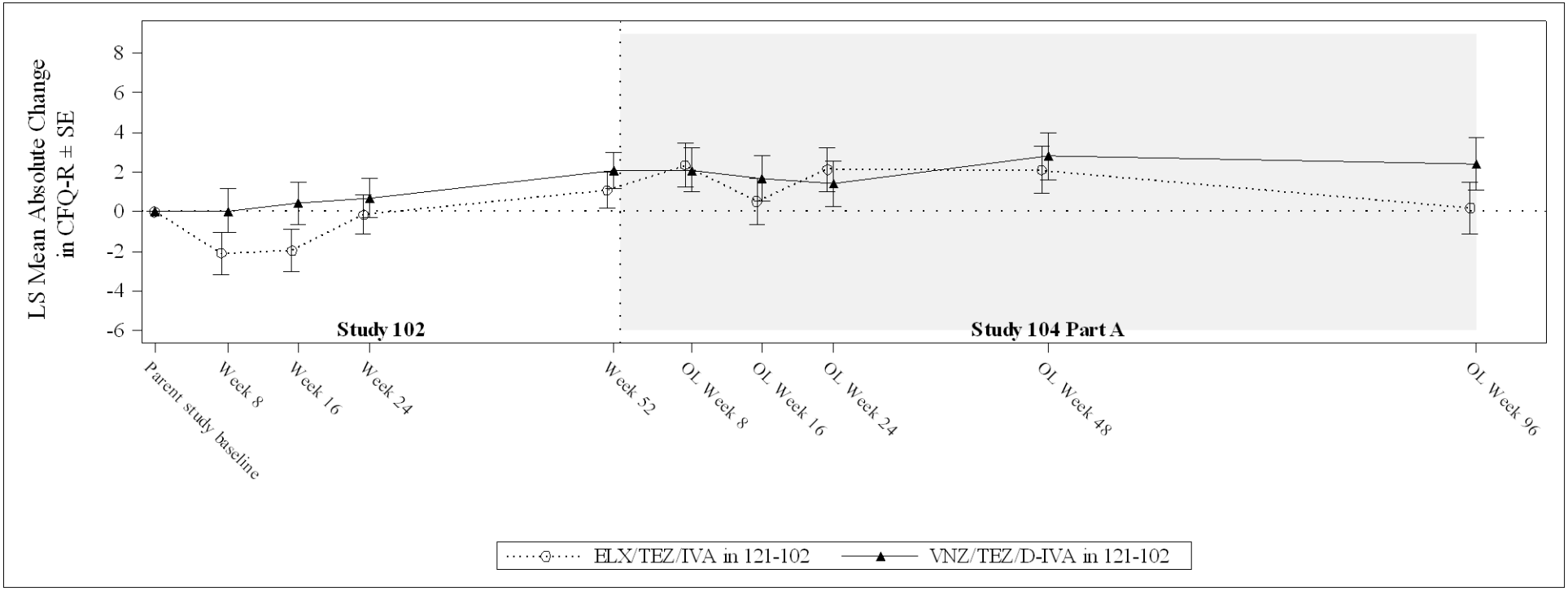
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

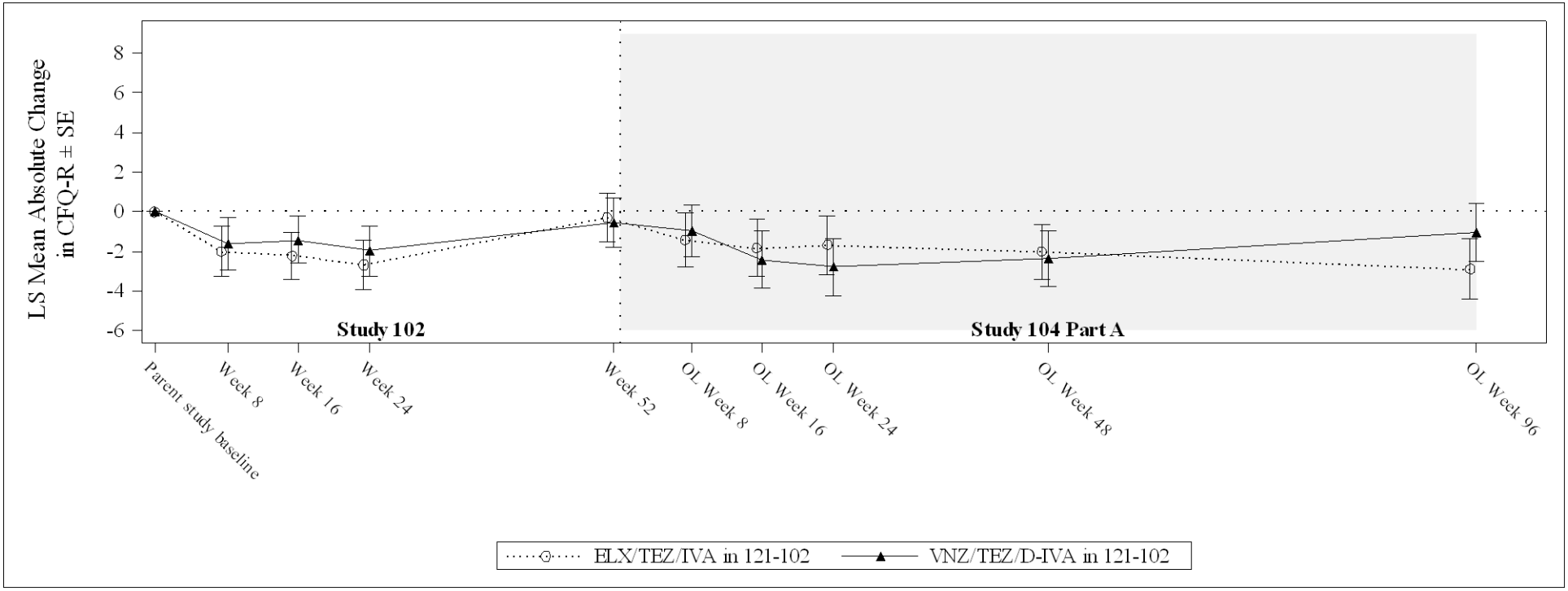
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
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Figure 14.2.6.4.1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

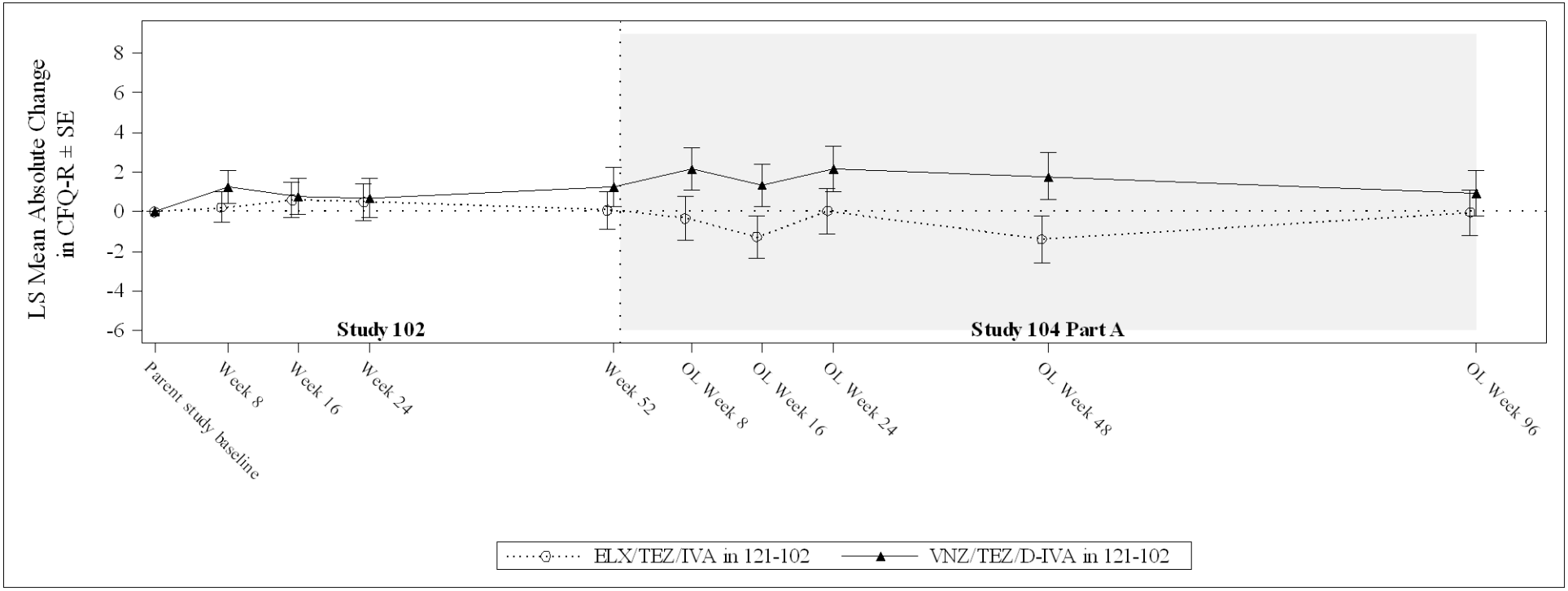
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

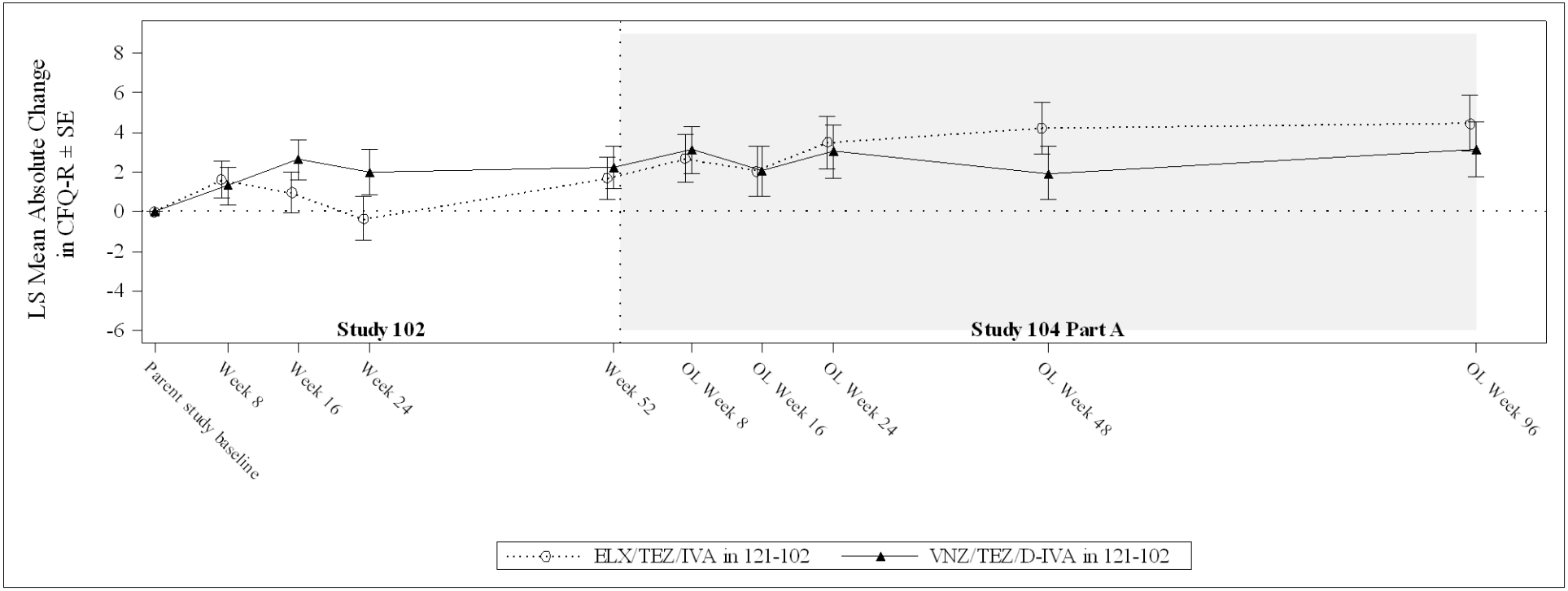
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.1a.ph
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Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

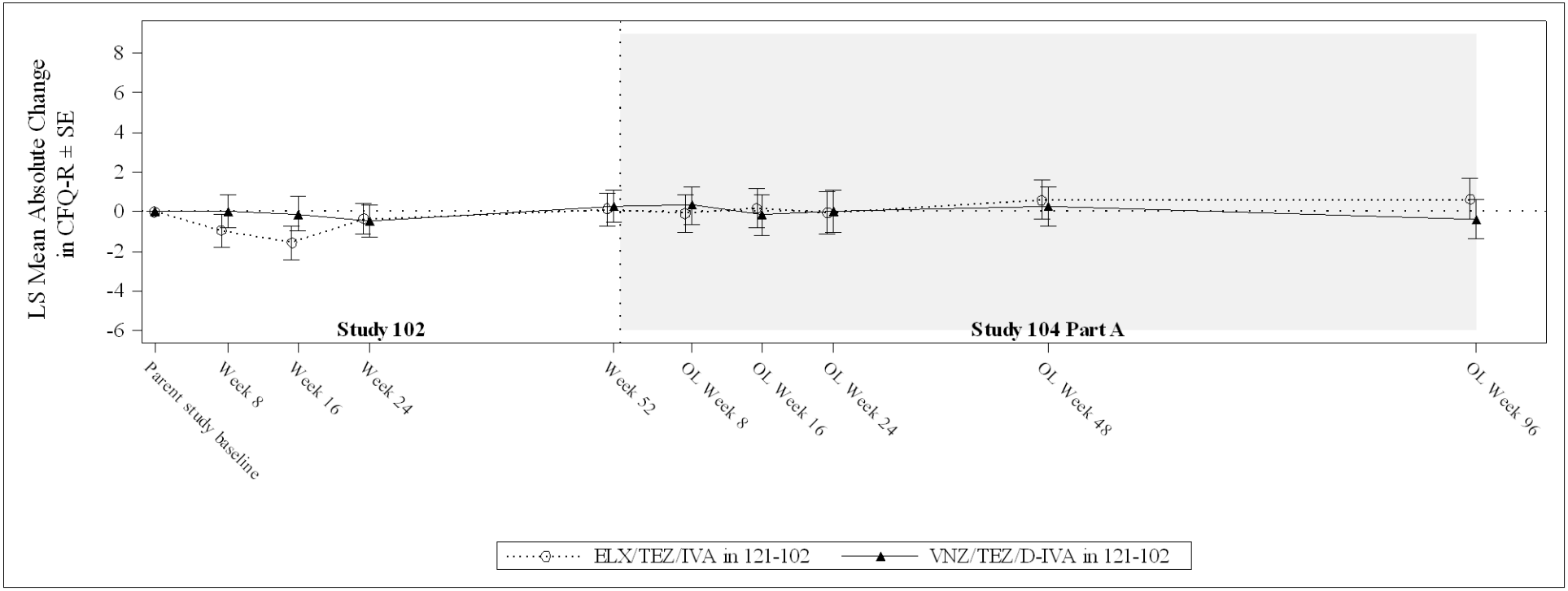
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

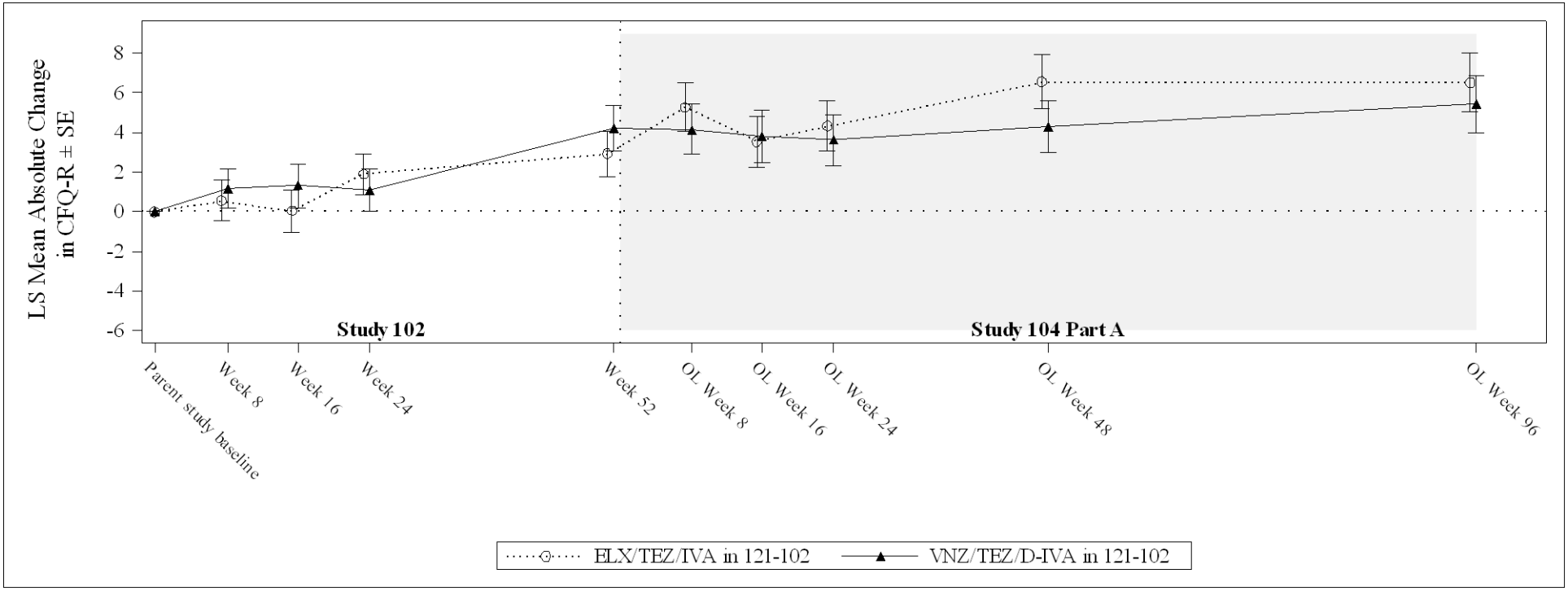
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.1a.ph
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Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

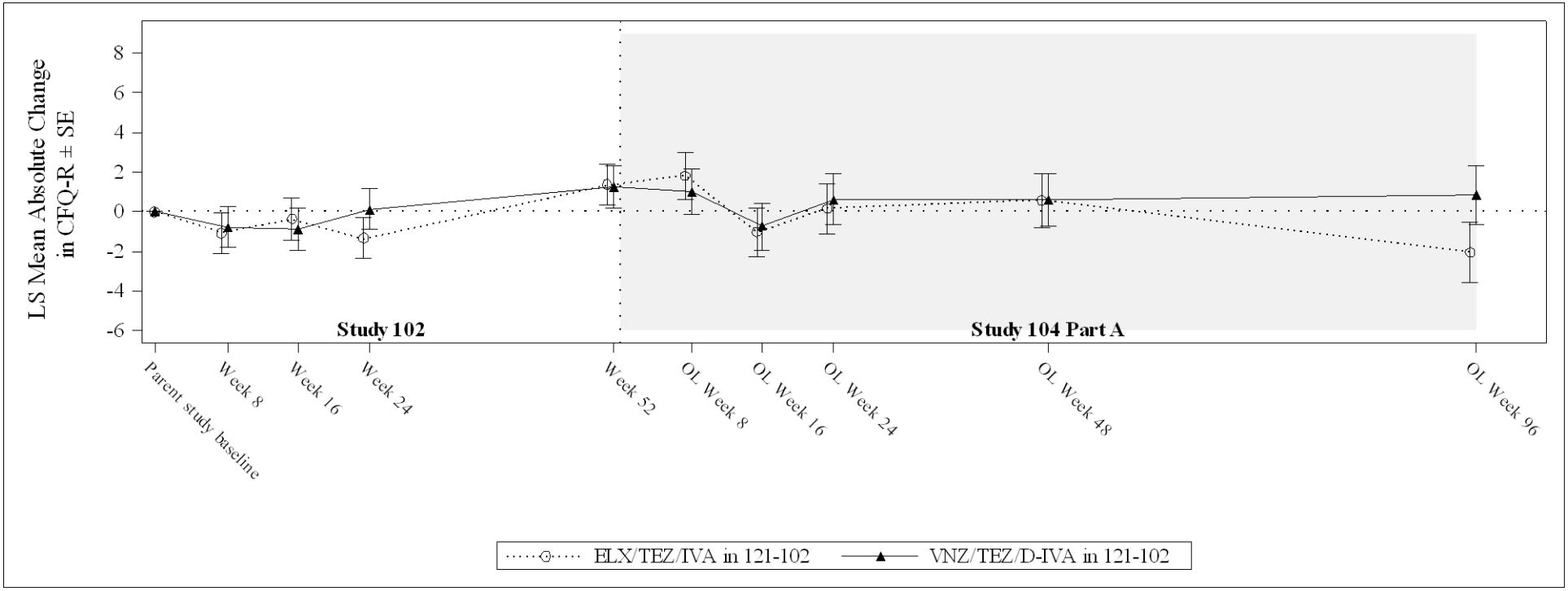
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

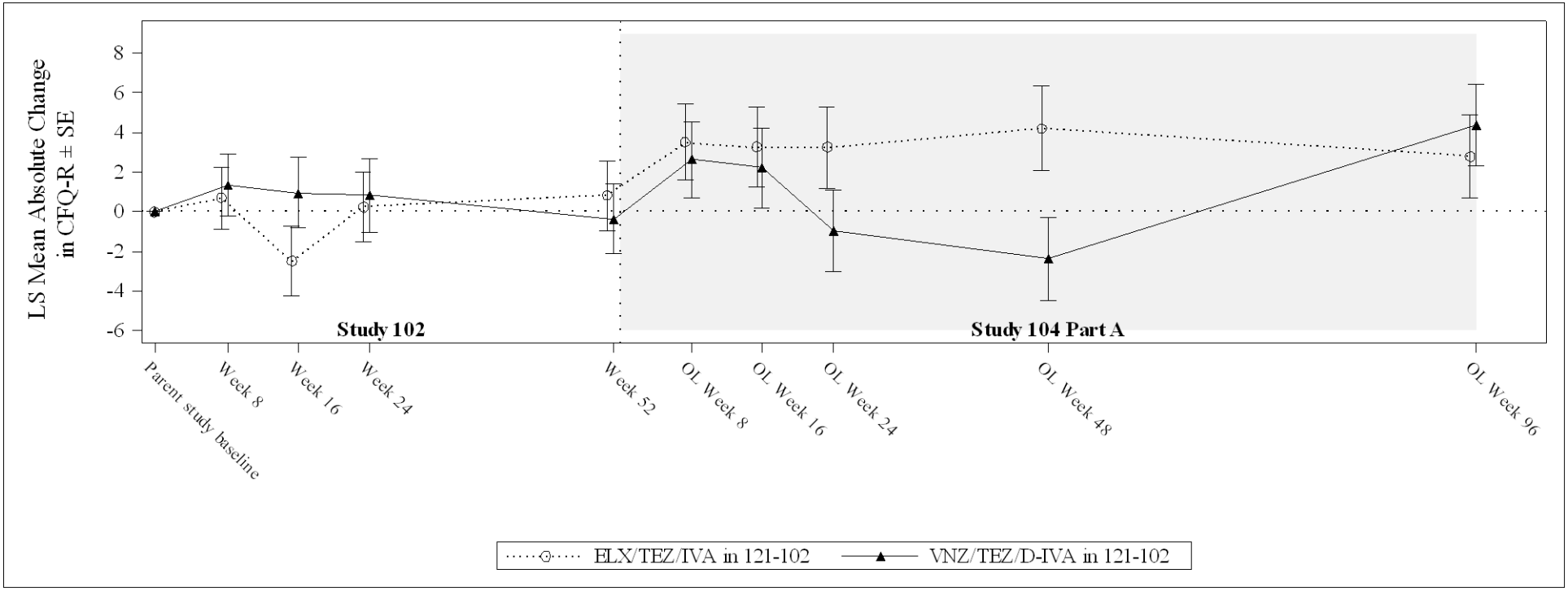
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

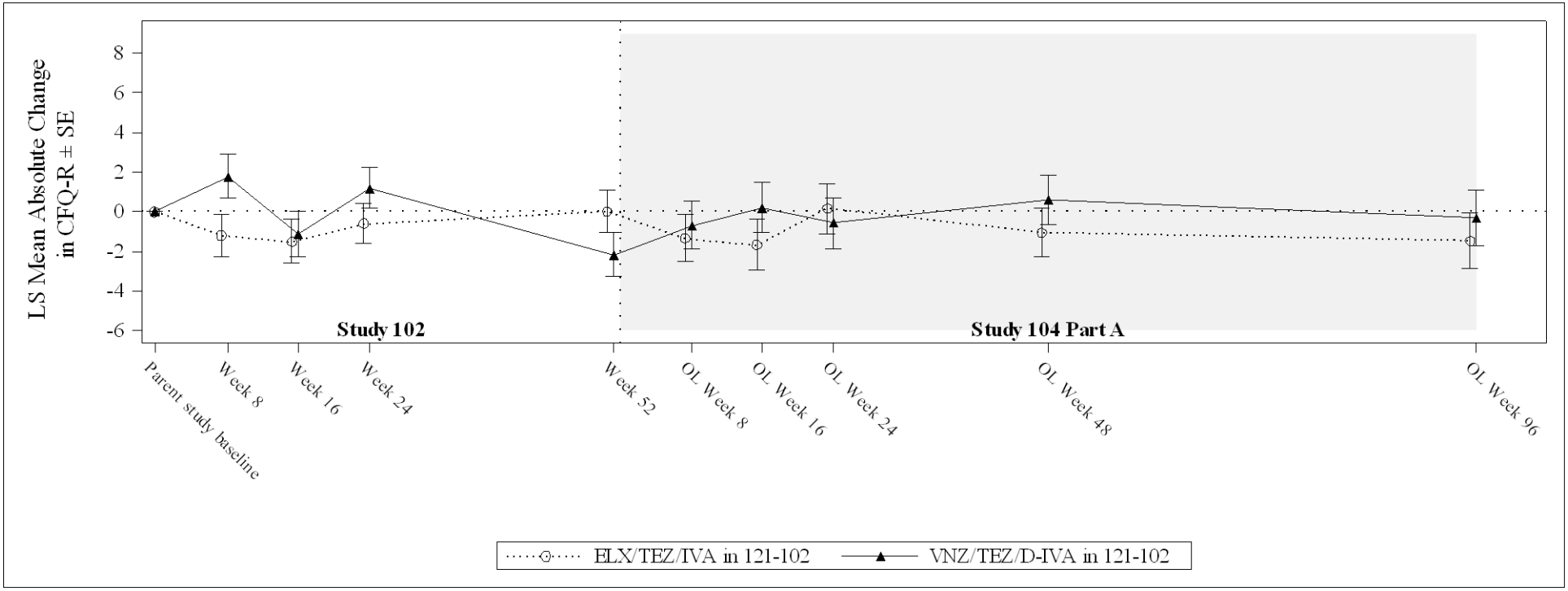
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

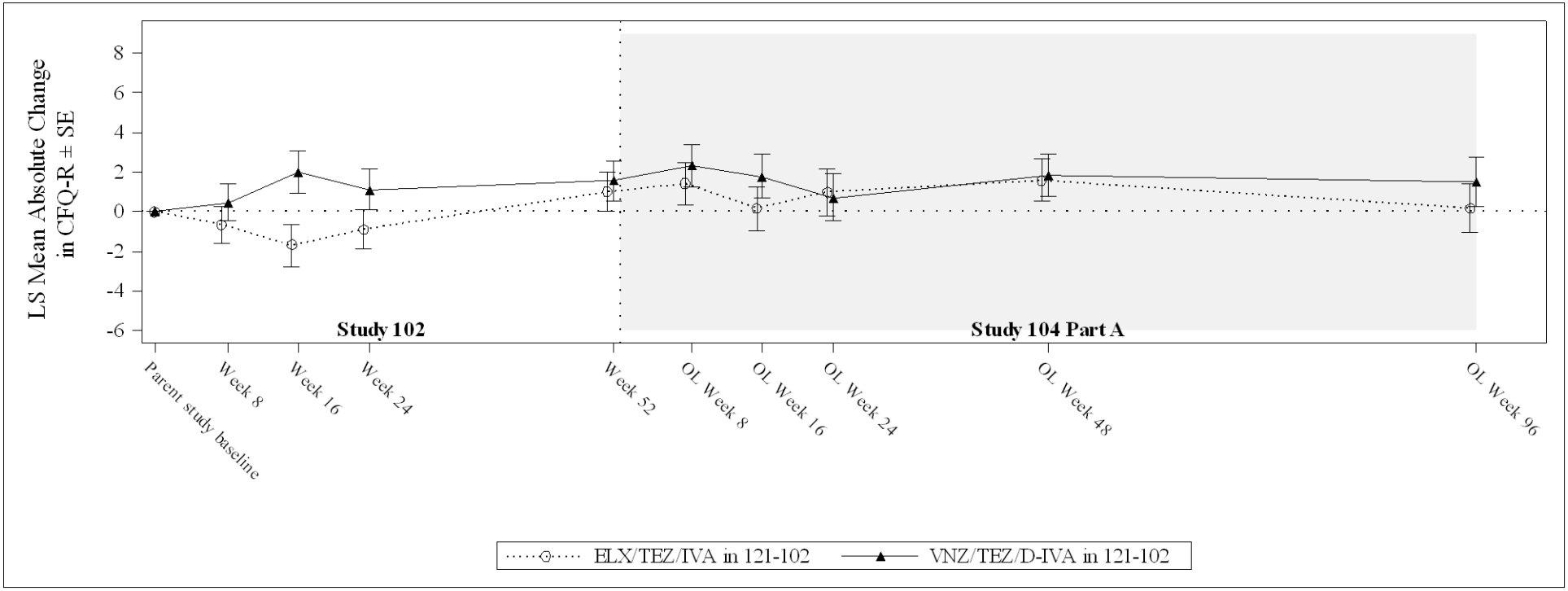
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

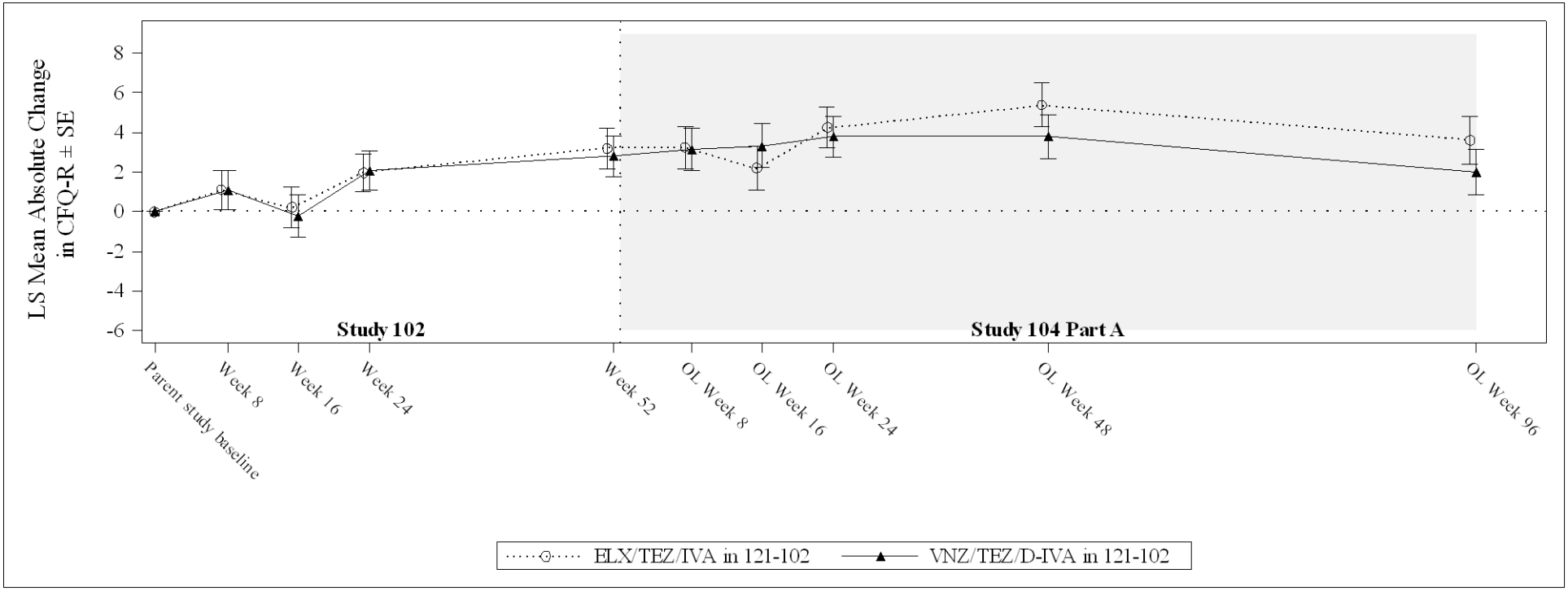
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social

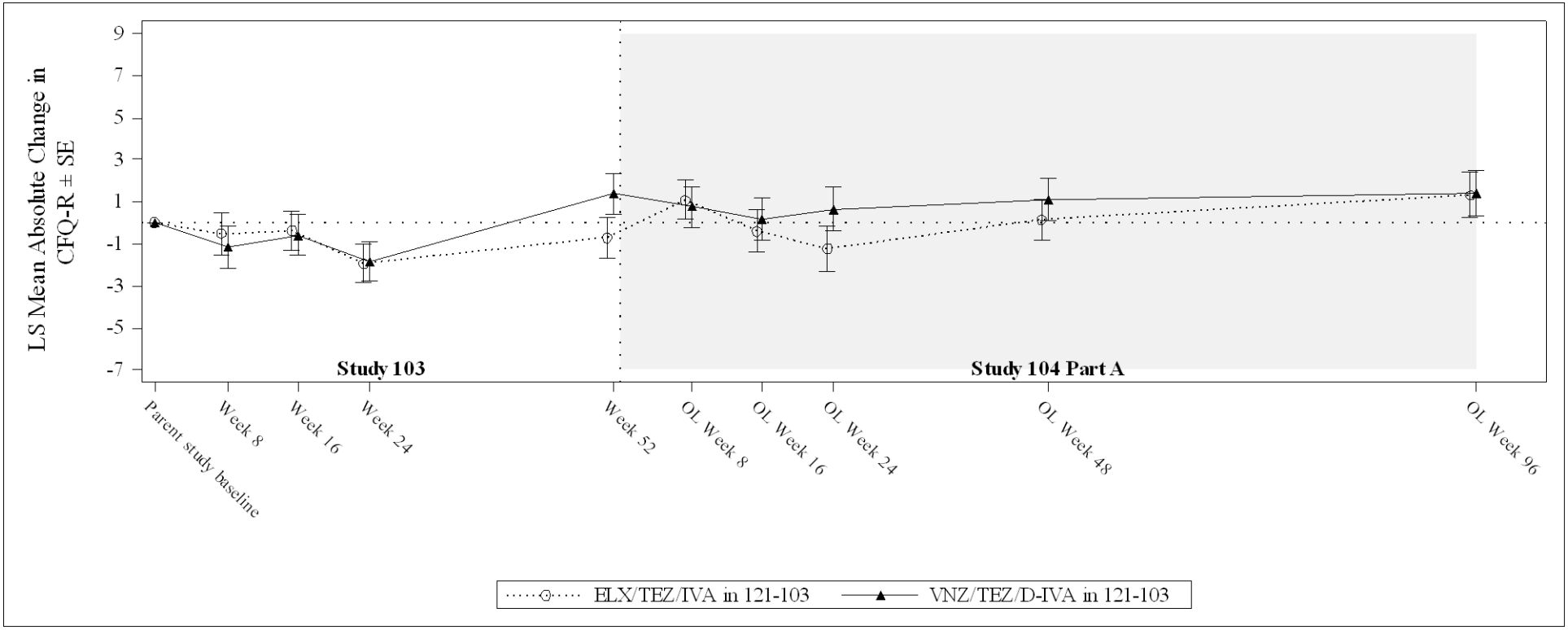


- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX20-121-104

Figure 14.2.6.4.2a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

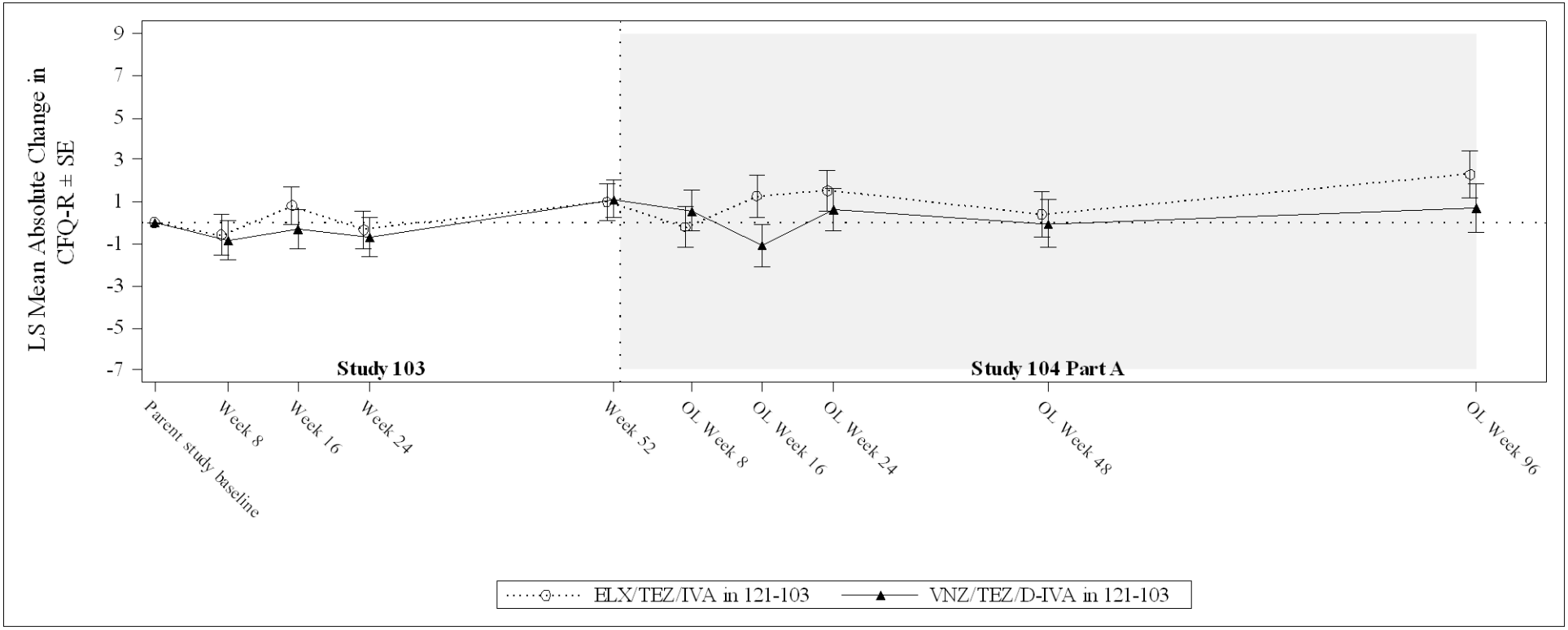
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Respiration



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), genotype group (F/F, F/G, F/RF, TCR/non-F), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.2a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

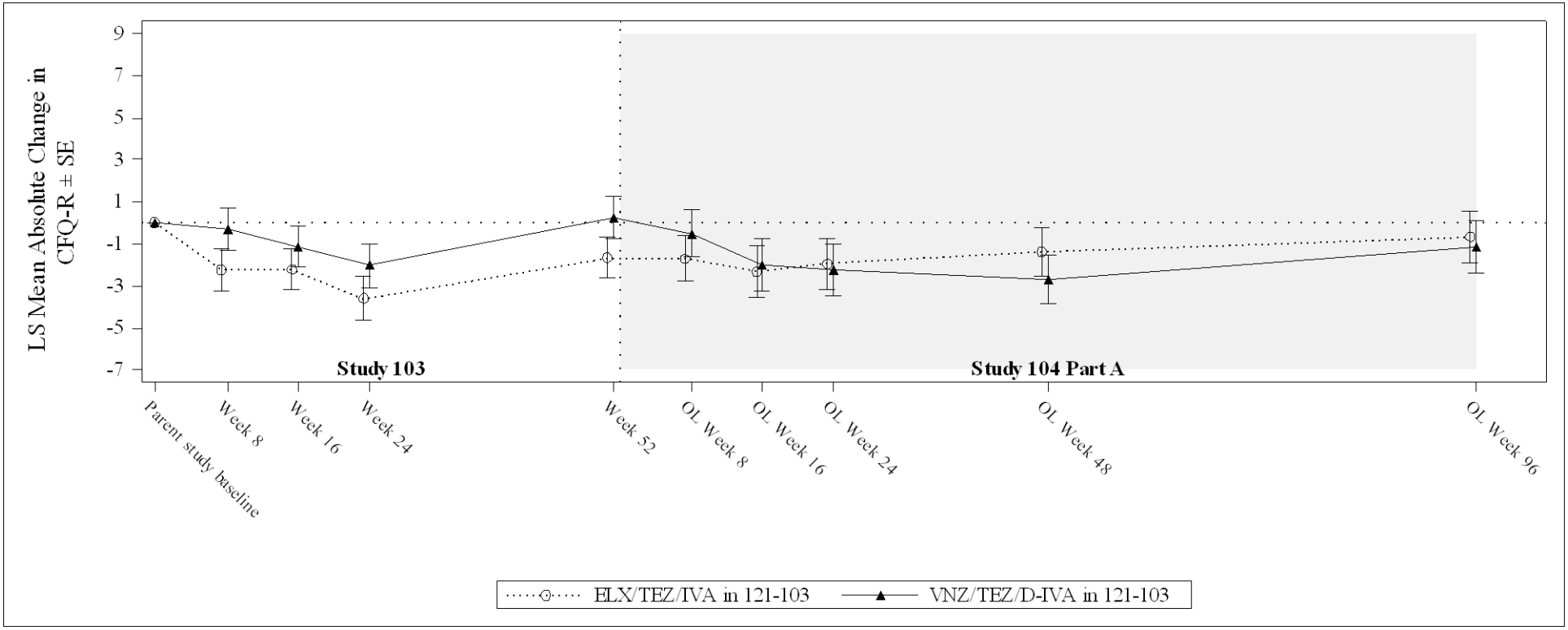
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Physical



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), genotype group (F/F, F/G, F/RF, TCR/non-F), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.2a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

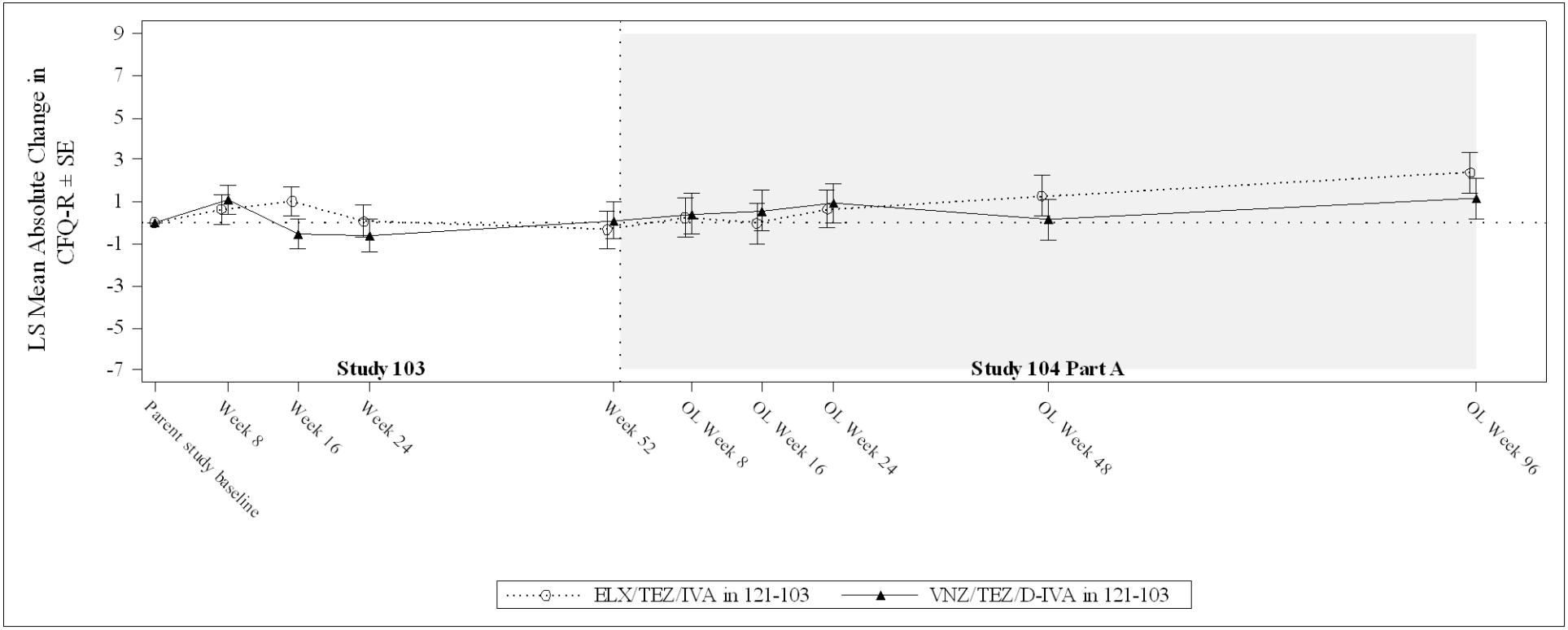
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Vitality



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), genotype group (F/F, F/G, F/RF, TCR/non-F), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.2a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

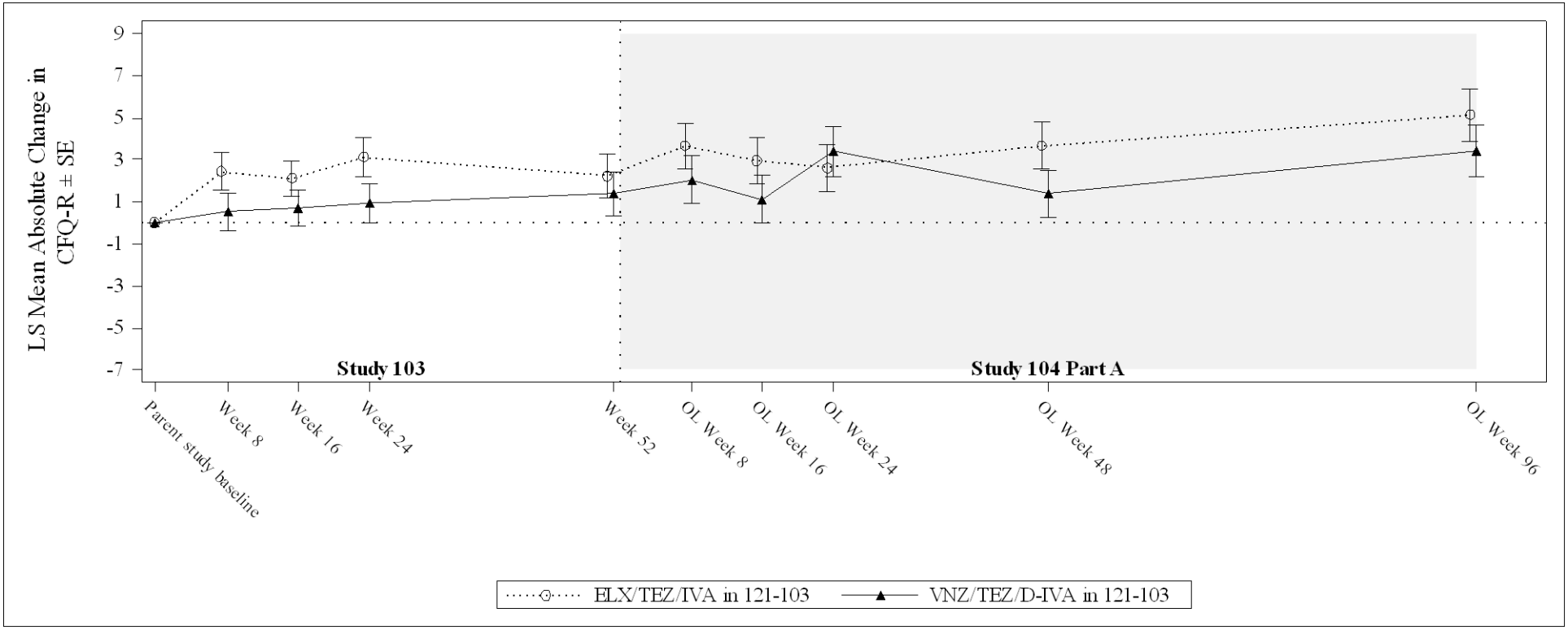
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Emotion



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), genotype group (F/F, F/G, F/RF, TCR/non-F), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.2a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

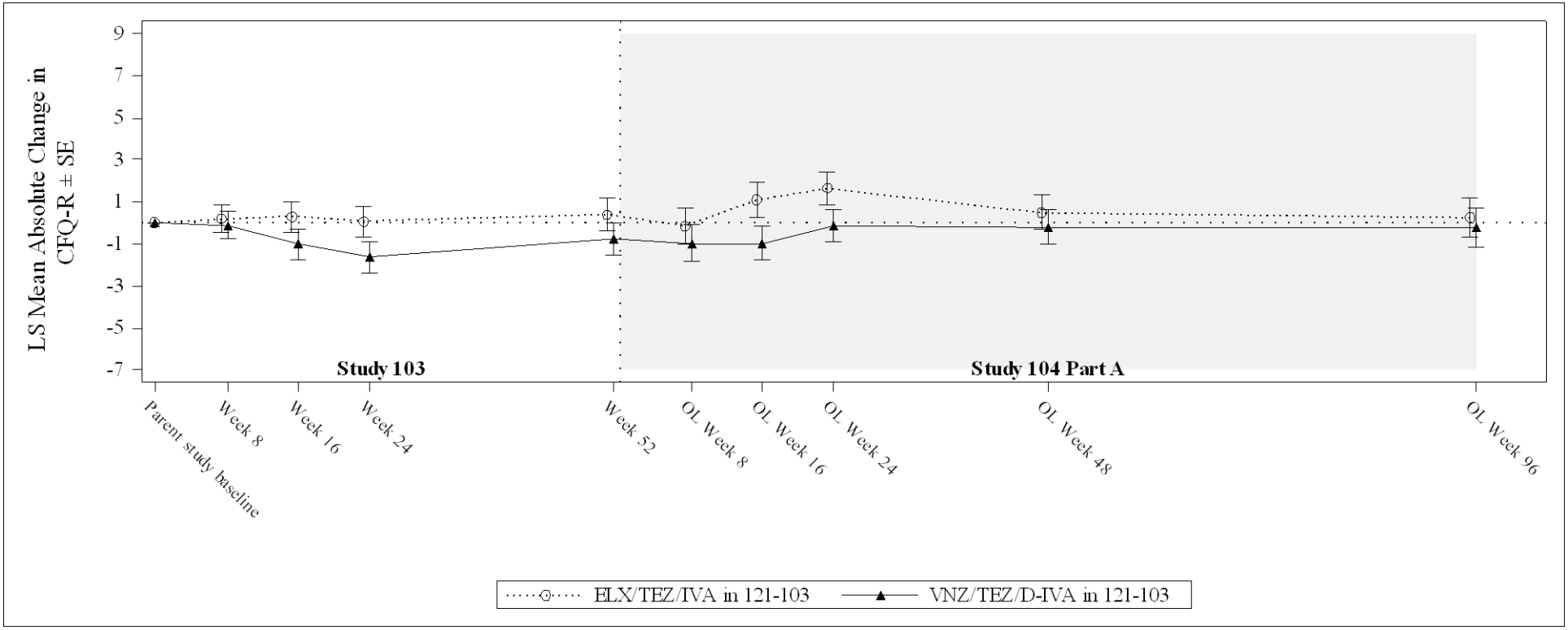
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Body



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), genotype group (F/F, F/G, F/RF, TCR/non-F), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.2a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

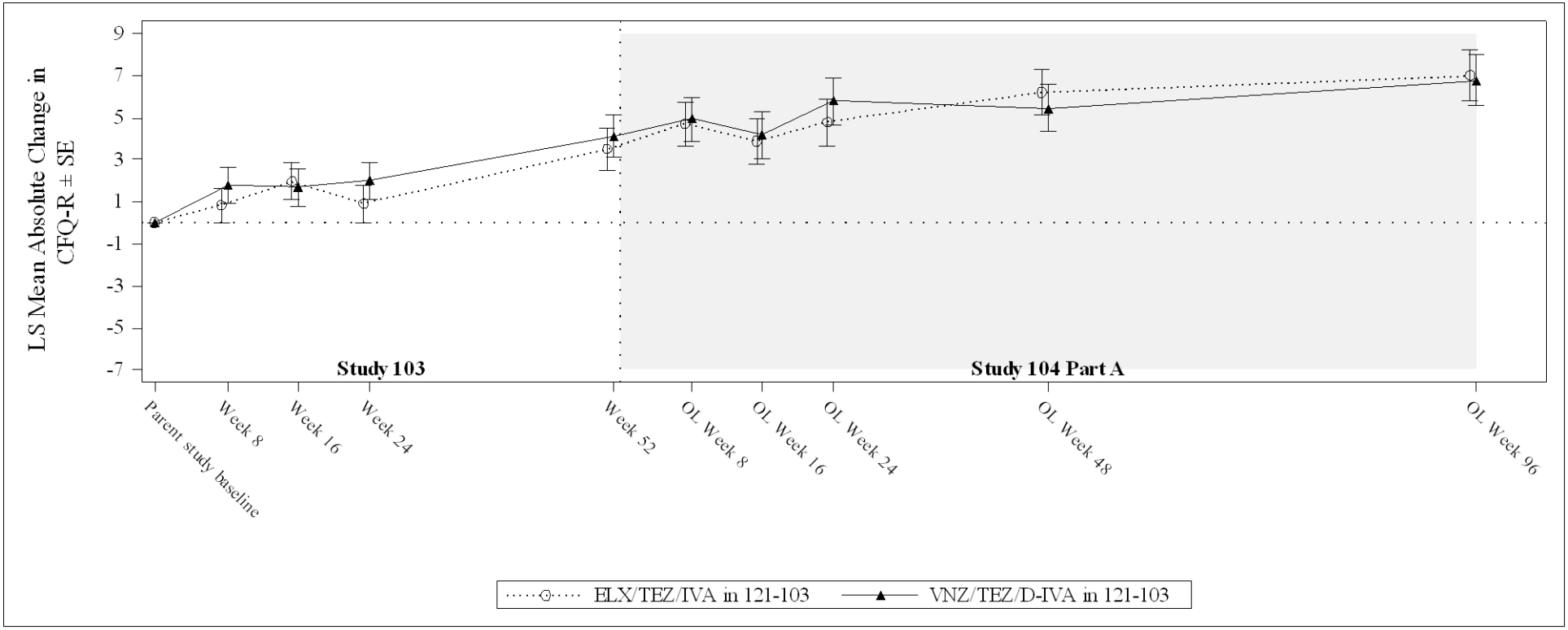
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Eat



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), genotype group (F/F, F/G, F/RF, TCR/non-F), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.2a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

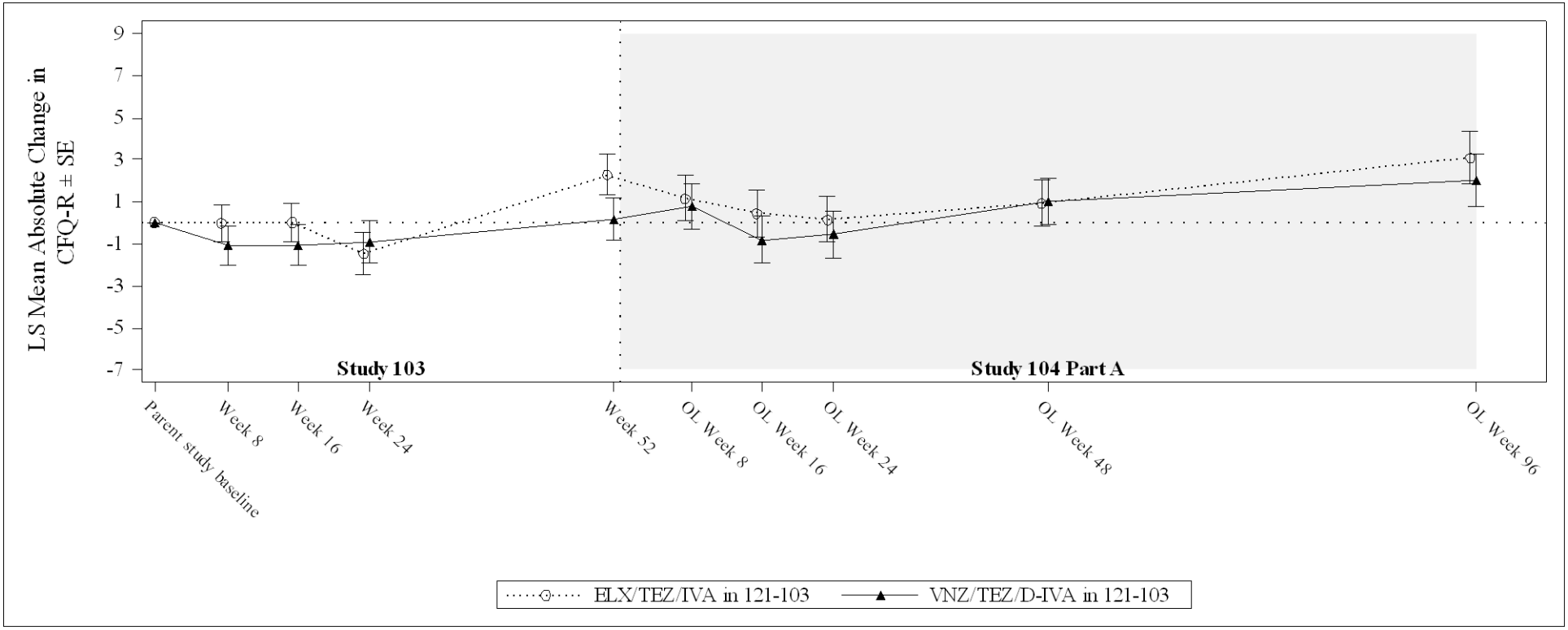
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Treatment Burden



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), genotype group (F/F, F/G, F/RF, TCR/non-F), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.2a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

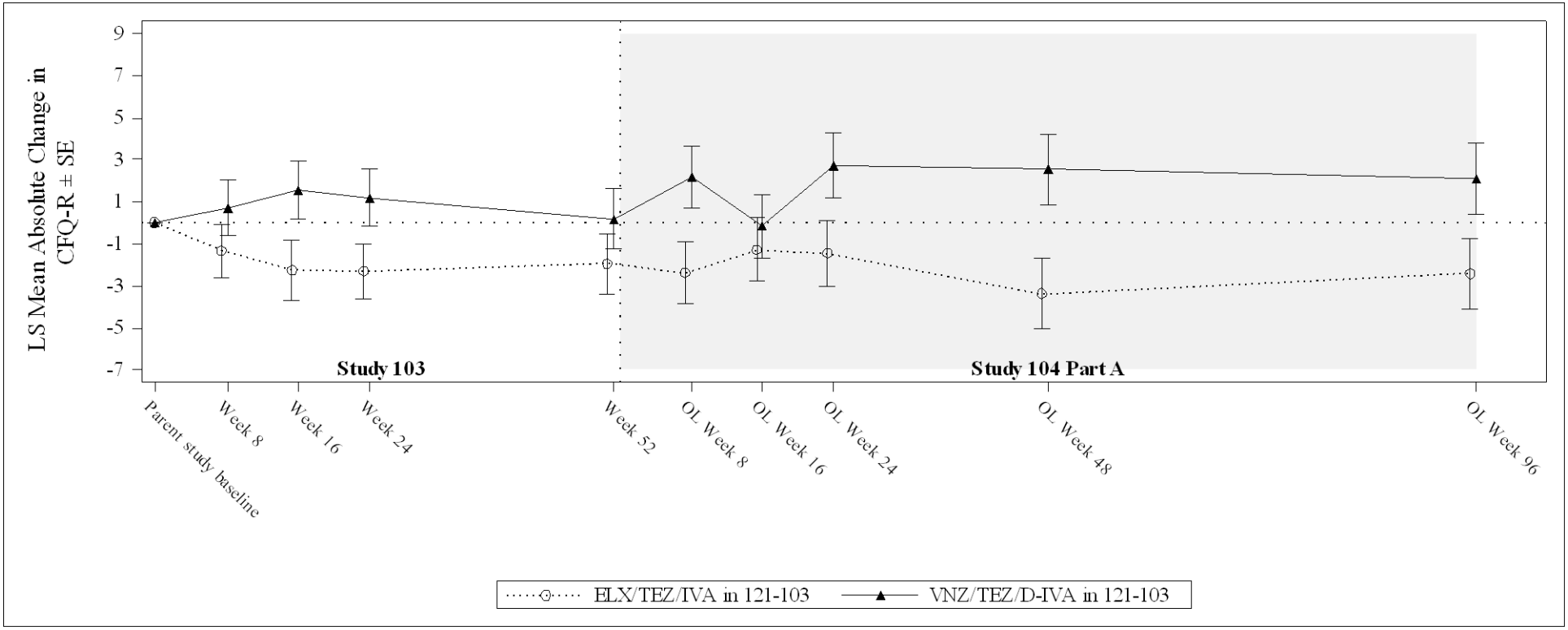
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Health Perceptions



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), genotype group (F/F, F/G, F/RF, TCR/non-F), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.2a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

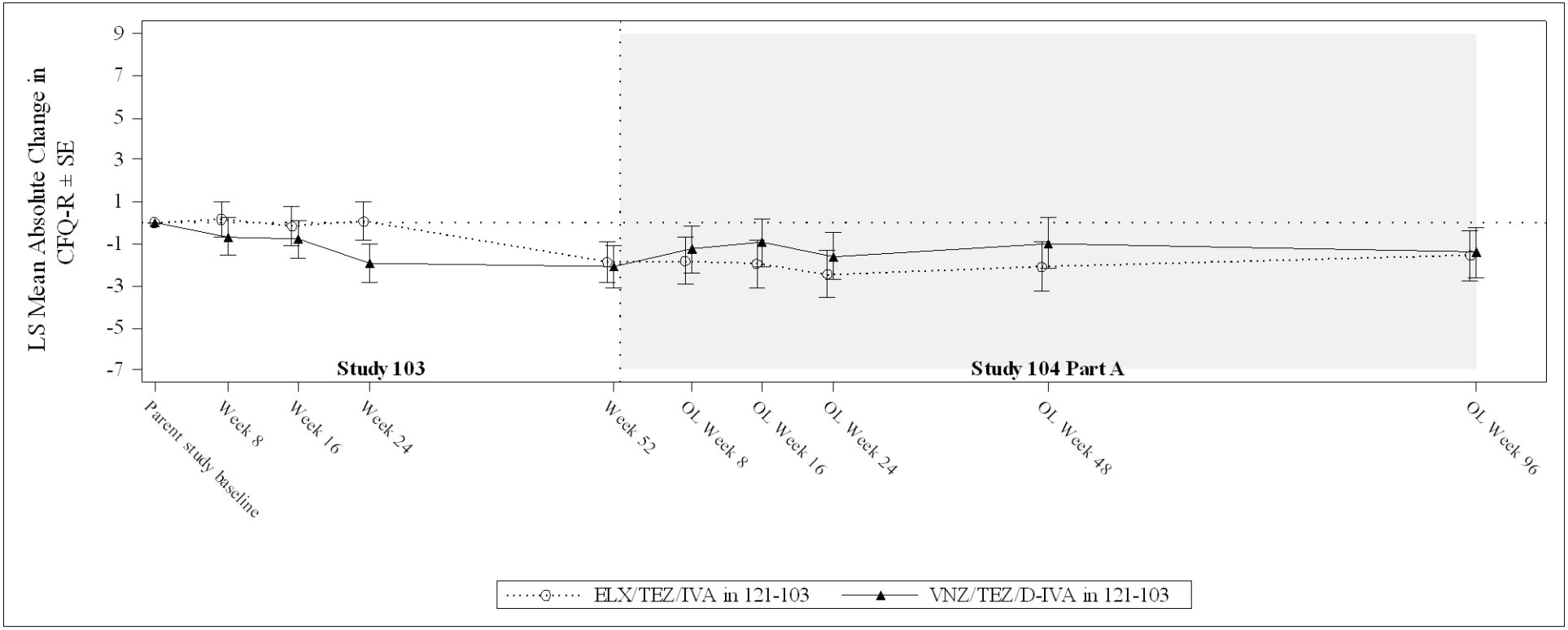
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Weight



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), genotype group (F/F, F/G, F/RF, TCR/non-F), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.2a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

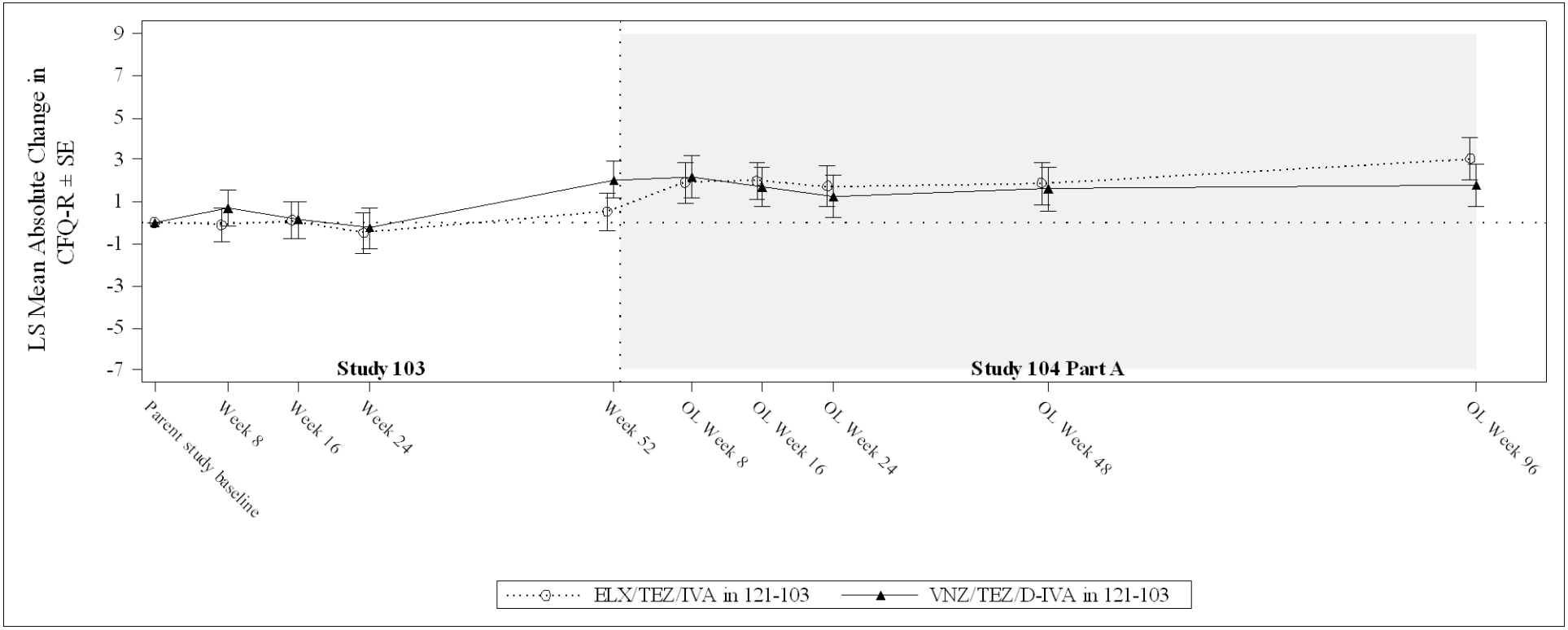
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Digestion



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), genotype group (F/F, F/G, F/RF, TCR/non-F), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.2a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

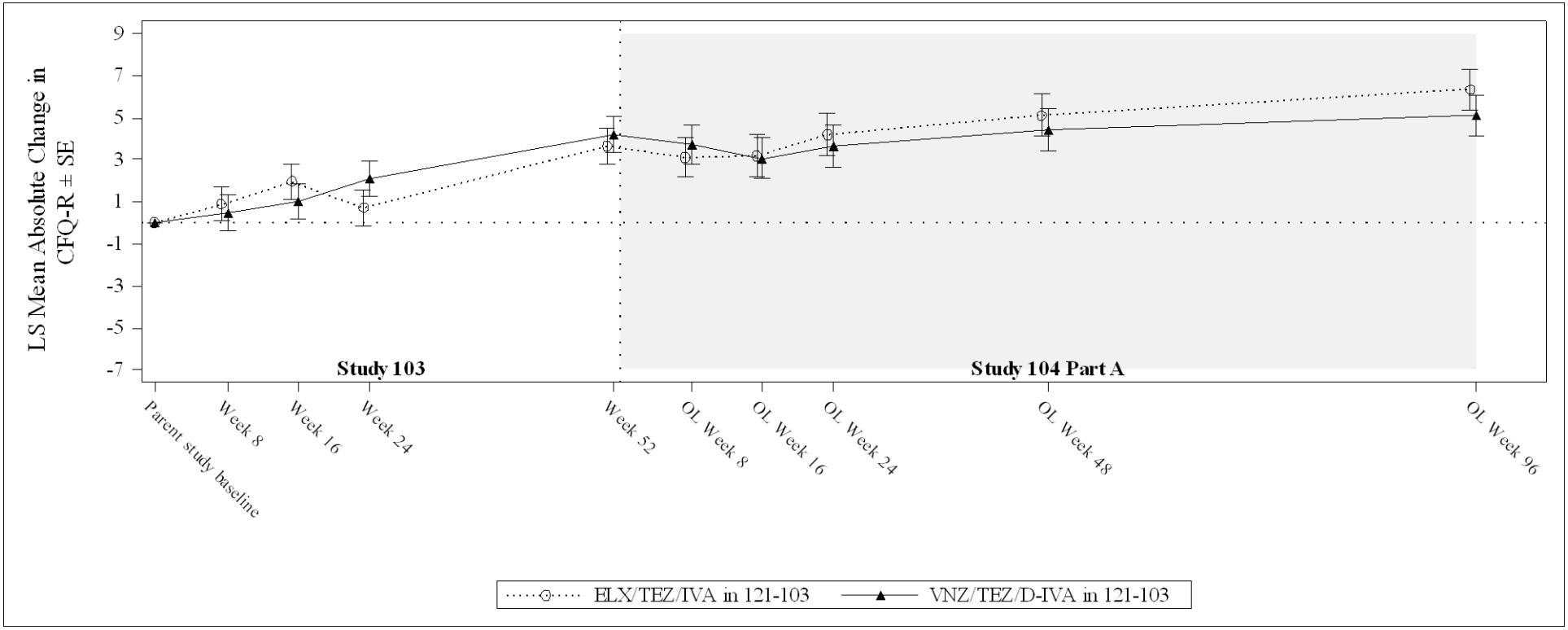
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Role



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), genotype group (F/F, F/G, F/RF, TCR/non-F), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.6.4.2a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

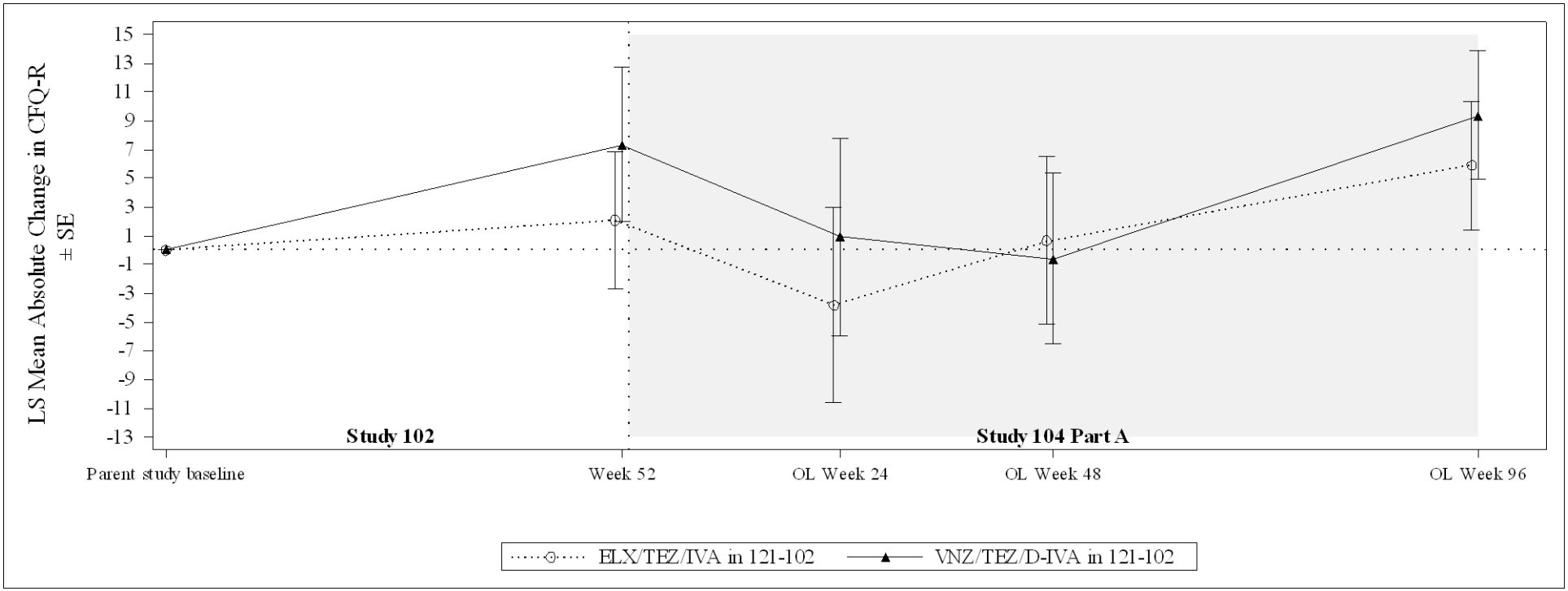
Version: Pooled 'Children Ages 12 and 13' Version and 'Adolescents and Adults' Version
Domain: Social



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, age at screening in the parent study (<18 vs ò18 years), genotype group (F/F, F/G, F/RF, TCR/non-F), and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.7.3a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

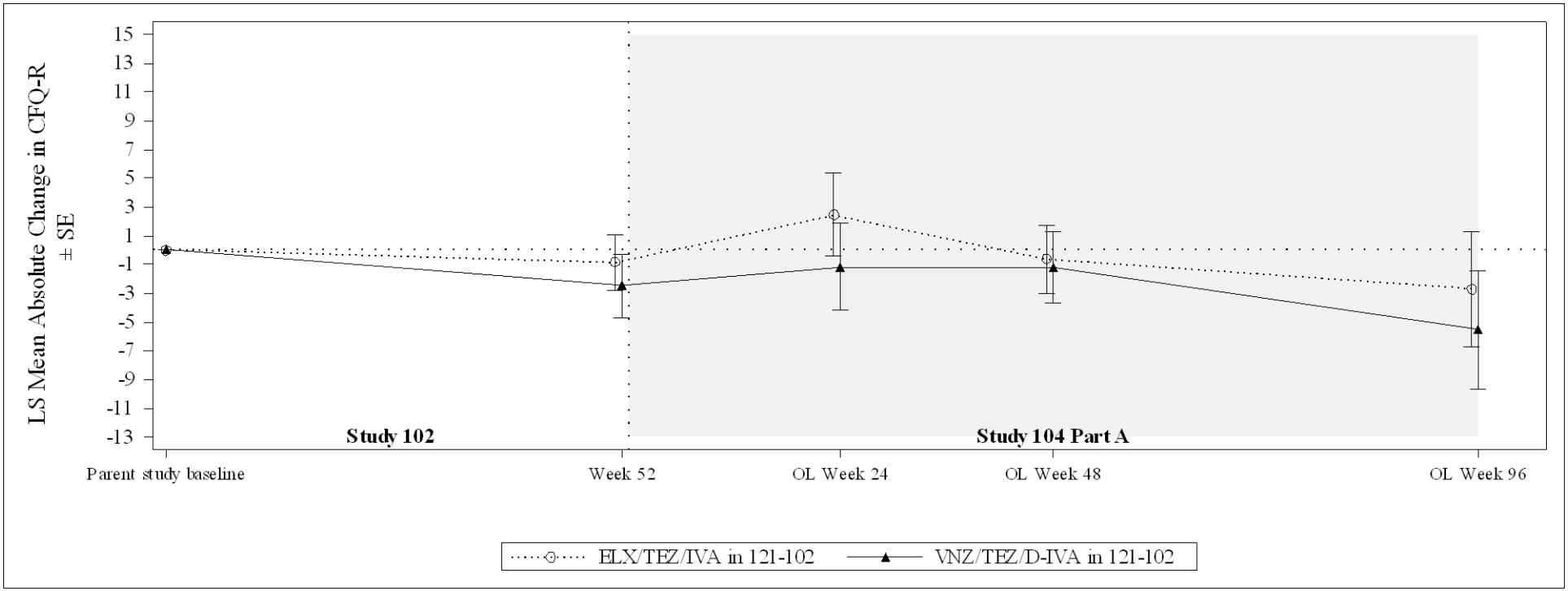
Domain: Effectiveness



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.7.3a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

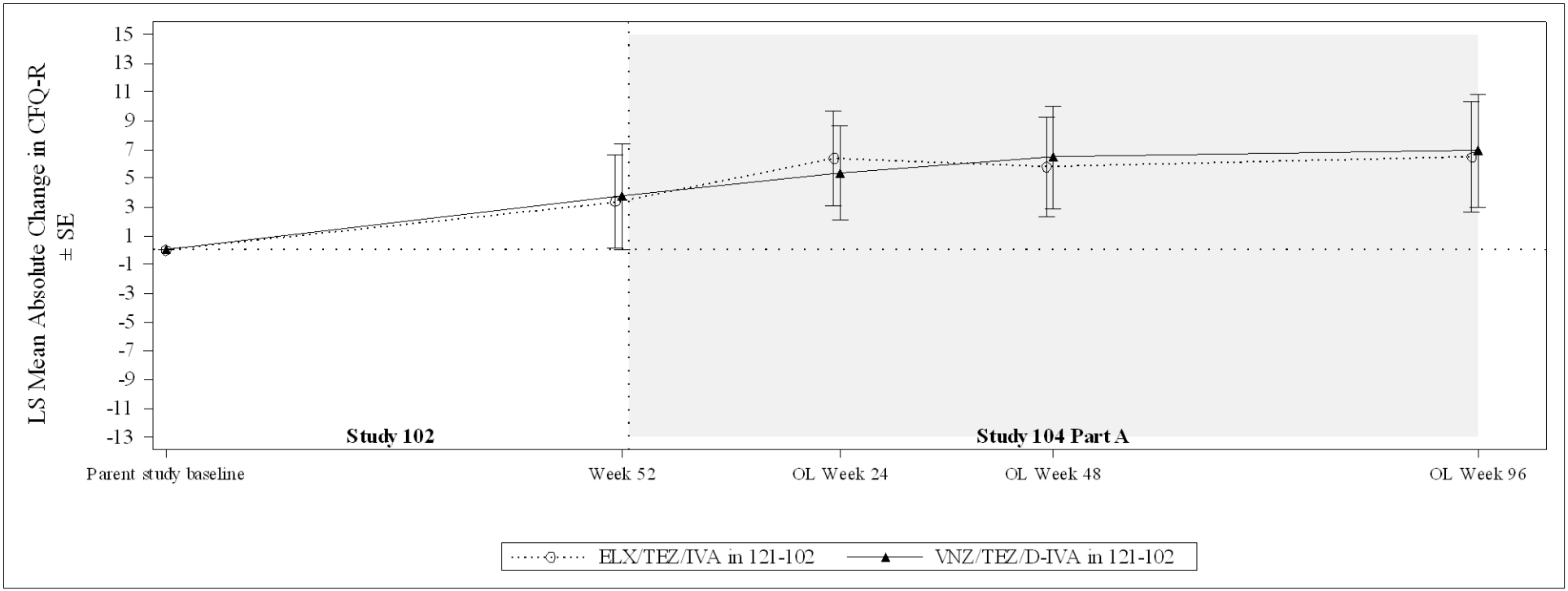
Domain: Side Effects



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.7.3a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

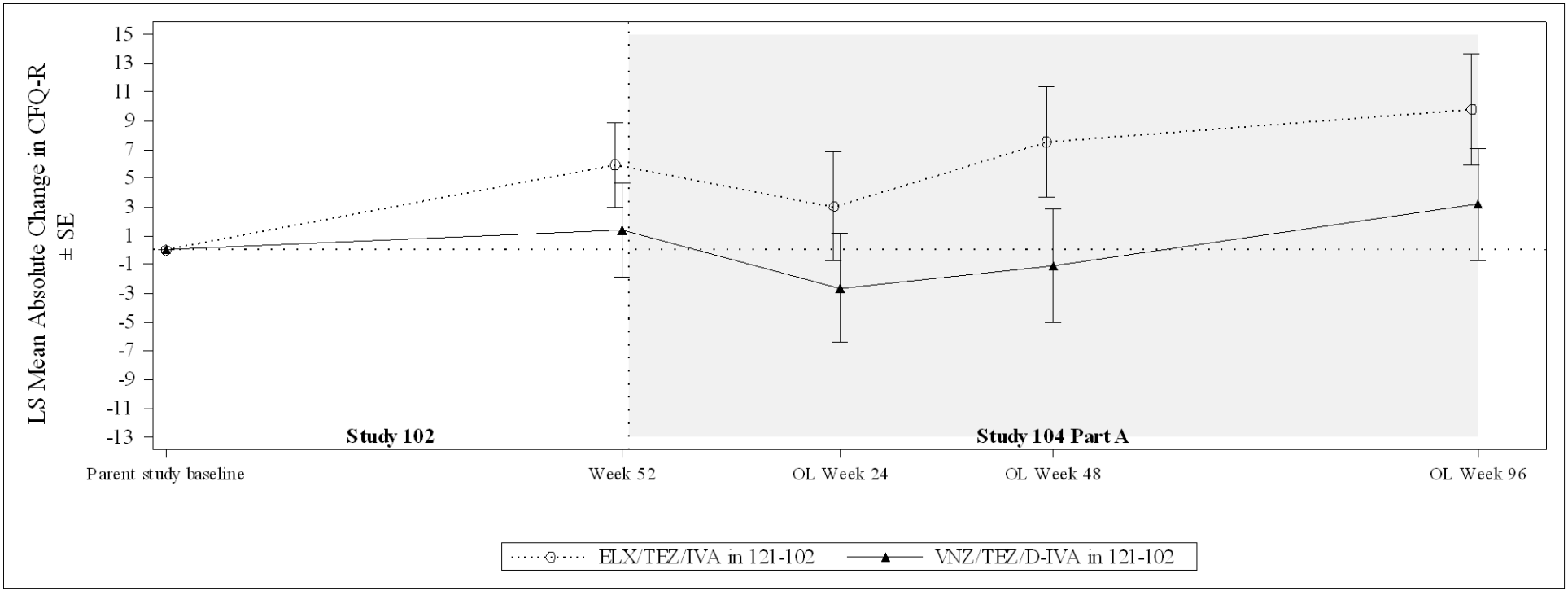
Domain: Convenience



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.7.3a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 102 Full Analysis Set and OL Full Analysis Set - Subjects from Study 102

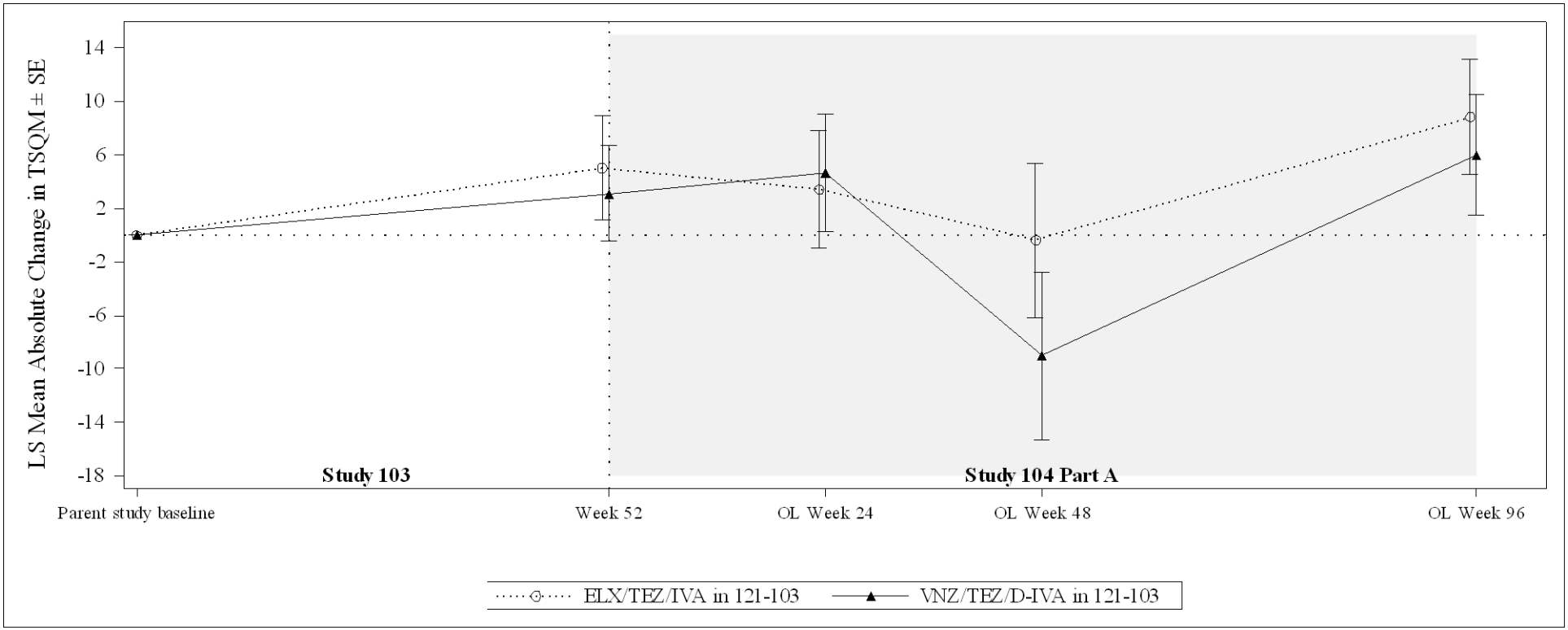
Domain: Global Satisfaction



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 102 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-102. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.7.4a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

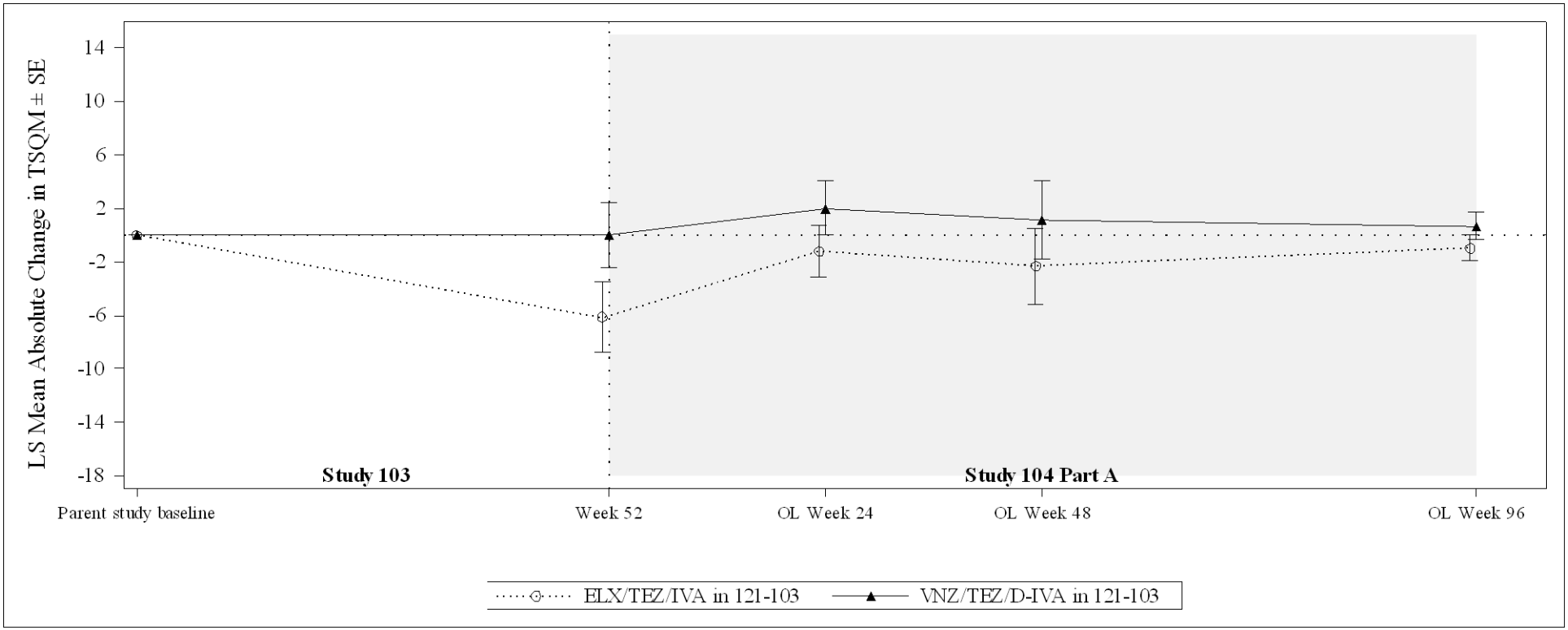
Domain: Effectiveness



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, genotype group (F/F, F/G, F/RF, TCR/non-F), with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.7.4a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

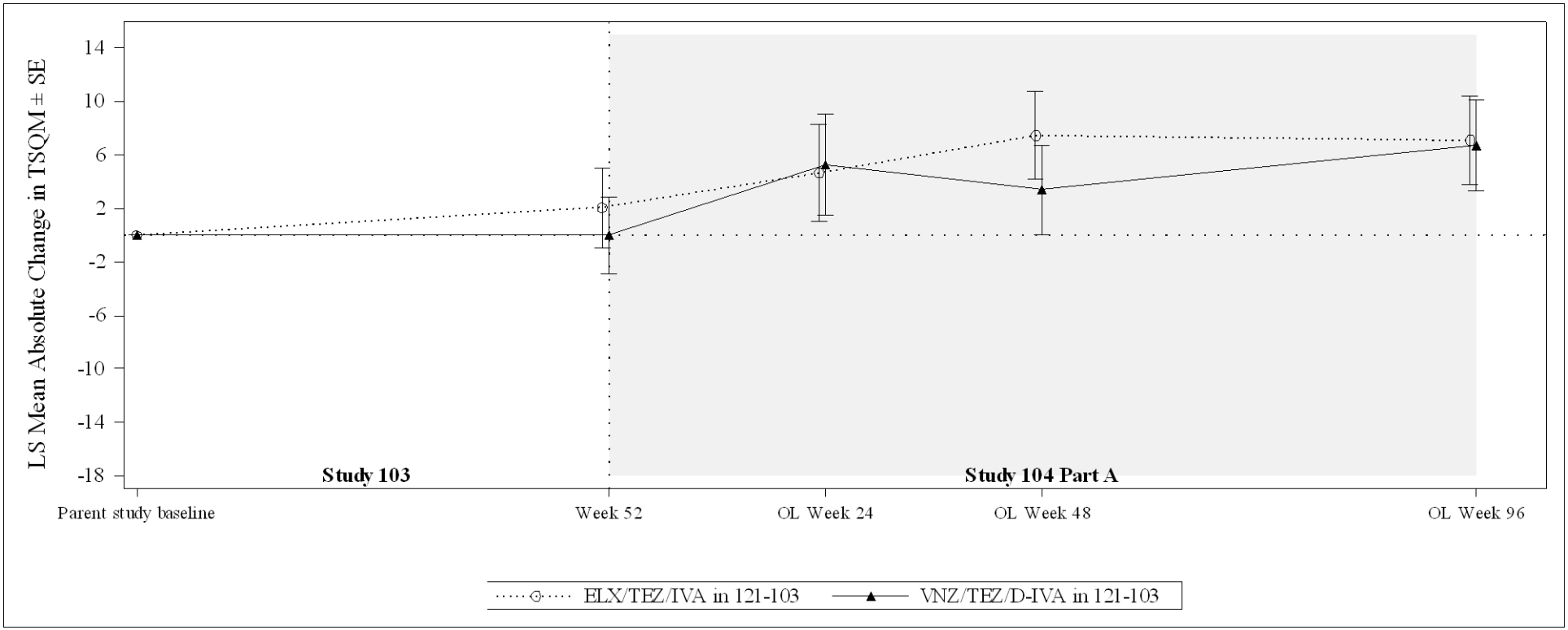
Domain: Side Effects



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, genotype group (F/F, F/G, F/RF, TCR/non-F), with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.7.4a.ph
MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Domain: Convenience

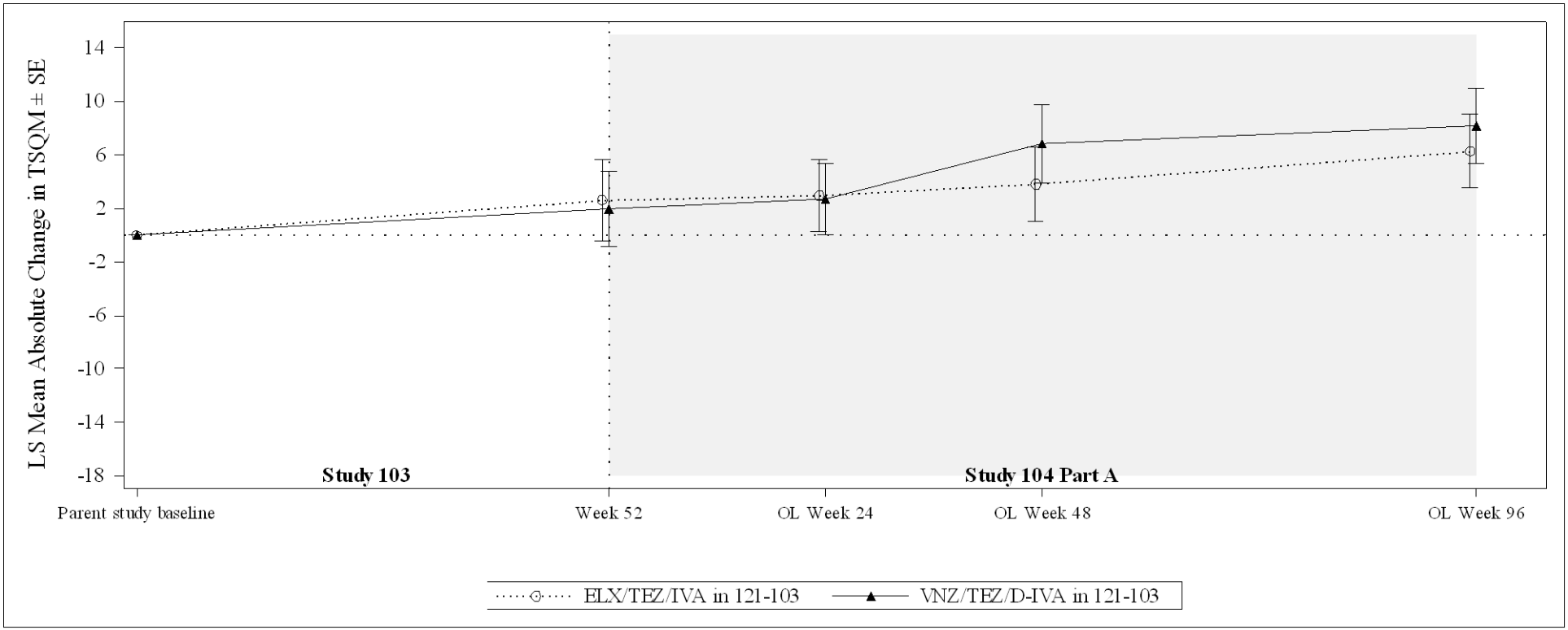


- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, genotype group (F/F, F/G, F/RF, TCR/non-F), with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.7.4a.ph

MMRM Analysis of Absolute Change from Parent Study Baseline in TSQM Domain Score for Subjects Aged ≥ 12 Years to <18 Years at the Date of Informed Consent at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Study 103 Full Analysis Set and OL Full Analysis Set - Subjects from Study 103

Domain: Global Satisfaction



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Study 103 Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits up to OL Part A Week 96 and is based on the OL Full Analysis Set for subjects from parent study 121-103. The model includes fixed categorical effects for treatment (as randomized in the parent study), visit, and treatment-by-visit interaction, genotype group (F/F, F/G, F/RF, TCR/non-F), with parent study baseline ppFEV1 and parent study baseline SwCl as continuous covariates. Covariance structure=UN, DF=Kenward-Roger.

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Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 24
Overall Study Observation Time	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
$ppFEV_1$ (percentage points)	
n	23
Mean (SD)	22.80 (3.31)
Median	24.00
Min, Max	12.29, 25.00
BMI (kg/m^2)	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
BMI z-score	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
Sweat Chloride (mmol/L)	
n	24
Mean (SD)	23.37 (2.24)
Median	24.00
Min, Max	16.14, 25.00

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 1.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint for F/MF
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 24
Weight (kg)	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
Weight z-score	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
Height (cm)	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
Height z-score	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
CFQ-R	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 1.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint for F/MF
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 24
Pulmonary Exacerbation	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00
$LCI_{2.5}$	
n	23
Mean (SD)	21.14 (5.84)
Median	24.00
Min, Max	4.14, 25.00
Safety	
n	24
Mean (SD)	24.05 (0.43)
Median	24.14
Min, Max	23.14, 25.00

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Zusatzanalysen zur Studie VX21-121-105

Table 1.1.2.1
Study VX21-121-105: Summary of Patients with Ongoing Antibiotic Medications at Baseline or at Week 24 for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline, N1	24
Subjects with 0 ongoing AB	17 (70.83)
Subjects with 1 ongoing AB	4 (16.67)
Subjects with ≥ 2 ongoing AB	3 (12.50)
Subjects with ≥ 1 ongoing IV AB	0
Week 24, N1	24
Subjects with 0 ongoing AB	17 (70.83)
Subjects with 1 ongoing AB	5 (20.83)
Subjects with ≥ 2 ongoing AB	2 (8.33)
Subjects with ≥ 1 ongoing IV AB	0

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- The ongoing antibiotic medications at baseline refer to those with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing antibiotic medications at Week 24 refer to those with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX21-121-105

Table 1.1.2.2
Study VX21-121-105: Summary of Patients with Antibiotic Medications during the Study Treatment Period for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
All subjects	24
Subjects with 0 AB	3 (12.50)
Subjects with 1-3 AB	16 (66.67)
Subjects with ≥ 4 AB	5 (20.83)
Subjects with 0 IV AB	22 (91.67)
Subjects with 1 IV AB	0
Subjects with ≥ 2 IV AB	2 (8.33)
Subjects with 0 ongoing antibiotic medication at baseline	17
Subjects with 0 AB	3 (17.65)
Subjects with 1-3 AB	13 (76.47)
Subjects with ≥ 4 AB	1 (5.88)
Subjects with 0 IV AB	16 (94.12)
Subjects with 1 IV AB	0
Subjects with ≥ 2 IV AB	1 (5.88)

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- Antibiotic medications during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX21-121-105

Table 1.1.3.1
Study VX21-121-105: Summary of Patients with Ongoing Physiotherapies at Baseline or at Week 24 for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline, N1	24
Subjects with 0 ongoing PT	9 (37.50)
Subjects with 1 ongoing PT	13 (54.17)
Subjects with ≥ 2 ongoing PT	2 (8.33)
Week 24, N1	24
Subjects with 0 ongoing PT	9 (37.50)
Subjects with 1 ongoing PT	12 (50.00)
Subjects with ≥ 2 ongoing PT	3 (12.50)

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- The ongoing physiotherapy at baseline is defined as a physiotherapy whose start date is prior to first dose date of study drug in the Treatment Period and the end date is ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing physiotherapy at Week 24 is defined as a physiotherapy whose start date is prior to Week 24 visit date and the end date is ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 1.1.3.2
Study VX21-121-105: Summary of Patients with Physiotherapies during the Study Treatment Period for F/MF Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
All subjects	24
Subjects with 0 PT	9 (37.50)
Subjects with 1 PT	12 (50.00)
Subjects with ≥ 2 PT	3 (12.50)
Subjects with 0 ongoing physiotherapies at baseline	9
Subjects with 0 PT	9 (100.00)
Subjects with 1 PT	0
Subjects with ≥ 2 PT	0

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- Physiotherapies during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX21-121-105

Table 1.1.4.1
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications at Baseline or at Week 24 for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline, N1	24
Subjects with 0 ongoing IM	2 (8.33)
Subjects with 1 ongoing IM	0
Subjects with ≥ 2 ongoing IM	22 (91.67)
Week 24, N1	24
Subjects with 0 ongoing IM	2 (8.33)
Subjects with 1 ongoing IM	0
Subjects with ≥ 2 ongoing IM	22 (91.67)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX21-121-105

Table 1.1.4.2
Study VX21-121-105: Summary of Patients with Inhaled Medications during the Study Treatment Period for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
All subjects	24
Subjects with 0 IM	1 (4.17)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	23 (95.83)
Subjects with 0 ongoing inhaled medication at baseline	2
Subjects with 0 IM	1 (50.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	1 (50.00)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

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Table 1.1.4.3
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications for Mucolytics at Baseline or at Week 24 for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline, N1	24
Subjects with 0 ongoing IM	2 (8.33)
Subjects with 1 ongoing IM	7 (29.17)
Subjects with ≥ 2 ongoing IM	15 (62.50)
Week 24, N1	24
Subjects with 0 ongoing IM	2 (8.33)
Subjects with 1 ongoing IM	7 (29.17)
Subjects with ≥ 2 ongoing IM	15 (62.50)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 1.1.4.4
Study VX21-121-105: Summary of Patients with Inhaled Medications for Mucolytics during the Study Treatment Period for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
All subjects	24
Subjects with 0 IM	2 (8.33)
Subjects with 1 IM	7 (29.17)
Subjects with ≥ 2 IM	15 (62.50)
Subjects with 0 ongoing inhaled medication at baseline	2
Subjects with 0 IM	2 (100.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	0

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 1.1.4.5
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications for Obstructive Airway Disease at Baseline or at Week 24 for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline, N1	24
Subjects with 0 ongoing IM	5 (20.83)
Subjects with 1 ongoing IM	11 (45.83)
Subjects with ≥ 2 ongoing IM	8 (33.33)
Week 24, N1	24
Subjects with 0 ongoing IM	5 (20.83)
Subjects with 1 ongoing IM	12 (50.00)
Subjects with ≥ 2 ongoing IM	7 (29.17)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

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Table 1.1.4.6
Study VX21-121-105: Summary of Patients with Inhaled Medications for Obstructive Airway Disease during the Study Treatment Period for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
All subjects	24
Subjects with 0 IM	4 (16.67)
Subjects with 1 IM	11 (45.83)
Subjects with ≥ 2 IM	9 (37.50)
Subjects with 0 ongoing inhaled medication at baseline	5
Subjects with 0 IM	4 (80.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	1 (20.00)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing..
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX21-121-105

Table 1.1.5.1
Study VX21-121-105: Summary of Patients with Ongoing CF-related Medications at Baseline or at Week 24 for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline, N1	24
Subjects with 0 ongoing CF-related medications	0
Subjects with 1 ongoing CF-related medications	1 (4.17)
Subjects with 2 ongoing CF-related medications	0
Subjects with 3 ongoing CF-related medications	3 (12.50)
Subjects with 4 ongoing CF-related medications	4 (16.67)
Subjects with ≥5 ongoing CF-related medications	16 (66.67)
Week 24, N1	24
Subjects with 0 ongoing CF-related medications	0
Subjects with 1 ongoing CF-related medications	1 (4.17)
Subjects with 2 ongoing CF-related medications	0
Subjects with 3 ongoing CF-related medications	3 (12.50)
Subjects with 4 ongoing CF-related medications	3 (12.50)
Subjects with ≥5 ongoing CF-related medications	17 (70.83)

- CF-related medications: CF co-medications are defined as those medications with
o ATC level 2 names of "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES", "DIGESTIVES, INCL. ENZYMES", "ANTIBACTERIALS FOR SYSTEMIC USE", "DRUGS USED IN DIABETES", "BILE AND LIVER THERAPY", "GENERAL NUTRIENTS";
o or ATC level 3 names of "DRUGS FOR CONSTIPATION", "PROPULSIVES";
o or ATC level 4 names of "MUCOLYTICS".
In addition, the route of administration for "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES" and "MUCOLYTICS" requires to be "RESPIRATORY (INHALATION)" and the route for "ANTIBACTERIALS FOR SYSTEMIC USE" requires to be "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- The ongoing CF-related medications at baseline refer to those CF-related medications with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing CF-related medications at Week 24 refer to those CF-related medications with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 1.2.1.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	94.25 (21.29)
Week 24	
n	20
Mean (SD)	97.22 (17.68)
Absolute Change at Week 24	
n	20
Mean (SD)	0.38 (7.11)
Absolute Change through Week 24 (MMRM)	
n	22
LS mean (SE)	2.48 (2.11)
95% CI of LS mean	(-2.03, 6.98)
P-value	0.2585

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 1.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	16.96 (2.15)
Week 24	
n	24
Mean (SD)	17.12 (2.41)
Absolute Change at Week 24	
n	24
Mean (SD)	0.15 (0.63)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	0.15 (0.13)
95% CI of LS mean	(-0.11, 0.42)
P-value	0.2440

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 1.2.1.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	0.08 (0.93)
Week 24	
n	24
Mean (SD)	-0.01 (1.04)
Absolute Change at Week 24	
n	24
Mean (SD)	-0.09 (0.32)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-0.09 (0.06)
95% CI of LS mean	(-0.22, 0.05)
P-value	0.1882

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 1.2.1.4.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	52.59 (18.88)
Week 24	
n	22
Mean (SD)	42.20 (15.76)
Absolute Change at Week 24	
n	22
Mean (SD)	-11.55 (10.36)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	-10.54 (2.06)
95% CI of LS mean	(-14.82, -6.26)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.4.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Non-missing value at Week 24, N1	22
Number of subjects with missing value at Week 24	2
SwCl <60 mmol/L at Week 24, n (%)	18 (75.00)
95% CI for the proportion	(53.29, 90.23)

- N1: number of subjects with non-missing SwCl at Week 24
- n: number of subjects with SwCl <60 mmol/L
- 95% CI is based on the Clopper-Pearson method

Table 1.2.1.4.3
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Non-missing value at Week 24, N1	22
Number of subjects with missing value at Week 24	2
SwCl <30 mmol/L at Week 24, n (%)	5 (20.83)
95% CI for the proportion	(7.13, 42.15)

- N1: number of subjects with non-missing SwCl at Week 24
- n: number of subjects with SwCl <30 mmol/L
- 95% CI is based on the Clopper-Pearson method

Zusatzanalysen zur Studie VX21-121-105

Table 1.2.1.5
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	30.73 (5.58)
Week 24	
n	24
Mean (SD)	32.34 (6.19)
Absolute Change at Week 24	
n	24
Mean (SD)	1.61 (1.30)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	1.61 (0.27)
95% CI of LS mean	(1.05, 2.17)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.1.6
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	0.00 (0.87)
Week 24	
n	24
Mean (SD)	-0.04 (0.96)
Absolute Change at Week 24	
n	24
Mean (SD)	-0.04 (0.22)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-0.04 (0.04)
95% CI of LS mean	(-0.13, 0.06)
P-value	0.4348

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 1.2.1.7
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	134.30 (9.31)
Week 24	
n	24
Mean (SD)	137.13 (9.47)
Absolute Change at Week 24	
n	24
Mean (SD)	2.83 (0.99)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	2.83 (0.20)
95% CI of LS mean	(2.41, 3.25)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 1.2.1.8
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	-0.07 (0.93)
Week 24	
n	24
Mean (SD)	-0.04 (0.94)
Absolute Change at Week 24	
n	24
Mean (SD)	0.03 (0.15)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	0.03 (0.03)
95% CI of LS mean	(-0.03, 0.09)
P-value	0.2782

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 1.2.1.9
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	21
Mean (SD)	6.92 (1.06)
Week 24	
n	17
Mean (SD)	6.47 (0.61)
Absolute Change at Week 24	
n	16
Mean (SD)	-0.24 (0.62)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	-0.12 (0.09)
95% CI of LS mean	(-0.33, 0.08)
P-value	0.2140

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	89.86 (7.93)
Week 4 (MMRM)	
n	23
LS mean (SE)	90.22 (1.85)
95% CI of LS mean	(86.38, 94.05)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	0.36 (1.85)
95% CI of LS mean	(-3.47, 4.20)
Week 8 (MMRM)	
n	23
LS mean (SE)	89.49 (2.42)
95% CI of LS mean	(84.47, 94.52)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	-0.36 (2.42)
95% CI of LS mean	(-5.39, 4.66)
Week 12 (MMRM)	
n	23
LS mean (SE)	91.67 (1.82)
95% CI of LS mean	(87.89, 95.44)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	1.81 (1.82)
95% CI of LS mean	(-1.96, 5.59)
Week 16 (MMRM)	
n	23
LS mean (SE)	91.67 (1.79)
95% CI of LS mean	(87.95, 95.38)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	1.81 (1.79)
95% CI of LS mean	(-1.90, 5.53)
Week 24	
n	24
Mean (SD)	89.24 (10.56)
Absolute Change at Week 24	
n	23
Mean (SD)	-0.72 (10.63)
Week 24 (MMRM)	
n	24
LS mean (SE)	89.13 (2.10)
95% CI of LS mean	(84.77, 93.49)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	-0.72 (2.10)
95% CI of LS mean	(-5.09, 3.64)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	0.54 (1.46)
95% CI of LS mean	(-2.49, 3.57)
P-value	0.7134

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Respiration

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Body

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Digestion

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Eat

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Emotion

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Physical

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Social

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	23 (95.83)
Week 4	23 (95.83)
Absolute Change at Week 4	23 (95.83)
Week 8	23 (95.83)
Absolute Change at Week 8	23 (95.83)
Week 12	23 (95.83)
Absolute Change at Week 12	23 (95.83)
Week 16	23 (95.83)
Absolute Change at Week 16	23 (95.83)
Week 24	24 (100.00)
Absolute Change at Week 24	23 (95.83)
Through Week 24	24 (100.00)
Absolute Change through Week 24	23 (95.83)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	91.62 (9.40)
Week 4 (MMRM)	
n	24
LS mean (SE)	83.56 (3.09)
95% CI of LS mean	(77.17, 89.96)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	-8.06 (3.09)
95% CI of LS mean	(-14.45, -1.66)
Week 8 (MMRM)	
n	24
LS mean (SE)	86.81 (3.66)
95% CI of LS mean	(79.24, 94.37)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	-4.81 (3.66)
95% CI of LS mean	(-12.38, 2.75)
Week 12 (MMRM)	
n	24
LS mean (SE)	93.06 (1.45)
95% CI of LS mean	(90.05, 96.06)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	1.44 (1.45)
95% CI of LS mean	(-1.57, 4.44)
Week 16 (MMRM)	
n	24
LS mean (SE)	91.90 (2.27)
95% CI of LS mean	(87.19, 96.60)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	0.28 (2.27)
95% CI of LS mean	(-4.43, 4.98)
Week 24	
n	24
Mean (SD)	88.43 (13.50)
Absolute Change at Week 24	
n	24
Mean (SD)	-3.19 (15.75)
Week 24 (MMRM)	
n	24
LS mean (SE)	88.43 (2.79)
95% CI of LS mean	(82.65, 94.21)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-3.19 (2.79)
95% CI of LS mean	(-8.97, 2.58)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	-1.46 (1.64)
95% CI of LS mean	(-4.85, 1.93)
P-value	0.3824

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Respiration

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Body

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Digestion

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Eat

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Emotion

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Health Perception

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Physical

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: School

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Treatment Burden

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Vitality

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for F/MF
Full Analysis Set

Domain: Weight

	VNZ/TEZ/D-IVA N = 24 n (%)
Baseline	24 (100.00)
Week 4	24 (100.00)
Absolute Change at Week 4	24 (100.00)
Week 8	24 (100.00)
Absolute Change at Week 8	24 (100.00)
Week 12	24 (100.00)
Absolute Change at Week 12	24 (100.00)
Week 16	24 (100.00)
Absolute Change at Week 16	24 (100.00)
Week 24	24 (100.00)
Absolute Change at Week 24	24 (100.00)
Through Week 24	24 (100.00)
Absolute Change through Week 24	24 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	90.82 (16.29)
Week 4 (MMRM)	
n	23
LS mean (SE)	91.30 (3.31)
95% CI of LS mean	(84.44, 98.16)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	0.48 (3.31)
95% CI of LS mean	(-6.38, 7.34)
Week 8 (MMRM)	
n	23
LS mean (SE)	90.34 (3.56)
95% CI of LS mean	(82.96, 97.72)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	-0.48 (3.56)
95% CI of LS mean	(-7.86, 6.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Body

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	90.34 (2.69)
95% CI of LS mean	(84.73, 95.95)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	-0.48 (2.69)
95% CI of LS mean	(-6.09, 5.13)
Week 16 (MMRM)	
n	23
LS mean (SE)	94.69 (1.82)
95% CI of LS mean	(90.91, 98.46)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	3.86 (1.82)
95% CI of LS mean	(0.09, 7.64)
Week 24	
n	24
Mean (SD)	94.44 (12.26)
Absolute Change at Week 24	
n	23
Mean (SD)	5.31 (15.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	96.14 (1.84)
95% CI of LS mean	(92.31, 99.96)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	5.31 (1.84)
95% CI of LS mean	(1.49, 9.14)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	4.59 (1.71)
95% CI of LS mean	(1.03, 8.15)
P-value	0.0139

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	81.16 (19.66)
Week 4 (MMRM)	
n	23
LS mean (SE)	89.86 (2.55)
95% CI of LS mean	(84.52, 95.19)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	8.70 (2.55)
95% CI of LS mean	(3.37, 14.03)
Week 8 (MMRM)	
n	23
LS mean (SE)	86.96 (4.19)
95% CI of LS mean	(78.24, 95.68)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	5.80 (4.19)
95% CI of LS mean	(-2.92, 14.52)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Digestion

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	82.61 (3.14)
95% CI of LS mean	(76.10, 89.12)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	1.45 (3.14)
95% CI of LS mean	(-5.06, 7.96)
Week 16 (MMRM)	
n	23
LS mean (SE)	86.96 (3.98)
95% CI of LS mean	(78.69, 95.23)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	5.80 (3.98)
95% CI of LS mean	(-2.47, 14.07)
Week 24	
n	24
Mean (SD)	87.50 (19.19)
Absolute Change at Week 24	
n	23
Mean (SD)	7.25 (28.35)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	88.41 (4.41)
95% CI of LS mean	(79.20, 97.61)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	7.25 (4.41)
95% CI of LS mean	(-1.96, 16.45)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	6.52 (3.07)
95% CI of LS mean	(0.07, 12.97)
P-value	0.0478

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	88.89 (17.41)
Week 4 (MMRM)	
n	23
LS mean (SE)	87.44 (3.04)
95% CI of LS mean	(81.10, 93.78)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	-1.45 (3.04)
95% CI of LS mean	(-7.79, 4.89)
Week 8 (MMRM)	
n	23
LS mean (SE)	86.47 (4.68)
95% CI of LS mean	(76.74, 96.21)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	-2.42 (4.68)
95% CI of LS mean	(-12.15, 7.32)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Eat

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	84.54 (4.18)
95% CI of LS mean	(75.85, 93.23)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	-4.35 (4.18)
95% CI of LS mean	(-13.04, 4.34)
Week 16 (MMRM)	
n	23
LS mean (SE)	85.02 (4.86)
95% CI of LS mean	(74.91, 95.14)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	-3.86 (4.86)
95% CI of LS mean	(-13.98, 6.25)
Week 24	
n	24
Mean (SD)	91.67 (17.10)
Absolute Change at Week 24	
n	23
Mean (SD)	2.42 (13.38)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	91.30 (2.79)
95% CI of LS mean	(85.42, 97.18)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	2.42 (2.79)
95% CI of LS mean	(-3.46, 8.29)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	-0.72 (3.46)
95% CI of LS mean	(-7.96, 6.51)
P-value	0.8363

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	84.42 (10.07)
Week 4 (MMRM)	
n	23
LS mean (SE)	83.70 (2.56)
95% CI of LS mean	(78.34, 89.06)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	-0.72 (2.56)
95% CI of LS mean	(-6.09, 4.64)
Week 8 (MMRM)	
n	23
LS mean (SE)	83.15 (2.53)
95% CI of LS mean	(77.81, 88.50)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	-1.27 (2.53)
95% CI of LS mean	(-6.61, 4.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Emotion

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	84.06 (3.37)
95% CI of LS mean	(76.99, 91.12)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	-0.36 (3.37)
95% CI of LS mean	(-7.43, 6.70)
Week 16 (MMRM)	
n	23
LS mean (SE)	81.16 (3.14)
95% CI of LS mean	(74.63, 87.68)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	-3.26 (3.14)
95% CI of LS mean	(-9.79, 3.26)
Week 24	
n	24
Mean (SD)	82.81 (14.76)
Absolute Change at Week 24	
n	23
Mean (SD)	-1.27 (9.93)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	83.15 (2.10)
95% CI of LS mean	(78.79, 87.51)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	-1.27 (2.10)
95% CI of LS mean	(-5.63, 3.09)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	-2.26 (2.40)
95% CI of LS mean	(-7.26, 2.73)
P-value	0.3559

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	89.37 (13.29)
Week 4 (MMRM)	
n	23
LS mean (SE)	87.92 (1.88)
95% CI of LS mean	(84.01, 91.84)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	-1.45 (1.88)
95% CI of LS mean	(-5.36, 2.47)
Week 8 (MMRM)	
n	23
LS mean (SE)	89.37 (2.78)
95% CI of LS mean	(83.61, 95.13)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	0.00 (2.78)
95% CI of LS mean	(-5.76, 5.76)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Physical

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	87.92 (3.73)
95% CI of LS mean	(80.18, 95.66)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	-1.45 (3.73)
95% CI of LS mean	(-9.19, 6.29)
Week 16 (MMRM)	
n	23
LS mean (SE)	87.44 (2.76)
95% CI of LS mean	(81.72, 93.16)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	-1.93 (2.76)
95% CI of LS mean	(-7.66, 3.79)
Week 24	
n	24
Mean (SD)	92.13 (11.80)
Absolute Change at Week 24	
n	23
Mean (SD)	2.42 (9.45)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	91.79 (1.76)
95% CI of LS mean	(88.12, 95.45)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	2.42 (1.76)
95% CI of LS mean	(-1.25, 6.08)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	0.24 (1.96)
95% CI of LS mean	(-3.84, 4.32)
P-value	0.9033

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	71.01 (15.66)
Week 4 (MMRM)	
n	23
LS mean (SE)	70.81 (2.71)
95% CI of LS mean	(65.17, 76.44)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	-0.21 (2.71)
95% CI of LS mean	(-5.84, 5.43)
Week 8 (MMRM)	
n	23
LS mean (SE)	70.39 (3.30)
95% CI of LS mean	(63.54, 77.25)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	-0.62 (3.30)
95% CI of LS mean	(-7.48, 6.23)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Social

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	71.84 (2.86)
95% CI of LS mean	(65.90, 77.79)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	0.83 (2.86)
95% CI of LS mean	(-5.12, 6.78)
Week 16 (MMRM)	
n	23
LS mean (SE)	73.08 (3.10)
95% CI of LS mean	(66.66, 79.51)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	2.07 (3.10)
95% CI of LS mean	(-4.36, 8.50)
Week 24	
n	24
Mean (SD)	75.89 (15.29)
Absolute Change at Week 24	
n	23
Mean (SD)	5.07 (17.73)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	76.09 (3.12)
95% CI of LS mean	(69.61, 82.57)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	5.07 (3.12)
95% CI of LS mean	(-1.41, 11.55)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	3.57 (2.85)
95% CI of LS mean	(-2.35, 9.50)
P-value	0.2241

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	23
Mean (SD)	78.99 (19.53)
Week 4 (MMRM)	
n	23
LS mean (SE)	81.16 (3.71)
95% CI of LS mean	(73.47, 88.85)
Absolute Change at Week 4 (MMRM)	
n	23
LS mean (SE)	2.17 (3.71)
95% CI of LS mean	(-5.52, 9.87)
Week 8 (MMRM)	
n	23
LS mean (SE)	84.06 (2.63)
95% CI of LS mean	(78.59, 89.53)
Absolute Change at Week 8 (MMRM)	
n	23
LS mean (SE)	5.07 (2.63)
95% CI of LS mean	(-0.40, 10.55)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Treatment Burden

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	23
LS mean (SE)	84.54 (2.55)
95% CI of LS mean	(79.25, 89.84)
Absolute Change at Week 12 (MMRM)	
n	23
LS mean (SE)	5.56 (2.55)
95% CI of LS mean	(0.26, 10.85)
Week 16 (MMRM)	
n	23
LS mean (SE)	79.23 (4.68)
95% CI of LS mean	(69.52, 88.94)
Absolute Change at Week 16 (MMRM)	
n	23
LS mean (SE)	0.24 (4.68)
95% CI of LS mean	(-9.47, 9.95)
Week 24	
n	24
Mean (SD)	84.26 (20.18)
Absolute Change at Week 24	
n	23
Mean (SD)	5.56 (15.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	84.54 (3.03)
95% CI of LS mean	(78.24, 90.84)
Absolute Change at Week 24 (MMRM)	
n	23
LS mean (SE)	5.56 (3.03)
95% CI of LS mean	(-0.74, 11.85)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	2.90 (2.81)
95% CI of LS mean	(-2.94, 8.73)
P-value	0.3136

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	82.41 (25.57)
Week 4 (MMRM)	
n	24
LS mean (SE)	80.56 (2.81)
95% CI of LS mean	(74.74, 86.37)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	-1.85 (2.81)
95% CI of LS mean	(-7.67, 3.96)
Week 8 (MMRM)	
n	24
LS mean (SE)	85.19 (2.21)
95% CI of LS mean	(80.61, 89.76)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	2.78 (2.21)
95% CI of LS mean	(-1.80, 7.35)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	84.26 (2.88)
95% CI of LS mean	(78.29, 90.23)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	1.85 (2.88)
95% CI of LS mean	(-4.12, 7.82)
Week 16 (MMRM)	
n	24
LS mean (SE)	86.11 (2.43)
95% CI of LS mean	(81.08, 91.14)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	3.70 (2.43)
95% CI of LS mean	(-1.33, 8.74)
Week 24	
n	24
Mean (SD)	86.11 (24.79)
Absolute Change at Week 24	
n	24
Mean (SD)	3.70 (7.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	86.11 (1.43)
95% CI of LS mean	(83.15, 89.07)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	3.70 (1.43)
95% CI of LS mean	(0.75, 6.66)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	3.70 (1.66)
95% CI of LS mean	(0.27, 7.14)
P-value	0.0357

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	81.48 (17.54)
Week 4 (MMRM)	
n	24
LS mean (SE)	82.41 (1.98)
95% CI of LS mean	(78.31, 86.51)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	0.93 (1.98)
95% CI of LS mean	(-3.18, 5.03)
Week 8 (MMRM)	
n	24
LS mean (SE)	82.87 (3.00)
95% CI of LS mean	(76.66, 89.08)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	1.39 (3.00)
95% CI of LS mean	(-4.82, 7.60)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	82.41 (2.55)
95% CI of LS mean	(77.12, 87.70)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	0.93 (2.55)
95% CI of LS mean	(-4.37, 6.22)
Week 16 (MMRM)	
n	24
LS mean (SE)	85.19 (2.12)
95% CI of LS mean	(80.79, 89.58)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	3.70 (2.12)
95% CI of LS mean	(-0.69, 8.10)
Week 24	
n	24
Mean (SD)	81.48 (20.11)
Absolute Change at Week 24	
n	24
Mean (SD)	0.00 (15.01)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	81.48 (3.02)
95% CI of LS mean	(75.24, 87.73)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	0.00 (3.02)
95% CI of LS mean	(-6.25, 6.25)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	1.85 (2.24)
95% CI of LS mean	(-2.79, 6.50)
P-value	0.4179

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	86.11 (23.91)
Week 4 (MMRM)	
n	24
LS mean (SE)	84.72 (3.27)
95% CI of LS mean	(77.93, 91.51)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	-1.39 (3.27)
95% CI of LS mean	(-8.18, 5.40)
Week 8 (MMRM)	
n	24
LS mean (SE)	88.19 (2.91)
95% CI of LS mean	(82.16, 94.22)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	2.08 (2.91)
95% CI of LS mean	(-3.95, 8.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	84.03 (3.61)
95% CI of LS mean	(76.53, 91.52)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	-2.08 (3.61)
95% CI of LS mean	(-9.58, 5.41)
Week 16 (MMRM)	
n	24
LS mean (SE)	86.11 (3.31)
95% CI of LS mean	(79.26, 92.97)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	0.00 (3.31)
95% CI of LS mean	(-6.86, 6.86)
Week 24	
n	24
Mean (SD)	85.42 (27.06)
Absolute Change at Week 24	
n	24
Mean (SD)	-0.69 (15.91)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	85.42 (3.27)
95% CI of LS mean	(78.64, 92.19)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-0.69 (3.27)
95% CI of LS mean	(-7.47, 6.08)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	-0.35 (3.03)
95% CI of LS mean	(-6.63, 5.94)
P-value	0.9099

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	89.72 (9.00)
Week 4 (MMRM)	
n	24
LS mean (SE)	89.72 (2.29)
95% CI of LS mean	(84.98, 94.47)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	0.00 (2.29)
95% CI of LS mean	(-4.75, 4.75)
Week 8 (MMRM)	
n	24
LS mean (SE)	90.00 (1.93)
95% CI of LS mean	(85.97, 94.03)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	0.28 (1.93)
95% CI of LS mean	(-3.75, 4.31)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	91.67 (1.53)
95% CI of LS mean	(88.50, 94.84)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	1.94 (1.53)
95% CI of LS mean	(-1.23, 5.11)
Week 16 (MMRM)	
n	24
LS mean (SE)	91.39 (1.89)
95% CI of LS mean	(87.48, 95.30)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	1.67 (1.89)
95% CI of LS mean	(-2.24, 5.57)
Week 24	
n	24
Mean (SD)	87.78 (12.69)
Absolute Change at Week 24	
n	24
Mean (SD)	-1.94 (11.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	87.78 (2.29)
95% CI of LS mean	(83.02, 92.53)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-1.94 (2.29)
95% CI of LS mean	(-6.70, 2.81)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	-0.14 (1.84)
95% CI of LS mean	(-3.96, 3.69)
P-value	0.9406

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	87.04 (14.53)
Week 4 (MMRM)	
n	24
LS mean (SE)	80.56 (3.15)
95% CI of LS mean	(74.03, 87.08)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	-6.48 (3.15)
95% CI of LS mean	(-13.01, 0.04)
Week 8 (MMRM)	
n	24
LS mean (SE)	82.41 (2.93)
95% CI of LS mean	(76.32, 88.49)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	-4.63 (2.93)
95% CI of LS mean	(-10.71, 1.46)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	86.57 (1.85)
95% CI of LS mean	(82.73, 90.42)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	-0.46 (1.85)
95% CI of LS mean	(-4.31, 3.38)
Week 16 (MMRM)	
n	24
LS mean (SE)	86.57 (2.41)
95% CI of LS mean	(81.59, 91.55)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	-0.46 (2.41)
95% CI of LS mean	(-5.44, 4.52)
Week 24	
n	24
Mean (SD)	88.43 (14.08)
Absolute Change at Week 24	
n	24
Mean (SD)	1.39 (11.50)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	88.43 (2.14)
95% CI of LS mean	(84.01, 92.85)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	1.39 (2.14)
95% CI of LS mean	(-3.03, 5.81)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	0.46 (1.52)
95% CI of LS mean	(-2.68, 3.61)
P-value	0.7633

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	94.62 (8.01)
Week 4 (MMRM)	
n	24
LS mean (SE)	90.80 (2.55)
95% CI of LS mean	(85.53, 96.07)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	-3.82 (2.55)
95% CI of LS mean	(-9.09, 1.45)
Week 8 (MMRM)	
n	24
LS mean (SE)	89.06 (2.75)
95% CI of LS mean	(83.37, 94.76)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	-5.56 (2.75)
95% CI of LS mean	(-11.25, 0.14)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	95.31 (1.38)
95% CI of LS mean	(92.40, 98.22)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	0.69 (1.38)
95% CI of LS mean	(-2.22, 3.61)
Week 16 (MMRM)	
n	24
LS mean (SE)	93.40 (2.21)
95% CI of LS mean	(88.76, 98.04)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	-1.22 (2.21)
95% CI of LS mean	(-5.85, 3.42)
Week 24	
n	24
Mean (SD)	93.40 (14.53)
Absolute Change at Week 24	
n	24
Mean (SD)	-1.22 (10.32)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	93.40 (2.17)
95% CI of LS mean	(88.87, 97.93)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-1.22 (2.17)
95% CI of LS mean	(-5.75, 3.32)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	-1.22 (1.72)
95% CI of LS mean	(-4.90, 2.47)
P-value	0.4916

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	85.42 (14.17)
Week 4 (MMRM)	
n	24
LS mean (SE)	81.60 (3.44)
95% CI of LS mean	(74.45, 88.75)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	-3.82 (3.44)
95% CI of LS mean	(-10.97, 3.33)
Week 8 (MMRM)	
n	24
LS mean (SE)	80.90 (3.18)
95% CI of LS mean	(74.32, 87.48)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	-4.51 (3.18)
95% CI of LS mean	(-11.09, 2.07)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	82.41 (2.59)
95% CI of LS mean	(77.01, 87.80)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	-3.01 (2.59)
95% CI of LS mean	(-8.40, 2.38)
Week 16 (MMRM)	
n	24
LS mean (SE)	87.85 (2.48)
95% CI of LS mean	(82.63, 93.06)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	2.43 (2.48)
95% CI of LS mean	(-2.79, 7.65)
Week 24	
n	24
Mean (SD)	84.72 (18.82)
Absolute Change at Week 24	
n	24
Mean (SD)	-0.69 (17.19)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	84.72 (3.40)
95% CI of LS mean	(77.69, 91.76)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-0.69 (3.40)
95% CI of LS mean	(-7.73, 6.34)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	0.87 (2.63)
95% CI of LS mean	(-4.61, 6.34)
P-value	0.7447

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	67.13 (23.74)
Week 4 (MMRM)	
n	24
LS mean (SE)	71.76 (3.29)
95% CI of LS mean	(64.90, 78.61)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	4.63 (3.29)
95% CI of LS mean	(-2.22, 11.48)
Week 8 (MMRM)	
n	24
LS mean (SE)	75.00 (4.08)
95% CI of LS mean	(66.47, 83.53)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	7.87 (4.08)
95% CI of LS mean	(-0.66, 16.40)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	71.30 (3.63)
95% CI of LS mean	(63.76, 78.83)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	4.17 (3.63)
95% CI of LS mean	(-3.37, 11.70)
Week 16 (MMRM)	
n	24
LS mean (SE)	74.54 (2.81)
95% CI of LS mean	(68.70, 80.37)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	7.41 (2.81)
95% CI of LS mean	(1.57, 13.24)
Week 24	
n	24
Mean (SD)	73.15 (24.72)
Absolute Change at Week 24	
n	24
Mean (SD)	6.02 (18.24)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	73.15 (3.56)
95% CI of LS mean	(65.79, 80.51)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	6.02 (3.56)
95% CI of LS mean	(-1.34, 13.38)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	6.71 (2.91)
95% CI of LS mean	(0.69, 12.74)
P-value	0.0306

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	79.44 (12.73)
Week 4 (MMRM)	
n	24
LS mean (SE)	80.00 (2.61)
95% CI of LS mean	(74.58, 85.42)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	0.56 (2.61)
95% CI of LS mean	(-4.86, 5.97)
Week 8 (MMRM)	
n	24
LS mean (SE)	80.00 (1.94)
95% CI of LS mean	(75.99, 84.01)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	0.56 (1.94)
95% CI of LS mean	(-3.45, 4.56)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	80.28 (2.25)
95% CI of LS mean	(75.61, 84.95)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	0.83 (2.25)
95% CI of LS mean	(-3.83, 5.50)
Week 16 (MMRM)	
n	24
LS mean (SE)	81.39 (2.82)
95% CI of LS mean	(75.54, 87.24)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	1.94 (2.82)
95% CI of LS mean	(-3.91, 7.80)
Week 24	
n	24
Mean (SD)	78.06 (15.41)
Absolute Change at Week 24	
n	24
Mean (SD)	-1.39 (12.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	78.06 (2.46)
95% CI of LS mean	(72.96, 83.15)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	-1.39 (2.46)
95% CI of LS mean	(-6.48, 3.71)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	0.28 (2.18)
95% CI of LS mean	(-4.24, 4.80)
P-value	0.8998

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Baseline	
n	24
Mean (SD)	63.89 (35.33)
Week 4 (MMRM)	
n	24
LS mean (SE)	70.83 (4.31)
95% CI of LS mean	(61.90, 79.77)
Absolute Change at Week 4 (MMRM)	
n	24
LS mean (SE)	6.94 (4.31)
95% CI of LS mean	(-1.99, 15.88)
Week 8 (MMRM)	
n	24
LS mean (SE)	70.83 (4.37)
95% CI of LS mean	(61.78, 79.89)
Absolute Change at Week 8 (MMRM)	
n	24
LS mean (SE)	6.94 (4.37)
95% CI of LS mean	(-2.11, 16.00)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 24
Week 12 (MMRM)	
n	24
LS mean (SE)	69.44 (5.41)
95% CI of LS mean	(58.23, 80.66)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	5.56 (5.41)
95% CI of LS mean	(-5.66, 16.77)
Week 16 (MMRM)	
n	24
LS mean (SE)	66.67 (5.71)
95% CI of LS mean	(54.80, 78.54)
Absolute Change at Week 16 (MMRM)	
n	24
LS mean (SE)	2.78 (5.71)
95% CI of LS mean	(-9.09, 14.65)
Week 24	
n	24
Mean (SD)	69.44 (40.43)
Absolute Change at Week 24	
n	24
Mean (SD)	5.56 (21.23)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 24
Week 24 (MMRM)	
n	24
LS mean (SE)	69.44 (4.47)
95% CI of LS mean	(60.17, 78.72)
Absolute Change at Week 24 (MMRM)	
n	24
LS mean (SE)	5.56 (4.47)
95% CI of LS mean	(-3.72, 14.83)
Absolute Change through Week 24 (MMRM)	
n	24
LS mean (SE)	4.17 (4.40)
95% CI of LS mean	(-4.95, 13.28)
P-value	0.3535

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.1.13
Study VX21-121-105: Summary of Pulmonary Exacerbations through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24
Total number of days (years) of the PEx analysis period	4040 (12.0)
Pulmonary exacerbations	
Number of subjects with events, n (%)	2 (8.33)
Total number of events	2
Observed event rate per year	0.17
Pulmonary exacerbations requiring hospitalization	
Number of subjects with events, n (%)	0
Total number of events	0
Observed event rate per year	0
Pulmonary exacerbations requiring IV antibiotic therapy	
Number of subjects with events, n (%)	0
Total number of events	0
Observed event rate per year	0
Pulmonary exacerbations requiring hospitalization or IV antibiotic therapy	
Number of subjects with events, n (%)	0
Total number of events	0
Observed event rate per year	0

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Zusatzanalysen zur Studie VX21-121-105

Table 1.2.1.14.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Any Pulmonary Exacerbation	
Overall	
Subjects with Events	2 (8.33)
Subjects Censored	22 (91.67)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Zusatzanalysen zur Studie VX21-121-105

Table 1.2.1.15.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization	
Overall	
Subjects with Events	0
Subjects Censored	24 (100.00)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring hospitalization during the PEx analysis period were censored at the PEx analysis period end date.

Zusatzanalysen zur Studie VX21-121-105

Table 1.2.1.16.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24 for F/MF
Full Analysis Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics	
Overall	
Subjects with Events	0
Subjects Censored	24 (100.00)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring IV antibiotics during the PEx analysis period were censored at the PEx analysis period end date.

Zusatzanalysen zur Studie VX21-121-105

Table 1.2.2.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.7089
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effects and baseline $ppFEV_1$ as covariate.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	104.07 (17.53)
Week 24	
n	10
Mean (SD)	102.94 (16.03)
Absolute Change at Week 24	
n	10
Mean (SD)	-1.83 (6.29)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	-2.06 (1.37)
95% CI of LS mean	(-5.32, 1.21)
P-value	0.1793

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	85.95 (21.22)
Week 24	
n	10
Mean (SD)	91.51 (18.18)
Absolute Change at Week 24	
n	10
Mean (SD)	2.60 (7.50)
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	4.40 (3.29)
95% CI of LS mean	(-2.94, 11.75)
P-value	0.2107

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.2.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.4544
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effects and baseline BMI as covariate.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	18.17 (2.39)
Week 24	
n	11
Mean (SD)	18.40 (2.56)
Absolute Change at Week 24	
n	11
Mean (SD)	0.23 (0.42)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	0.23 (0.13)
95% CI of LS mean	(-0.07, 0.53)
P-value	0.1207

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	15.94 (1.27)
Week 24	
n	13
Mean (SD)	16.04 (1.72)
Absolute Change at Week 24	
n	13
Mean (SD)	0.09 (0.78)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	0.09 (0.22)
95% CI of LS mean	(-0.39, 0.57)
P-value	0.6819

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.3524
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline BMI z-score as covariate.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	0.47 (0.91)
Week 24	
n	11
Mean (SD)	0.44 (0.94)
Absolute Change at Week 24	
n	11
Mean (SD)	-0.04 (0.13)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	-0.04 (0.04)
95% CI of LS mean	(-0.12, 0.05)
P-value	0.3910

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	-0.26 (0.84)
Week 24	
n	13
Mean (SD)	-0.39 (1.00)
Absolute Change at Week 24	
n	13
Mean (SD)	-0.13 (0.42)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-0.13 (0.12)
95% CI of LS mean	(-0.39, 0.12)
P-value	0.2795

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.9086
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effects and baseline sweat chloride as covariate.
- N/C: model does not converge.

Table 1.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	48.14 (20.22)
Week 24	
n	10
Mean (SD)	39.85 (16.97)
Absolute Change at Week 24	
n	10
Mean (SD)	-10.40 (9.51)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	-7.62 (2.48)
95% CI of LS mean	(-13.20, -2.05)
P-value	0.0127

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	56.67 (17.42)
Week 24	
n	12
Mean (SD)	44.17 (15.14)
Absolute Change at Week 24	
n	12
Mean (SD)	-12.50 (11.35)
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	-13.27 (3.36)
95% CI of LS mean	(-20.69, -5.85)
P-value	0.0024

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 1.2.2.4.2.1
Study VX21-121-105: Subgroup Factor Test for
Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.8130
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Chi-square test.

Table 1.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 1.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 1.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Non-missing value at Week 24, N1	10
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	8 (72.73)
95% CI for the proportion	(39.03, 93.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 1.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Non-missing value at Week 24, N1	12
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	10 (76.92)
95% CI for the proportion	(46.19, 94.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 1.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 1.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Zusatzanalysen zur Studie VX21-121-105

Table 1.2.2.4.3.1
Study VX21-121-105: Subgroup Factor Test for
Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Chi-square test.

Table 1.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 1.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 1.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 1.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 1.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 1.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 1.2.2.5.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.6517
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effects and baseline weight as covariate.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	33.31 (4.69)
Week 24	
n	11
Mean (SD)	35.11 (5.26)
Absolute Change at Week 24	
n	11
Mean (SD)	1.80 (0.87)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	1.80 (0.26)
95% CI of LS mean	(1.21, 2.40)
P-value	0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	28.55 (5.48)
Week 24	
n	13
Mean (SD)	29.99 (6.11)
Absolute Change at Week 24	
n	13
Mean (SD)	1.45 (1.60)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	1.45 (0.45)
95% CI of LS mean	(0.46, 2.43)
P-value	0.0079

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.6.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.6578
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effects and baseline weight z-score as covariate.
- N/C: model does not converge.

Table 1.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA
	N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	0.16 (0.80)
Week 24	
n	11
Mean (SD)	0.15 (0.85)
Absolute Change at Week 24	
n	11
Mean (SD)	-0.01 (0.11)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	-0.01 (0.03)
95% CI of LS mean	(-0.09, 0.07)
P-value	0.7696

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	-0.14 (0.94)
Week 24	
n	13
Mean (SD)	-0.20 (1.05)
Absolute Change at Week 24	
n	13
Mean (SD)	-0.06 (0.29)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-0.06 (0.08)
95% CI of LS mean	(-0.24, 0.12)
P-value	0.5004

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.7.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.7490
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effects and baseline height as covariate.
- N/C: model does not converge.

Table 1.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	135.48 (7.56)
Week 24	
n	11
Mean (SD)	138.21 (7.55)
Absolute Change at Week 24	
n	11
Mean (SD)	2.73 (0.78)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	2.73 (0.25)
95% CI of LS mean	(2.17, 3.28)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	133.31 (10.78)
Week 24	
n	13
Mean (SD)	136.22 (11.06)
Absolute Change at Week 24	
n	13
Mean (SD)	2.92 (1.16)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	2.92 (0.32)
95% CI of LS mean	(2.22, 3.62)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.8.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.3427
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline height z-score as covariate.
- N/C: model does not converge.

Table 1.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	-0.32 (0.85)
Week 24	
n	11
Mean (SD)	-0.28 (0.86)
Absolute Change at Week 24	
n	11
Mean (SD)	0.04 (0.14)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	0.04 (0.04)
95% CI of LS mean	(-0.05, 0.14)
P-value	0.3514

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	0.14 (0.98)
Week 24	
n	13
Mean (SD)	0.17 (0.98)
Absolute Change at Week 24	
n	13
Mean (SD)	0.03 (0.16)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	0.03 (0.04)
95% CI of LS mean	(-0.07, 0.12)
P-value	0.5641

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 1.2.2.9.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.4223
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline $LCI_{2.5}$ as covariate.
- N/C: model does not converge.

Table 1.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	10
Mean (SD)	6.94 (0.98)
Week 24	
n	8
Mean (SD)	6.45 (0.67)
Absolute Change at Week 24	
n	8
Mean (SD)	-0.21 (0.64)
Absolute Change through Week 24 (MMRM)	
n	8
LS mean (SE)	-0.17 (0.12)
95% CI of LS mean	(-0.45, 0.11)
P-value	0.1976

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	11
Mean (SD)	6.91 (1.18)
Week 24	
n	9
Mean (SD)	6.50 (0.58)
Absolute Change at Week 24	
n	8
Mean (SD)	-0.26 (0.63)
Absolute Change through Week 24 (MMRM)	
n	8
LS mean (SE)	0.24 (0.24)
95% CI of LS mean	(-0.37, 0.86)
P-value	0.3496

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.9564
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Respiratory domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	87.88 (6.83)
Week 4 (MMRM)	
n	11
LS mean (SE)	89.39 (3.13)
95% CI of LS mean	(82.42, 96.36)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	1.52 (3.13)
95% CI of LS mean	(-5.46, 8.49)
Week 8 (MMRM)	
n	11
LS mean (SE)	90.91 (2.79)
95% CI of LS mean	(84.69, 97.13)
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	3.03 (2.79)
95% CI of LS mean	(-3.19, 9.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Week 12 (MMRM)	
n	11
LS mean (SE)	91.67 (1.92)
95% CI of LS mean	(87.39, 95.94)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	3.79 (1.92)
95% CI of LS mean	(-0.49, 8.06)
Week 16 (MMRM)	
n	11
LS mean (SE)	89.39 (3.16)
95% CI of LS mean	(82.27, 96.52)
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	1.52 (3.16)
95% CI of LS mean	(-5.61, 8.64)
Week 24	
n	11
Mean (SD)	91.67 (8.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 24	
n	11
Mean (SD)	3.79 (10.78)
Week 24 (MMRM)	
n	11
LS mean (SE)	91.67 (2.77)
95% CI of LS mean	(85.42, 97.91)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	3.79 (2.77)
95% CI of LS mean	(-2.45, 10.03)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	2.65 (2.57)
95% CI of LS mean	(-3.19, 8.49)
P-value	0.3301

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	91.67 (8.70)
Week 4 (MMRM)	
n	12
LS mean (SE)	90.97 (2.18)
95% CI of LS mean	(86.16, 95.78)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-0.69 (2.18)
95% CI of LS mean	(-5.51, 4.12)
Week 8 (MMRM)	
n	12
LS mean (SE)	88.19 (4.03)
95% CI of LS mean	(79.29, 97.09)
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	-3.47 (4.03)
95% CI of LS mean	(-12.37, 5.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Week 12 (MMRM)	
n	12
LS mean (SE)	91.67 (3.27)
95% CI of LS mean	(84.39, 98.95)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	0.00 (3.27)
95% CI of LS mean	(-7.28, 7.28)
Week 16 (MMRM)	
n	12
LS mean (SE)	93.75 (2.15)
95% CI of LS mean	(89.00, 98.50)
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	2.08 (2.15)
95% CI of LS mean	(-2.67, 6.83)
Week 24	
n	13
Mean (SD)	87.18 (12.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 24	
n	12
Mean (SD)	-4.86 (9.03)
Week 24 (MMRM)	
n	13
LS mean (SE)	86.81 (2.83)
95% CI of LS mean	(80.52, 93.09)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	-4.86 (2.83)
95% CI of LS mean	(-11.15, 1.43)
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	-1.39 (1.63)
95% CI of LS mean	(-5.02, 2.24)
P-value	0.4145

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.5972
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Respiratory domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	90.91 (9.71)
Week 4 (MMRM)	
n	11
LS mean (SE)	83.33 (4.66)
95% CI of LS mean	(72.85, 93.82)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	-7.58 (4.66)
95% CI of LS mean	(-18.06, 2.91)
Week 8 (MMRM)	
n	11
LS mean (SE)	88.89 (5.73)
95% CI of LS mean	(76.09, 101.68)
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	-2.02 (5.73)
95% CI of LS mean	(-14.82, 10.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Week 12 (MMRM)	
n	11
LS mean (SE)	93.43 (2.28)
95% CI of LS mean	(87.73, 99.14)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	2.53 (2.28)
95% CI of LS mean	(-3.18, 8.23)
Week 16 (MMRM)	
n	11
LS mean (SE)	88.38 (4.79)
95% CI of LS mean	(77.38, 99.39)
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	-2.53 (4.79)
95% CI of LS mean	(-13.53, 8.48)
Week 24	
n	11
Mean (SD)	88.38 (13.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 24	
n	11
Mean (SD)	-2.53 (15.19)
Week 24 (MMRM)	
n	11
LS mean (SE)	88.38 (4.81)
95% CI of LS mean	(77.43, 99.34)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-2.53 (4.81)
95% CI of LS mean	(-13.48, 8.43)
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	-2.53 (4.11)
95% CI of LS mean	(-12.13, 7.08)
P-value	0.5572

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	92.22 (9.48)
Week 4 (MMRM)	
n	13
LS mean (SE)	83.76 (4.53)
95% CI of LS mean	(73.85, 93.67)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-8.46 (4.53)
95% CI of LS mean	(-18.37, 1.44)
Week 8 (MMRM)	
n	13
LS mean (SE)	85.04 (4.80)
95% CI of LS mean	(74.59, 95.49)
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	-7.18 (4.80)
95% CI of LS mean	(-17.63, 3.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Week 12 (MMRM)	
n	13
LS mean (SE)	92.74 (2.15)
95% CI of LS mean	(88.03, 97.44)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	0.51 (2.15)
95% CI of LS mean	(-4.19, 5.22)
Week 16 (MMRM)	
n	13
LS mean (SE)	94.87 (2.75)
95% CI of LS mean	(88.74, 101.00)
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	2.65 (2.75)
95% CI of LS mean	(-3.48, 8.78)
Week 24	
n	13
Mean (SD)	88.46 (14.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 24	
n	13
Mean (SD)	-3.76 (16.81)
Week 24 (MMRM)	
n	13
LS mean (SE)	88.46 (4.07)
95% CI of LS mean	(79.59, 97.33)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	-3.76 (4.07)
95% CI of LS mean	(-12.63, 5.11)
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-0.56 (1.84)
95% CI of LS mean	(-4.59, 3.48)
P-value	0.7678

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Body

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.4469
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Body domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Digestion

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.1011
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Digestion domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Eat

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.2829
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Eat domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Emotion

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.2133
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Emotion domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Physical

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.1715
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Physical domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Social

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.3944
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Social domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Treatment Burden

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.7733
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Treatment Burden domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	85.86 (21.14)
Week 4 (MMRM)	
n	11
LS mean (SE)	90.91 (8.20)
95% CI of LS mean	(56.07, 125.75)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	5.05 (8.20)
95% CI of LS mean	(-29.79, 39.89)
Week 8 (MMRM)	
n	11
LS mean (SE)	93.94 (5.47)
95% CI of LS mean	(24.50, 163.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	8.08 (5.47)
95% CI of LS mean	(-61.36, 77.52)
Week 12 (MMRM)	
n	11
LS mean (SE)	91.92 (8.00)
95% CI of LS mean	(26.07, 157.77)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	6.06 (8.00)
95% CI of LS mean	(-59.79, 71.91)
Week 16 (MMRM)	
n	11
LS mean (SE)	92.93 (6.68)
95% CI of LS mean	(8.03, 177.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	7.07 (6.68)
95% CI of LS mean	(-77.83, 91.97)
Week 24	
n	11
Mean (SD)	94.95 (9.11)
Absolute Change at Week 24	
n	11
Mean (SD)	9.09 (18.47)
Week 24 (MMRM)	
n	11
LS mean (SE)	94.95 (5.55)
95% CI of LS mean	(24.39, 165.51)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	9.09 (5.55)
95% CI of LS mean	(-61.47, 79.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	8.08 (6.01)
95% CI of LS mean	(-68.32, 84.49)
P-value	0.4073

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	95.37 (8.81)
Week 4 (MMRM)	
n	12
LS mean (SE)	91.67 (4.22)
95% CI of LS mean	(82.32, 101.02)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-3.70 (4.22)
95% CI of LS mean	(-13.05, 5.65)
Week 8 (MMRM)	
n	12
LS mean (SE)	87.04 (4.55)
95% CI of LS mean	(77.00, 97.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	-8.33 (4.55)
95% CI of LS mean	(-18.37, 1.70)
Week 12 (MMRM)	
n	12
LS mean (SE)	88.89 (3.47)
95% CI of LS mean	(81.24, 96.54)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	-6.48 (3.47)
95% CI of LS mean	(-14.13, 1.17)
Week 16 (MMRM)	
n	12
LS mean (SE)	96.30 (3.90)
95% CI of LS mean	(87.57, 105.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	0.93 (3.90)
95% CI of LS mean	(-7.80, 9.65)
Week 24	
n	13
Mean (SD)	94.02 (14.78)
Absolute Change at Week 24	
n	12
Mean (SD)	1.85 (11.44)
Week 24 (MMRM)	
n	13
LS mean (SE)	97.22 (3.72)
95% CI of LS mean	(88.88, 105.56)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	1.85 (3.72)
95% CI of LS mean	(-6.49, 10.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	1.39 (3.78)
95% CI of LS mean	(-7.09, 9.87)
P-value	0.7214

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	81.82 (22.92)
Week 4 (MMRM)	
n	11
LS mean (SE)	87.88 (3.06)
95% CI of LS mean	(81.02, 94.74)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	6.06 (3.06)
95% CI of LS mean	(-0.80, 12.92)
Week 8 (MMRM)	
n	11
LS mean (SE)	78.79 (7.04)
95% CI of LS mean	(62.86, 94.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	-3.03 (7.04)
95% CI of LS mean	(-18.96, 12.90)
Week 12 (MMRM)	
n	11
LS mean (SE)	78.79 (4.14)
95% CI of LS mean	(69.35, 88.22)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	-3.03 (4.14)
95% CI of LS mean	(-12.47, 6.40)
Week 16 (MMRM)	
n	11
LS mean (SE)	81.82 (6.69)
95% CI of LS mean	(66.78, 96.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	0.00 (6.69)
95% CI of LS mean	(-15.03, 15.03)
Week 24	
n	11
Mean (SD)	87.88 (16.82)
Absolute Change at Week 24	
n	11
Mean (SD)	6.06 (32.72)
Week 24 (MMRM)	
n	11
LS mean (SE)	87.88 (7.64)
95% CI of LS mean	(69.77, 105.99)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	6.06 (7.64)
95% CI of LS mean	(-12.05, 24.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	3.03 (5.68)
95% CI of LS mean	(-10.74, 16.80)
P-value	0.6123

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	80.56 (17.16)
Week 4 (MMRM)	
n	12
LS mean (SE)	91.67 (4.79)
95% CI of LS mean	(81.96, 101.38)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	11.11 (4.79)
95% CI of LS mean	(1.40, 20.82)
Week 8 (MMRM)	
n	12
LS mean (SE)	94.44 (4.79)
95% CI of LS mean	(84.73, 104.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	13.89 (4.79)
95% CI of LS mean	(4.18, 23.60)
Week 12 (MMRM)	
n	12
LS mean (SE)	86.11 (4.79)
95% CI of LS mean	(76.40, 95.82)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	5.56 (4.79)
95% CI of LS mean	(-4.16, 15.27)
Week 16 (MMRM)	
n	12
LS mean (SE)	91.67 (4.79)
95% CI of LS mean	(81.96, 101.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	11.11 (4.79)
95% CI of LS mean	(1.40, 20.82)
Week 24	
n	13
Mean (SD)	87.18 (21.68)
Absolute Change at Week 24	
n	12
Mean (SD)	8.33 (25.13)
Week 24 (MMRM)	
n	13
LS mean (SE)	88.89 (4.79)
95% CI of LS mean	(79.18, 98.60)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	8.33 (4.79)
95% CI of LS mean	(-1.38, 18.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	9.72 (3.88)
95% CI of LS mean	(1.65, 17.79)
P-value	0.0206

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	82.83 (22.42)
Week 4 (MMRM)	
n	11
LS mean (SE)	82.83 (5.87)
95% CI of LS mean	(69.73, 95.93)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	0.00 (5.87)
95% CI of LS mean	(-13.10, 13.10)
Week 8 (MMRM)	
n	11
LS mean (SE)	86.87 (4.90)
95% CI of LS mean	(75.62, 98.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	4.04 (4.90)
95% CI of LS mean	(-7.20, 15.29)
Week 12 (MMRM)	
n	11
LS mean (SE)	81.82 (5.66)
95% CI of LS mean	(69.11, 94.52)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	-1.01 (5.66)
95% CI of LS mean	(-13.72, 11.70)
Week 16 (MMRM)	
n	11
LS mean (SE)	76.77 (9.39)
95% CI of LS mean	(55.77, 97.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	-6.06 (9.39)
95% CI of LS mean	(-27.06, 14.94)
Week 24	
n	11
Mean (SD)	87.88 (23.02)
Absolute Change at Week 24	
n	11
Mean (SD)	5.05 (12.54)
Week 24 (MMRM)	
n	11
LS mean (SE)	87.88 (4.04)
95% CI of LS mean	(78.59, 97.16)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	5.05 (4.04)
95% CI of LS mean	(-4.23, 14.33)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	-0.51 (6.18)
95% CI of LS mean	(-14.44, 13.43)
P-value	0.9366

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	94.44 (8.86)
Week 4 (MMRM)	
n	12
LS mean (SE)	91.67 (2.25)
95% CI of LS mean	(86.54, 96.80)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-2.78 (2.25)
95% CI of LS mean	(-7.91, 2.35)
Week 8 (MMRM)	
n	12
LS mean (SE)	86.11 (7.94)
95% CI of LS mean	(68.62, 103.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	-8.33 (7.94)
95% CI of LS mean	(-25.82, 9.15)
Week 12 (MMRM)	
n	12
LS mean (SE)	87.04 (6.71)
95% CI of LS mean	(72.20, 101.87)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	-7.41 (6.71)
95% CI of LS mean	(-22.24, 7.43)
Week 16 (MMRM)	
n	12
LS mean (SE)	92.59 (5.15)
95% CI of LS mean	(81.01, 104.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	-1.85 (5.15)
95% CI of LS mean	(-13.44, 9.73)
Week 24	
n	13
Mean (SD)	94.87 (9.75)
Absolute Change at Week 24	
n	12
Mean (SD)	0.00 (14.21)
Week 24 (MMRM)	
n	13
LS mean (SE)	94.44 (4.74)
95% CI of LS mean	(83.74, 105.15)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	0.00 (4.74)
95% CI of LS mean	(-10.70, 10.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	-0.93 (4.77)
95% CI of LS mean	(-11.70, 9.85)
P-value	0.8503

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	79.55 (10.11)
Week 4 (MMRM)	
n	11
LS mean (SE)	81.06 (4.10)
95% CI of LS mean	(71.47, 90.65)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	1.52 (4.10)
95% CI of LS mean	(-8.07, 11.10)
Week 8 (MMRM)	
n	11
LS mean (SE)	82.20 (3.81)
95% CI of LS mean	(72.78, 91.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	2.65 (3.81)
95% CI of LS mean	(-6.76, 12.07)
Week 12 (MMRM)	
n	11
LS mean (SE)	84.09 (5.55)
95% CI of LS mean	(71.03, 97.15)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	4.55 (5.55)
95% CI of LS mean	(-8.51, 17.60)
Week 16 (MMRM)	
n	11
LS mean (SE)	79.55 (5.38)
95% CI of LS mean	(67.40, 91.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	0.00 (5.38)
95% CI of LS mean	(-12.15, 12.15)
Week 24	
n	11
Mean (SD)	80.68 (13.85)
Absolute Change at Week 24	
n	11
Mean (SD)	1.14 (6.99)
Week 24 (MMRM)	
n	11
LS mean (SE)	80.68 (2.20)
95% CI of LS mean	(75.40, 85.96)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	1.14 (2.20)
95% CI of LS mean	(-4.15, 6.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	0.57 (3.41)
95% CI of LS mean	(-7.33, 8.47)
P-value	0.8718

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	88.89 (8.01)
Week 4 (MMRM)	
n	12
LS mean (SE)	86.11 (3.44)
95% CI of LS mean	(78.50, 93.72)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-2.78 (3.44)
95% CI of LS mean	(-10.38, 4.83)
Week 8 (MMRM)	
n	12
LS mean (SE)	84.03 (3.49)
95% CI of LS mean	(76.27, 91.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	-4.86 (3.49)
95% CI of LS mean	(-12.62, 2.90)
Week 12 (MMRM)	
n	12
LS mean (SE)	84.03 (4.28)
95% CI of LS mean	(74.51, 93.54)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	-4.86 (4.28)
95% CI of LS mean	(-14.38, 4.66)
Week 16 (MMRM)	
n	12
LS mean (SE)	82.64 (3.73)
95% CI of LS mean	(74.29, 90.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	-6.25 (3.73)
95% CI of LS mean	(-14.60, 2.10)
Week 24	
n	13
Mean (SD)	84.62 (15.81)
Absolute Change at Week 24	
n	12
Mean (SD)	-3.47 (11.90)
Week 24 (MMRM)	
n	13
LS mean (SE)	85.42 (3.63)
95% CI of LS mean	(77.23, 93.61)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	-3.47 (3.63)
95% CI of LS mean	(-11.66, 4.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	-4.86 (3.57)
95% CI of LS mean	(-12.90, 3.17)
P-value	0.2054

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	88.38 (15.21)
Week 4 (MMRM)	
n	11
LS mean (SE)	89.39 (2.91)
95% CI of LS mean	(82.89, 95.90)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	1.01 (2.91)
95% CI of LS mean	(-5.50, 7.52)
Week 8 (MMRM)	
n	11
LS mean (SE)	90.91 (3.58)
95% CI of LS mean	(82.92, 98.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	2.53 (3.58)
95% CI of LS mean	(-5.47, 10.52)
Week 12 (MMRM)	
n	11
LS mean (SE)	91.92 (2.88)
95% CI of LS mean	(85.39, 98.45)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	3.54 (2.88)
95% CI of LS mean	(-2.99, 10.06)
Week 16 (MMRM)	
n	11
LS mean (SE)	90.40 (2.83)
95% CI of LS mean	(84.02, 96.79)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	2.02 (2.83)
95% CI of LS mean	(-4.36, 8.40)
Week 24	
n	11
Mean (SD)	93.94 (12.29)
Absolute Change at Week 24	
n	11
Mean (SD)	5.56 (10.54)
Week 24 (MMRM)	
n	11
LS mean (SE)	93.94 (2.83)
95% CI of LS mean	(87.36, 100.52)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	5.56 (2.83)
95% CI of LS mean	(-1.03, 12.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	3.79 (2.48)
95% CI of LS mean	(-1.79, 9.37)
P-value	0.1597

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	90.28 (11.87)
Week 4 (MMRM)	
n	12
LS mean (SE)	86.57 (2.44)
95% CI of LS mean	(81.16, 91.99)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-3.70 (2.44)
95% CI of LS mean	(-9.12, 1.71)
Week 8 (MMRM)	
n	12
LS mean (SE)	87.96 (4.30)
95% CI of LS mean	(78.48, 97.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	-2.31 (4.30)
95% CI of LS mean	(-11.80, 7.17)
Week 12 (MMRM)	
n	12
LS mean (SE)	84.26 (6.72)
95% CI of LS mean	(69.42, 99.10)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	-6.02 (6.72)
95% CI of LS mean	(-20.86, 8.82)
Week 16 (MMRM)	
n	12
LS mean (SE)	84.72 (4.47)
95% CI of LS mean	(74.87, 94.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	-5.56 (4.47)
95% CI of LS mean	(-15.40, 4.29)
Week 24	
n	13
Mean (SD)	90.60 (11.65)
Absolute Change at Week 24	
n	12
Mean (SD)	-0.46 (7.66)
Week 24 (MMRM)	
n	13
LS mean (SE)	89.81 (2.17)
95% CI of LS mean	(84.98, 94.64)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	-0.46 (2.17)
95% CI of LS mean	(-5.29, 4.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	-3.01 (2.87)
95% CI of LS mean	(-9.34, 3.32)
P-value	0.3169

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	74.03 (12.84)
Week 4 (MMRM)	
n	11
LS mean (SE)	75.76 (3.40)
95% CI of LS mean	(68.15, 83.36)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	1.73 (3.40)
95% CI of LS mean	(-5.88, 9.34)
Week 8 (MMRM)	
n	11
LS mean (SE)	76.19 (4.02)
95% CI of LS mean	(67.21, 85.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	2.16 (4.02)
95% CI of LS mean	(-6.81, 11.14)
Week 12 (MMRM)	
n	11
LS mean (SE)	76.19 (3.87)
95% CI of LS mean	(67.45, 84.94)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	2.16 (3.87)
95% CI of LS mean	(-6.58, 10.91)
Week 16 (MMRM)	
n	11
LS mean (SE)	78.79 (3.34)
95% CI of LS mean	(71.26, 86.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	4.76 (3.34)
95% CI of LS mean	(-2.77, 12.29)
Week 24	
n	11
Mean (SD)	79.87 (11.54)
Absolute Change at Week 24	
n	11
Mean (SD)	5.84 (17.80)
Week 24 (MMRM)	
n	11
LS mean (SE)	79.87 (3.66)
95% CI of LS mean	(71.61, 88.13)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	5.84 (3.66)
95% CI of LS mean	(-2.41, 14.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	5.30 (3.06)
95% CI of LS mean	(-1.56, 12.16)
P-value	0.1153

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	68.25 (17.97)
Week 4 (MMRM)	
n	12
LS mean (SE)	66.27 (4.03)
95% CI of LS mean	(57.31, 75.23)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-1.98 (4.03)
95% CI of LS mean	(-10.95, 6.98)
Week 8 (MMRM)	
n	12
LS mean (SE)	65.08 (5.34)
95% CI of LS mean	(53.03, 77.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	-3.17 (5.34)
95% CI of LS mean	(-15.22, 8.87)
Week 12 (MMRM)	
n	12
LS mean (SE)	67.86 (4.57)
95% CI of LS mean	(57.63, 78.09)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	-0.40 (4.57)
95% CI of LS mean	(-10.62, 9.83)
Week 16 (MMRM)	
n	12
LS mean (SE)	67.86 (5.13)
95% CI of LS mean	(56.48, 79.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	-0.40 (5.13)
95% CI of LS mean	(-11.77, 10.98)
Week 24	
n	13
Mean (SD)	72.53 (17.62)
Absolute Change at Week 24	
n	12
Mean (SD)	4.37 (18.44)
Week 24 (MMRM)	
n	13
LS mean (SE)	72.62 (4.86)
95% CI of LS mean	(61.81, 83.43)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	4.37 (4.86)
95% CI of LS mean	(-6.44, 15.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	1.98 (4.66)
95% CI of LS mean	(-8.39, 12.36)
P-value	0.6793

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	76.26 (18.61)
Week 4 (MMRM)	
n	11
LS mean (SE)	81.82 (6.41)
95% CI of LS mean	(67.50, 96.13)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	5.56 (6.41)
95% CI of LS mean	(-8.76, 19.87)
Week 8 (MMRM)	
n	11
LS mean (SE)	80.81 (3.73)
95% CI of LS mean	(72.34, 89.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	4.55 (3.73)
95% CI of LS mean	(-3.92, 13.02)
Week 12 (MMRM)	
n	11
LS mean (SE)	83.84 (4.43)
95% CI of LS mean	(73.84, 93.84)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	7.58 (4.43)
95% CI of LS mean	(-2.42, 17.57)
Week 16 (MMRM)	
n	11
LS mean (SE)	74.75 (5.03)
95% CI of LS mean	(63.01, 86.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	-1.52 (5.03)
95% CI of LS mean	(-13.25, 10.22)
Week 24	
n	11
Mean (SD)	82.83 (21.87)
Absolute Change at Week 24	
n	11
Mean (SD)	6.57 (10.78)
Week 24 (MMRM)	
n	11
LS mean (SE)	82.83 (3.67)
95% CI of LS mean	(74.20, 91.46)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	6.57 (3.67)
95% CI of LS mean	(-2.07, 15.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	2.53 (4.00)
95% CI of LS mean	(-7.04, 12.09)
P-value	0.5487

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	12
Mean (SD)	81.48 (20.83)
Week 4 (MMRM)	
n	12
LS mean (SE)	80.56 (4.31)
95% CI of LS mean	(71.03, 90.08)
Absolute Change at Week 4 (MMRM)	
n	12
LS mean (SE)	-0.93 (4.31)
95% CI of LS mean	(-10.46, 8.60)
Week 8 (MMRM)	
n	12
LS mean (SE)	87.04 (3.91)
95% CI of LS mean	(78.27, 95.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	12
LS mean (SE)	5.56 (3.91)
95% CI of LS mean	(-3.21, 14.32)
Week 12 (MMRM)	
n	12
LS mean (SE)	85.19 (3.09)
95% CI of LS mean	(78.30, 92.07)
Absolute Change at Week 12 (MMRM)	
n	12
LS mean (SE)	3.70 (3.09)
95% CI of LS mean	(-3.19, 10.59)
Week 16 (MMRM)	
n	12
LS mean (SE)	83.33 (7.88)
95% CI of LS mean	(65.94, 100.73)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	12
LS mean (SE)	1.85 (7.88)
95% CI of LS mean	(-15.54, 19.25)
Week 24	
n	13
Mean (SD)	85.47 (19.45)
Absolute Change at Week 24	
n	12
Mean (SD)	4.63 (18.63)
Week 24 (MMRM)	
n	13
LS mean (SE)	86.11 (4.93)
95% CI of LS mean	(75.17, 97.05)
Absolute Change at Week 24 (MMRM)	
n	12
LS mean (SE)	4.63 (4.93)
95% CI of LS mean	(-6.31, 15.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	12
LS mean (SE)	3.24 (4.12)
95% CI of LS mean	(-6.08, 12.56)
P-value	0.4514

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.7487
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Body (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.5876
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Digestion (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.6182
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Eat (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.9255
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Emotion (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.7776
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Health Perceptions (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.8032
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Physical (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.9151
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R School (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.9211
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Treatment Burden (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.6174
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Vitality (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.6889
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Weight (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	88.89 (18.59)
Week 4 (MMRM)	
n	11
LS mean (SE)	86.87 (3.58)
95% CI of LS mean	(79.28, 94.45)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	-2.02 (3.58)
95% CI of LS mean	(-9.61, 5.57)
Week 8 (MMRM)	
n	11
LS mean (SE)	93.94 (3.58)
95% CI of LS mean	(86.35, 101.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	5.05 (3.58)
95% CI of LS mean	(-2.54, 12.64)
Week 12 (MMRM)	
n	11
LS mean (SE)	90.91 (3.58)
95% CI of LS mean	(83.32, 98.49)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	2.02 (3.58)
95% CI of LS mean	(-5.57, 9.61)
Week 16 (MMRM)	
n	11
LS mean (SE)	92.93 (3.58)
95% CI of LS mean	(85.34, 100.52)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	4.04 (3.58)
95% CI of LS mean	(-3.55, 11.63)
Week 24	
n	11
Mean (SD)	91.92 (18.65)
Absolute Change at Week 24	
n	11
Mean (SD)	3.03 (7.19)
Week 24 (MMRM)	
n	11
LS mean (SE)	91.92 (3.58)
95% CI of LS mean	(84.33, 99.51)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	3.03 (3.58)
95% CI of LS mean	(-4.56, 10.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	3.54 (3.28)
95% CI of LS mean	(-3.65, 10.72)
P-value	0.3029

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	76.92 (29.90)
Week 4 (MMRM)	
n	13
LS mean (SE)	75.21 (3.86)
95% CI of LS mean	(66.78, 83.65)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-1.71 (3.86)
95% CI of LS mean	(-10.15, 6.73)
Week 8 (MMRM)	
n	13
LS mean (SE)	77.78 (3.39)
95% CI of LS mean	(70.40, 85.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	0.85 (3.39)
95% CI of LS mean	(-6.53, 8.23)
Week 12 (MMRM)	
n	13
LS mean (SE)	78.63 (4.59)
95% CI of LS mean	(68.63, 88.64)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	1.71 (4.59)
95% CI of LS mean	(-8.29, 11.71)
Week 16 (MMRM)	
n	13
LS mean (SE)	80.34 (2.72)
95% CI of LS mean	(74.37, 86.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	3.42 (2.72)
95% CI of LS mean	(-2.55, 9.39)
Week 24	
n	13
Mean (SD)	81.20 (28.83)
Absolute Change at Week 24	
n	13
Mean (SD)	4.27 (7.23)
Week 24 (MMRM)	
n	13
LS mean (SE)	81.20 (1.99)
95% CI of LS mean	(76.83, 85.56)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	4.27 (1.99)
95% CI of LS mean	(-0.09, 8.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	3.85 (1.98)
95% CI of LS mean	(-0.50, 8.20)
P-value	0.0777

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	76.77 (19.53)
Week 4 (MMRM)	
n	11
LS mean (SE)	76.77 (3.00)
95% CI of LS mean	(70.07, 83.47)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	0.00 (3.00)
95% CI of LS mean	(-6.70, 6.70)
Week 8 (MMRM)	
n	11
LS mean (SE)	78.79 (5.81)
95% CI of LS mean	(65.76, 91.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	2.02 (5.81)
95% CI of LS mean	(-11.01, 15.05)
Week 12 (MMRM)	
n	11
LS mean (SE)	79.80 (3.54)
95% CI of LS mean	(71.74, 87.85)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	3.03 (3.54)
95% CI of LS mean	(-5.02, 11.09)
Week 16 (MMRM)	
n	11
LS mean (SE)	81.82 (4.06)
95% CI of LS mean	(72.35, 91.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	5.05 (4.06)
95% CI of LS mean	(-4.41, 14.52)
Week 24	
n	11
Mean (SD)	81.82 (15.13)
Absolute Change at Week 24	
n	11
Mean (SD)	5.05 (12.54)
Week 24 (MMRM)	
n	11
LS mean (SE)	81.82 (3.52)
95% CI of LS mean	(73.52, 90.11)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	5.05 (3.52)
95% CI of LS mean	(-3.24, 13.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	5.05 (3.57)
95% CI of LS mean	(-3.43, 13.54)
P-value	0.2010

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	85.47 (15.31)
Week 4 (MMRM)	
n	13
LS mean (SE)	87.18 (2.39)
95% CI of LS mean	(81.85, 92.51)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	1.71 (2.39)
95% CI of LS mean	(-3.62, 7.04)
Week 8 (MMRM)	
n	13
LS mean (SE)	86.32 (3.52)
95% CI of LS mean	(78.53, 94.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	0.85 (3.52)
95% CI of LS mean	(-6.94, 8.65)
Week 12 (MMRM)	
n	13
LS mean (SE)	84.62 (3.74)
95% CI of LS mean	(76.45, 92.78)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	-0.85 (3.74)
95% CI of LS mean	(-9.02, 7.31)
Week 16 (MMRM)	
n	13
LS mean (SE)	88.03 (2.96)
95% CI of LS mean	(81.44, 94.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	2.56 (2.96)
95% CI of LS mean	(-4.03, 9.16)
Week 24	
n	13
Mean (SD)	81.20 (24.17)
Absolute Change at Week 24	
n	13
Mean (SD)	-4.27 (16.06)
Week 24 (MMRM)	
n	13
LS mean (SE)	81.20 (5.84)
95% CI of LS mean	(68.33, 94.07)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	-4.27 (5.84)
95% CI of LS mean	(-17.14, 8.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-0.85 (4.11)
95% CI of LS mean	(-10.00, 8.29)
P-value	0.8393

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	80.30 (32.33)
Week 4 (MMRM)	
n	11
LS mean (SE)	81.82 (9.10)
95% CI of LS mean	(44.14, 119.50)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	1.52 (9.10)
95% CI of LS mean	(-36.16, 39.19)
Week 8 (MMRM)	
n	11
LS mean (SE)	84.85 (8.07)
95% CI of LS mean	(44.31, 125.38)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	4.55 (8.07)
95% CI of LS mean	(-35.99, 45.08)
Week 12 (MMRM)	
n	11
LS mean (SE)	80.30 (8.10)
95% CI of LS mean	(50.20, 110.41)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	0.00 (8.10)
95% CI of LS mean	(-30.10, 30.10)
Week 16 (MMRM)	
n	11
LS mean (SE)	81.82 (9.97)
95% CI of LS mean	(46.06, 117.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	1.52 (9.97)
95% CI of LS mean	(-34.24, 37.27)
Week 24	
n	11
Mean (SD)	78.79 (36.58)
Absolute Change at Week 24	
n	11
Mean (SD)	-1.52 (21.67)
Week 24 (MMRM)	
n	11
LS mean (SE)	78.79 (9.63)
95% CI of LS mean	(46.17, 111.41)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-1.52 (9.63)
95% CI of LS mean	(-34.14, 31.11)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	0.00 (9.75)
95% CI of LS mean	(-34.37, 34.37)
P-value	>0.9999

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	91.03 (12.94)
Week 4 (MMRM)	
n	13
LS mean (SE)	87.18 (4.29)
95% CI of LS mean	(77.79, 96.57)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-3.85 (4.29)
95% CI of LS mean	(-13.24, 5.55)
Week 8 (MMRM)	
n	13
LS mean (SE)	91.03 (3.79)
95% CI of LS mean	(82.73, 99.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	0.00 (3.79)
95% CI of LS mean	(-8.30, 8.30)
Week 12 (MMRM)	
n	13
LS mean (SE)	87.18 (4.32)
95% CI of LS mean	(77.76, 96.60)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	-3.85 (4.32)
95% CI of LS mean	(-13.26, 5.57)
Week 16 (MMRM)	
n	13
LS mean (SE)	89.74 (3.57)
95% CI of LS mean	(81.94, 97.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	-1.28 (3.57)
95% CI of LS mean	(-9.09, 6.52)
Week 24	
n	13
Mean (SD)	91.03 (14.62)
Absolute Change at Week 24	
n	13
Mean (SD)	0.00 (9.62)
Week 24 (MMRM)	
n	13
LS mean (SE)	91.03 (2.72)
95% CI of LS mean	(85.07, 96.98)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	0.00 (2.72)
95% CI of LS mean	(-5.95, 5.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-0.64 (2.28)
95% CI of LS mean	(-5.65, 4.37)
P-value	0.7840

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	90.91 (10.01)
Week 4 (MMRM)	
n	11
LS mean (SE)	92.12 (3.66)
95% CI of LS mean	(83.88, 100.36)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	1.21 (3.66)
95% CI of LS mean	(-7.03, 9.45)
Week 8 (MMRM)	
n	11
LS mean (SE)	92.12 (2.21)
95% CI of LS mean	(87.13, 97.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	1.21 (2.21)
95% CI of LS mean	(-3.78, 6.21)
Week 12 (MMRM)	
n	11
LS mean (SE)	92.12 (2.91)
95% CI of LS mean	(85.35, 98.89)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	1.21 (2.91)
95% CI of LS mean	(-5.56, 7.98)
Week 16 (MMRM)	
n	11
LS mean (SE)	92.73 (2.69)
95% CI of LS mean	(86.40, 99.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	1.82 (2.69)
95% CI of LS mean	(-4.51, 8.15)
Week 24	
n	11
Mean (SD)	87.88 (13.27)
Absolute Change at Week 24	
n	11
Mean (SD)	-3.03 (11.30)
Week 24 (MMRM)	
n	11
LS mean (SE)	87.88 (3.52)
95% CI of LS mean	(79.89, 95.87)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-3.03 (3.52)
95% CI of LS mean	(-11.02, 4.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	-0.61 (2.60)
95% CI of LS mean	(-6.43, 5.22)
P-value	0.8204

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	88.72 (8.34)
Week 4 (MMRM)	
n	13
LS mean (SE)	87.69 (2.96)
95% CI of LS mean	(81.19, 94.20)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-1.03 (2.96)
95% CI of LS mean	(-7.53, 5.48)
Week 8 (MMRM)	
n	13
LS mean (SE)	88.21 (3.09)
95% CI of LS mean	(81.41, 95.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	-0.51 (3.09)
95% CI of LS mean	(-7.30, 6.28)
Week 12 (MMRM)	
n	13
LS mean (SE)	91.28 (1.51)
95% CI of LS mean	(87.91, 94.65)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	2.56 (1.51)
95% CI of LS mean	(-0.80, 5.93)
Week 16 (MMRM)	
n	13
LS mean (SE)	90.26 (2.73)
95% CI of LS mean	(84.27, 96.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	1.54 (2.73)
95% CI of LS mean	(-4.44, 7.52)
Week 24	
n	13
Mean (SD)	87.69 (12.72)
Absolute Change at Week 24	
n	13
Mean (SD)	-1.03 (11.17)
Week 24 (MMRM)	
n	13
LS mean (SE)	87.69 (3.16)
95% CI of LS mean	(80.79, 94.60)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	-1.03 (3.16)
95% CI of LS mean	(-7.93, 5.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	0.26 (2.71)
95% CI of LS mean	(-5.69, 6.20)
P-value	0.9264

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	88.89 (14.05)
Week 4 (MMRM)	
n	11
LS mean (SE)	80.81 (2.77)
95% CI of LS mean	(74.59, 87.03)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	-8.08 (2.77)
95% CI of LS mean	(-14.30, -1.86)
Week 8 (MMRM)	
n	11
LS mean (SE)	84.85 (3.03)
95% CI of LS mean	(78.05, 91.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	-4.04 (3.03)
95% CI of LS mean	(-10.84, 2.76)
Week 12 (MMRM)	
n	11
LS mean (SE)	88.89 (3.21)
95% CI of LS mean	(81.69, 96.09)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	0.00 (3.21)
95% CI of LS mean	(-7.20, 7.20)
Week 16 (MMRM)	
n	11
LS mean (SE)	90.91 (3.05)
95% CI of LS mean	(84.02, 97.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	2.02 (3.05)
95% CI of LS mean	(-4.87, 8.91)
Week 24	
n	11
Mean (SD)	86.87 (14.76)
Absolute Change at Week 24	
n	11
Mean (SD)	-2.02 (10.91)
Week 24 (MMRM)	
n	11
LS mean (SE)	86.87 (3.14)
95% CI of LS mean	(79.87, 93.87)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-2.02 (3.14)
95% CI of LS mean	(-9.02, 4.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	0.00 (2.22)
95% CI of LS mean	(-5.02, 5.02)
P-value	>0.9999

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	85.47 (15.31)
Week 4 (MMRM)	
n	13
LS mean (SE)	80.34 (5.55)
95% CI of LS mean	(68.21, 92.48)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-5.13 (5.55)
95% CI of LS mean	(-17.26, 7.01)
Week 8 (MMRM)	
n	13
LS mean (SE)	80.34 (5.30)
95% CI of LS mean	(68.67, 92.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	-5.13 (5.30)
95% CI of LS mean	(-16.80, 6.55)
Week 12 (MMRM)	
n	13
LS mean (SE)	84.62 (2.68)
95% CI of LS mean	(78.52, 90.71)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	-0.85 (2.68)
95% CI of LS mean	(-6.95, 5.24)
Week 16 (MMRM)	
n	13
LS mean (SE)	82.91 (3.71)
95% CI of LS mean	(74.81, 91.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	-2.56 (3.71)
95% CI of LS mean	(-10.66, 5.53)
Week 24	
n	13
Mean (SD)	89.74 (13.95)
Absolute Change at Week 24	
n	13
Mean (SD)	4.27 (11.60)
Week 24 (MMRM)	
n	13
LS mean (SE)	89.74 (2.91)
95% CI of LS mean	(83.39, 96.10)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	4.27 (2.91)
95% CI of LS mean	(-2.08, 10.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	0.85 (2.31)
95% CI of LS mean	(-4.24, 5.95)
P-value	0.7188

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	96.59 (4.49)
Week 4 (MMRM)	
n	11
LS mean (SE)	93.18 (2.45)
95% CI of LS mean	(87.71, 98.65)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	-3.41 (2.45)
95% CI of LS mean	(-8.88, 2.06)
Week 8 (MMRM)	
n	11
LS mean (SE)	90.53 (4.15)
95% CI of LS mean	(81.28, 99.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	-6.06 (4.15)
95% CI of LS mean	(-15.31, 3.19)
Week 12 (MMRM)	
n	11
LS mean (SE)	95.83 (2.95)
95% CI of LS mean	(89.25, 102.42)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	-0.76 (2.95)
95% CI of LS mean	(-7.34, 5.83)
Week 16 (MMRM)	
n	11
LS mean (SE)	96.97 (1.88)
95% CI of LS mean	(92.76, 101.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	0.38 (1.88)
95% CI of LS mean	(-3.83, 4.58)
Week 24	
n	11
Mean (SD)	96.21 (5.73)
Absolute Change at Week 24	
n	11
Mean (SD)	-0.38 (5.42)
Week 24 (MMRM)	
n	11
LS mean (SE)	96.21 (1.65)
95% CI of LS mean	(92.51, 99.91)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-0.38 (1.65)
95% CI of LS mean	(-4.08, 3.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	0.00 (1.68)
95% CI of LS mean	(-3.77, 3.77)
P-value	>0.9999

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	92.95 (9.97)
Week 4 (MMRM)	
n	13
LS mean (SE)	88.78 (4.40)
95% CI of LS mean	(79.20, 98.36)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-4.17 (4.40)
95% CI of LS mean	(-13.75, 5.41)
Week 8 (MMRM)	
n	13
LS mean (SE)	87.82 (4.08)
95% CI of LS mean	(78.93, 96.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	-5.13 (4.08)
95% CI of LS mean	(-14.02, 3.76)
Week 12 (MMRM)	
n	13
LS mean (SE)	94.87 (0.87)
95% CI of LS mean	(92.76, 96.98)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	1.92 (0.87)
95% CI of LS mean	(-0.18, 4.03)
Week 16 (MMRM)	
n	13
LS mean (SE)	90.38 (3.92)
95% CI of LS mean	(81.79, 98.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	-2.56 (3.92)
95% CI of LS mean	(-11.16, 6.03)
Week 24	
n	13
Mean (SD)	91.03 (19.08)
Absolute Change at Week 24	
n	13
Mean (SD)	-1.92 (13.35)
Week 24 (MMRM)	
n	13
LS mean (SE)	91.03 (3.92)
95% CI of LS mean	(82.46, 99.59)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	-1.92 (3.92)
95% CI of LS mean	(-10.49, 6.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-2.24 (3.02)
95% CI of LS mean	(-8.92, 4.44)
P-value	0.4739

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	85.61 (15.41)
Week 4 (MMRM)	
n	11
LS mean (SE)	80.30 (4.67)
95% CI of LS mean	(69.81, 90.79)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	-5.30 (4.67)
95% CI of LS mean	(-15.79, 5.19)
Week 8 (MMRM)	
n	11
LS mean (SE)	78.79 (4.59)
95% CI of LS mean	(68.53, 89.04)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	-6.82 (4.59)
95% CI of LS mean	(-17.07, 3.44)
Week 12 (MMRM)	
n	11
LS mean (SE)	79.04 (4.63)
95% CI of LS mean	(68.57, 89.51)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	-6.57 (4.63)
95% CI of LS mean	(-17.04, 3.90)
Week 16 (MMRM)	
n	11
LS mean (SE)	90.91 (3.83)
95% CI of LS mean	(82.15, 99.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	5.30 (3.83)
95% CI of LS mean	(-3.45, 14.06)
Week 24	
n	11
Mean (SD)	83.33 (18.63)
Absolute Change at Week 24	
n	11
Mean (SD)	-2.27 (19.75)
Week 24 (MMRM)	
n	11
LS mean (SE)	83.33 (5.43)
95% CI of LS mean	(71.20, 95.47)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-2.27 (5.43)
95% CI of LS mean	(-14.41, 9.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	1.52 (4.44)
95% CI of LS mean	(-8.48, 11.51)
P-value	0.7407

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	85.26 (13.67)
Week 4 (MMRM)	
n	13
LS mean (SE)	82.69 (5.11)
95% CI of LS mean	(71.52, 93.87)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	-2.56 (5.11)
95% CI of LS mean	(-13.74, 8.61)
Week 8 (MMRM)	
n	13
LS mean (SE)	82.69 (4.73)
95% CI of LS mean	(72.29, 93.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	-2.56 (4.73)
95% CI of LS mean	(-12.97, 7.84)
Week 12 (MMRM)	
n	13
LS mean (SE)	85.26 (2.88)
95% CI of LS mean	(78.95, 91.56)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	0.00 (2.88)
95% CI of LS mean	(-6.30, 6.30)
Week 16 (MMRM)	
n	13
LS mean (SE)	85.26 (3.13)
95% CI of LS mean	(78.29, 92.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	0.00 (3.13)
95% CI of LS mean	(-6.96, 6.96)
Week 24	
n	13
Mean (SD)	85.90 (19.66)
Absolute Change at Week 24	
n	13
Mean (SD)	0.64 (15.39)
Week 24 (MMRM)	
n	13
LS mean (SE)	85.90 (4.30)
95% CI of LS mean	(76.52, 95.28)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	0.64 (4.30)
95% CI of LS mean	(-8.74, 10.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	0.32 (3.10)
95% CI of LS mean	(-6.49, 7.13)
P-value	0.9194

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	69.70 (21.71)
Week 4 (MMRM)	
n	11
LS mean (SE)	76.77 (5.48)
95% CI of LS mean	(64.26, 89.28)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	7.07 (5.48)
95% CI of LS mean	(-5.44, 19.58)
Week 8 (MMRM)	
n	11
LS mean (SE)	74.75 (5.40)
95% CI of LS mean	(62.48, 87.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	5.05 (5.40)
95% CI of LS mean	(-7.21, 17.31)
Week 12 (MMRM)	
n	11
LS mean (SE)	72.73 (6.83)
95% CI of LS mean	(57.39, 88.07)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	3.03 (6.83)
95% CI of LS mean	(-12.31, 18.37)
Week 16 (MMRM)	
n	11
LS mean (SE)	77.78 (5.34)
95% CI of LS mean	(65.78, 89.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	8.08 (5.34)
95% CI of LS mean	(-3.91, 20.07)
Week 24	
n	11
Mean (SD)	76.77 (20.76)
Absolute Change at Week 24	
n	11
Mean (SD)	7.07 (22.37)
Week 24 (MMRM)	
n	11
LS mean (SE)	76.77 (5.82)
95% CI of LS mean	(63.69, 89.85)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	7.07 (5.82)
95% CI of LS mean	(-6.01, 20.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	7.58 (5.09)
95% CI of LS mean	(-3.88, 19.04)
P-value	0.1697

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	64.96 (26.00)
Week 4 (MMRM)	
n	13
LS mean (SE)	67.52 (3.99)
95% CI of LS mean	(58.73, 76.31)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	2.56 (3.99)
95% CI of LS mean	(-6.22, 11.35)
Week 8 (MMRM)	
n	13
LS mean (SE)	75.21 (6.23)
95% CI of LS mean	(61.45, 88.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	10.26 (6.23)
95% CI of LS mean	(-3.51, 24.02)
Week 12 (MMRM)	
n	13
LS mean (SE)	70.09 (3.76)
95% CI of LS mean	(61.84, 78.33)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	5.13 (3.76)
95% CI of LS mean	(-3.12, 13.37)
Week 16 (MMRM)	
n	13
LS mean (SE)	71.79 (2.43)
95% CI of LS mean	(66.34, 77.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	6.84 (2.43)
95% CI of LS mean	(1.38, 12.30)
Week 24	
n	13
Mean (SD)	70.09 (28.10)
Absolute Change at Week 24	
n	13
Mean (SD)	5.13 (14.78)
Week 24 (MMRM)	
n	13
LS mean (SE)	70.09 (4.16)
95% CI of LS mean	(60.98, 79.19)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	5.13 (4.16)
95% CI of LS mean	(-3.97, 14.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	5.98 (2.98)
95% CI of LS mean	(-0.61, 12.58)
P-value	0.0711

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	78.79 (11.08)
Week 4 (MMRM)	
n	11
LS mean (SE)	78.79 (3.87)
95% CI of LS mean	(69.96, 87.62)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	0.00 (3.87)
95% CI of LS mean	(-8.83, 8.83)
Week 8 (MMRM)	
n	11
LS mean (SE)	78.18 (2.14)
95% CI of LS mean	(73.39, 82.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	-0.61 (2.14)
95% CI of LS mean	(-5.40, 4.19)
Week 12 (MMRM)	
n	11
LS mean (SE)	78.18 (3.05)
95% CI of LS mean	(71.36, 85.01)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	-0.61 (3.05)
95% CI of LS mean	(-7.43, 6.22)
Week 16 (MMRM)	
n	11
LS mean (SE)	83.03 (4.75)
95% CI of LS mean	(72.21, 93.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	4.24 (4.75)
95% CI of LS mean	(-6.58, 15.07)
Week 24	
n	11
Mean (SD)	77.58 (15.57)
Absolute Change at Week 24	
n	11
Mean (SD)	-1.21 (12.59)
Week 24 (MMRM)	
n	11
LS mean (SE)	77.58 (3.82)
95% CI of LS mean	(69.05, 86.10)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	-1.21 (3.82)
95% CI of LS mean	(-9.74, 7.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	1.52 (3.58)
95% CI of LS mean	(-6.64, 9.67)
P-value	0.6822

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	80.00 (14.40)
Week 4 (MMRM)	
n	13
LS mean (SE)	81.03 (4.07)
95% CI of LS mean	(72.14, 89.91)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	1.03 (4.07)
95% CI of LS mean	(-7.86, 9.91)
Week 8 (MMRM)	
n	13
LS mean (SE)	81.54 (3.09)
95% CI of LS mean	(74.77, 88.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	1.54 (3.09)
95% CI of LS mean	(-5.23, 8.31)
Week 12 (MMRM)	
n	13
LS mean (SE)	82.05 (3.02)
95% CI of LS mean	(75.42, 88.68)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	2.05 (3.02)
95% CI of LS mean	(-4.58, 8.68)
Week 16 (MMRM)	
n	13
LS mean (SE)	80.00 (4.04)
95% CI of LS mean	(71.18, 88.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	0.00 (4.04)
95% CI of LS mean	(-8.82, 8.82)
Week 24	
n	13
Mean (SD)	78.46 (15.91)
Absolute Change at Week 24	
n	13
Mean (SD)	-1.54 (12.52)
Week 24 (MMRM)	
n	13
LS mean (SE)	78.46 (3.43)
95% CI of LS mean	(70.95, 85.97)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	-1.54 (3.43)
95% CI of LS mean	(-9.05, 5.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	-0.77 (3.21)
95% CI of LS mean	(-7.81, 6.28)
P-value	0.8149

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Baseline	
n	11
Mean (SD)	72.73 (29.13)
Week 4 (MMRM)	
n	11
LS mean (SE)	78.79 (6.60)
95% CI of LS mean	(63.77, 93.81)
Absolute Change at Week 4 (MMRM)	
n	11
LS mean (SE)	6.06 (6.60)
95% CI of LS mean	(-8.96, 21.08)
Week 8 (MMRM)	
n	11
LS mean (SE)	81.82 (6.81)
95% CI of LS mean	(66.39, 97.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 8 (MMRM)	
n	11
LS mean (SE)	9.09 (6.81)
95% CI of LS mean	(-6.34, 24.52)
Week 12 (MMRM)	
n	11
LS mean (SE)	75.76 (9.70)
95% CI of LS mean	(53.97, 97.55)
Absolute Change at Week 12 (MMRM)	
n	11
LS mean (SE)	3.03 (9.70)
95% CI of LS mean	(-18.76, 24.82)
Week 16 (MMRM)	
n	11
LS mean (SE)	75.76 (8.91)
95% CI of LS mean	(55.77, 95.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change at Week 16 (MMRM)	
n	11
LS mean (SE)	3.03 (8.91)
95% CI of LS mean	(-16.95, 23.01)
Week 24	
n	11
Mean (SD)	78.79 (34.23)
Absolute Change at Week 24	
n	11
Mean (SD)	6.06 (25.03)
Week 24 (MMRM)	
n	11
LS mean (SE)	78.79 (8.86)
95% CI of LS mean	(58.82, 98.75)
Absolute Change at Week 24 (MMRM)	
n	11
LS mean (SE)	6.06 (8.86)
95% CI of LS mean	(-13.90, 26.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 11
Absolute Change through Week 24 (MMRM)	
n	11
LS mean (SE)	4.55 (8.46)
95% CI of LS mean	(-14.51, 23.60)
P-value	0.6038

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Baseline	
n	13
Mean (SD)	56.41 (39.40)
Week 4 (MMRM)	
n	13
LS mean (SE)	64.10 (6.73)
95% CI of LS mean	(49.28, 78.93)
Absolute Change at Week 4 (MMRM)	
n	13
LS mean (SE)	7.69 (6.73)
95% CI of LS mean	(-7.14, 22.52)
Week 8 (MMRM)	
n	13
LS mean (SE)	61.54 (6.42)
95% CI of LS mean	(47.42, 75.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 8 (MMRM)	
n	13
LS mean (SE)	5.13 (6.42)
95% CI of LS mean	(-8.99, 19.24)
Week 12 (MMRM)	
n	13
LS mean (SE)	64.10 (7.68)
95% CI of LS mean	(47.17, 81.04)
Absolute Change at Week 12 (MMRM)	
n	13
LS mean (SE)	7.69 (7.68)
95% CI of LS mean	(-9.24, 24.63)
Week 16 (MMRM)	
n	13
LS mean (SE)	58.97 (8.73)
95% CI of LS mean	(39.56, 78.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change at Week 16 (MMRM)	
n	13
LS mean (SE)	2.56 (8.73)
95% CI of LS mean	(-16.85, 21.98)
Week 24	
n	13
Mean (SD)	61.54 (44.82)
Absolute Change at Week 24	
n	13
Mean (SD)	5.13 (18.49)
Week 24 (MMRM)	
n	13
LS mean (SE)	61.54 (5.35)
95% CI of LS mean	(49.74, 73.34)
Absolute Change at Week 24 (MMRM)	
n	13
LS mean (SE)	5.13 (5.35)
95% CI of LS mean	(-6.67, 16.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 13
Absolute Change through Week 24 (MMRM)	
n	13
LS mean (SE)	3.85 (5.74)
95% CI of LS mean	(-8.93, 16.62)
P-value	0.5179

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups for F/MF
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 1.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period for F/MF
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Any Pulmonary Exacerbation	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 1.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period for F/MF
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring Hospitalization	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 1.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period for F/MF
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring IV Antibiotic Therapy	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 1.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period for F/MF
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring Hospitalization or IV Antibiotic Therapy	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 1.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 1.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 1.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 1.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 1.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 1.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 1.2.2.14.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation during the PEx Analysis Period for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 1.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.15.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 1.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.16.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period for F/MF
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 1.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 1.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups for F/MF
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Zusatzanalysen zur Studie VX21-121-105

Table 1.3.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any TEAEs	22 (91.67)
Respiratory, thoracic and mediastinal disorders	17 (70.83)
Cough	11 (45.83)
Nasal congestion	4 (16.67)
Oropharyngeal pain	3 (12.50)
Infections and infestations	13 (54.17)
Upper respiratory tract infection	5 (20.83)
Gastrointestinal disorders	8 (33.33)
Abdominal pain upper	3 (12.50)
General disorders and administration site conditions	7 (29.17)
Pyrexia	4 (16.67)
Fatigue	3 (12.50)
Investigations	6 (25.00)
Nervous system disorders	4 (16.67)
Headache	3 (12.50)
Injury, poisoning and procedural complications	3 (12.50)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any TEAEs	22 (91.67)
Grade 1/Mild	7 (29.17)
Grade 2/Moderate	15 (62.50)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Respiratory, thoracic and mediastinal disorders	17 (70.83)
Grade 1/Mild	8 (33.33)
Grade 2/Moderate	9 (37.50)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Cough	11 (45.83)
Grade 1/Mild	4 (16.67)
Grade 2/Moderate	7 (29.17)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Nasal congestion	4 (16.67)
Grade 1/Mild	4 (16.67)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 24 n (%)
Oropharyngeal pain	3 (12.50)
Grade 1/Mild	3 (12.50)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Infections and infestations	13 (54.17)
Grade 1/Mild	7 (29.17)
Grade 2/Moderate	6 (25.00)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Upper respiratory tract infection	5 (20.83)
Grade 1/Mild	4 (16.67)
Grade 2/Moderate	1 (4.17)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Gastrointestinal disorders	8 (33.33)
Grade 1/Mild	6 (25.00)
Grade 2/Moderate	2 (8.33)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 24 n (%)
Abdominal pain upper	3 (12.50)
Grade 1/Mild	2 (8.33)
Grade 2/Moderate	1 (4.17)
Grade 3/Severe	0
Grade 4/Life Threatening	0
General disorders and administration site conditions	7 (29.17)
Grade 1/Mild	6 (25.00)
Grade 2/Moderate	1 (4.17)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Pyrexia	4 (16.67)
Grade 1/Mild	4 (16.67)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Fatigue	3 (12.50)
Grade 1/Mild	3 (12.50)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 24 n (%)
Investigations	6 (25.00)
Grade 1/Mild	5 (20.83)
Grade 2/Moderate	1 (4.17)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Nervous system disorders	4 (16.67)
Grade 1/Mild	4 (16.67)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Headache	3 (12.50)
Grade 1/Mild	3 (12.50)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Injury, poisoning and procedural complications	3 (12.50)
Grade 1/Mild	2 (8.33)
Grade 2/Moderate	1 (4.17)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Zusatzanalysen zur Studie VX21-121-105

Table 1.3.1.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 24 n (%)

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.1.3
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any Serious TEAEs	1 (4.17)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Zusatzanalysen zur Studie VX21-121-105

Table 1.3.1.4
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 24 n (%)

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Zusatzanalysen zur Studie VX21-121-105

Table 1.3.1.11
Study VX21-121-105: Summary of Death for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.

Zusatzanalysen zur Studie VX21-121-105

Table 1.3.1.12
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events for F/MF
Safety Set

	VNZ/TEZ/D-IVA N = 24 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	3 (12.50)
Subjects with non-severe events (Maximum Grade 1/2)	3 (12.50)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Zusatzanalysen zur Studie VX21-121-105

Table 1.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Subjects with any TEAEs	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.1083
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-
Respiratory, thoracic and mediastinal disorders	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.4755
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 11 n (%)
Subjects with any TEAEs	9 (81.82)
Respiratory, thoracic and mediastinal disorders	7 (63.64)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 13 n (%)
Subjects with any TEAEs	13 (100.00)
Respiratory, thoracic and mediastinal disorders	10 (76.92)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.1
Study VX21-121-105: Subgroup Factor Test for Grade 3/4/5 TEAEs by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Zusatzanalysen zur Studie VX21-121-105

Table 1.3.2.3.1
Study VX21-121-105: Subgroup Factor Test for Serious TEAEs by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.1
Study VX21-121-105: Subgroup Factor Test for TEAEs Leading to Treatment Discontinuation by SOC and PT for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor for F/MF
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 1.3.2.11.1
Study VX21-121-105: Subgroup Factor Test for Death for F/MF
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.1
Study VX21-121-105: Subgroup Factor Test for Treatment-emergent Infective Pulmonary Exacerbation Events for F/MF
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 17 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 7 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 11 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 13 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 15 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 1.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor for F/MF
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 6 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint for non-(F/MF)
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 54
Overall Study Observation Time	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
$ppFEV_1$ (percentage points)	
n	54
Mean (SD)	23.51 (2.46)
Median	24.14
Min, Max	12.00, 25.57
BMI (kg/m^2)	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
BMI z-score	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
Sweat Chloride (mmol/L)	
n	54
Mean (SD)	23.90 (1.61)
Median	24.14
Min, Max	16.14, 25.57

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 2.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint for non-(F/MF)
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 54
Weight (kg)	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
Weight z-score	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
Height (cm)	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
Height z-score	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
CFQ-R	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 2.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint for non-(F/MF)
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 54
Pulmonary Exacerbation	
n	54
Mean (SD)	24.20 (0.50)
Median	24.14
Min, Max	23.14, 25.57
$LCI_{2.5}$	
n	53
Mean (SD)	22.65 (4.60)
Median	24.14
Min, Max	3.86, 25.57
Safety	
n	54
Mean (SD)	23.95 (1.96)
Median	24.14
Min, Max	10.29, 25.57

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Zusatzanalysen zur Studie VX21-121-105

Table 2.1.2.1
Study VX21-121-105: Summary of Patients with Ongoing Antibiotic Medications at Baseline or at Week 24 non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline, N1	54
Subjects with 0 ongoing AB	46 (85.19)
Subjects with 1 ongoing AB	8 (14.81)
Subjects with ≥ 2 ongoing AB	0
Subjects with ≥ 1 ongoing IV AB	0
Week 24, N1	54
Subjects with 0 ongoing AB	49 (90.74)
Subjects with 1 ongoing AB	5 (9.26)
Subjects with ≥ 2 ongoing AB	0
Subjects with ≥ 1 ongoing IV AB	0

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- The ongoing antibiotic medications at baseline refer to those with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing antibiotic medications at Week 24 refer to those with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX21-121-105

Table 2.1.2.2
Study VX21-121-105: Summary of Patients with Antibiotic Medications during the Study Treatment Period non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
All subjects	54
Subjects with 0 AB	24 (44.44)
Subjects with 1-3 AB	28 (51.85)
Subjects with ≥ 4 AB	2 (3.70)
Subjects with 0 IV AB	51 (94.44)
Subjects with 1 IV AB	3 (5.56)
Subjects with ≥ 2 IV AB	0
Subjects with 0 ongoing antibiotic medication at baseline	46
Subjects with 0 AB	24 (52.17)
Subjects with 1-3 AB	21 (45.65)
Subjects with ≥ 4 AB	1 (2.17)
Subjects with 0 IV AB	43 (93.48)
Subjects with 1 IV AB	3 (6.52)
Subjects with ≥ 2 IV AB	0

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- Antibiotic medications during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX21-121-105

Table 2.1.3.1
Study VX21-121-105: Summary of Patients with Ongoing Physiotherapies at Baseline or at Week 24 non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline, N1	54
Subjects with 0 ongoing PT	12 (22.22)
Subjects with 1 ongoing PT	37 (68.52)
Subjects with ≥ 2 ongoing PT	5 (9.26)
Week 24, N1	54
Subjects with 0 ongoing PT	12 (22.22)
Subjects with 1 ongoing PT	37 (68.52)
Subjects with ≥ 2 ongoing PT	5 (9.26)

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- The ongoing physiotherapy at baseline is defined as a physiotherapy whose start date is prior to first dose date of study drug in the Treatment Period and the end date is ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing physiotherapy at Week 24 is defined as a physiotherapy whose start date is prior to Week 24 visit date and the end date is ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX21-121-105

Table 2.1.3.2
Study VX21-121-105: Summary of Patients with Physiotherapies during the Study Treatment Period non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
All subjects	54
Subjects with 0 PT	12 (22.22)
Subjects with 1 PT	37 (68.52)
Subjects with ≥ 2 PT	5 (9.26)
Subjects with 0 ongoing physiotherapies at baseline	12
Subjects with 0 PT	12 (100.00)
Subjects with 1 PT	0
Subjects with ≥ 2 PT	0

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- Physiotherapies during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX21-121-105

Table 2.1.4.1
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications at Baseline or at Week 24 non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline, N1	54
Subjects with 0 ongoing IM	4 (7.41)
Subjects with 1 ongoing IM	6 (11.11)
Subjects with ≥ 2 ongoing IM	44 (81.48)
Week 24, N1	54
Subjects with 0 ongoing IM	4 (7.41)
Subjects with 1 ongoing IM	6 (11.11)
Subjects with ≥ 2 ongoing IM	44 (81.48)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX21-121-105

Table 2.1.4.2
Study VX21-121-105: Summary of Patients with Inhaled Medications during the Study Treatment Period non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
All subjects	54
Subjects with 0 IM	4 (7.41)
Subjects with 1 IM	6 (11.11)
Subjects with ≥ 2 IM	44 (81.48)
Subjects with 0 ongoing inhaled medication at baseline	4
Subjects with 0 IM	4 (100.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	0

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 2.1.4.3
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications for Mucolytics at Baseline or at Week 24 non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline, N1	54
Subjects with 0 ongoing IM	9 (16.67)
Subjects with 1 ongoing IM	19 (35.19)
Subjects with ≥ 2 ongoing IM	26 (48.15)
Week 24, N1	54
Subjects with 0 ongoing IM	9 (16.67)
Subjects with 1 ongoing IM	19 (35.19)
Subjects with ≥ 2 ongoing IM	26 (48.15)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 2.1.4.4
Study VX21-121-105: Summary of Patients with Inhaled Medications for Mucolytics during the Study Treatment Period non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
All subjects	54
Subjects with 0 IM	9 (16.67)
Subjects with 1 IM	19 (35.19)
Subjects with ≥ 2 IM	26 (48.15)
Subjects with 0 ongoing inhaled medication at baseline	9
Subjects with 0 IM	9 (100.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	0

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Table 2.1.4.5
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications for Obstructive Airway Disease at Baseline or at Week 24 non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline, N1	54
Subjects with 0 ongoing IM	13 (24.07)
Subjects with 1 ongoing IM	24 (44.44)
Subjects with ≥ 2 ongoing IM	17 (31.48)
Week 24, N1	54
Subjects with 0 ongoing IM	13 (24.07)
Subjects with 1 ongoing IM	23 (42.59)
Subjects with ≥ 2 ongoing IM	18 (33.33)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 2.1.4.6
Study VX21-121-105: Summary of Patients with Inhaled Medications for Obstructive Airway Disease during the Study Treatment Period non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
All subjects	54
Subjects with 0 IM	13 (24.07)
Subjects with 1 IM	23 (42.59)
Subjects with ≥ 2 IM	18 (33.33)
Subjects with 0 ongoing inhaled medication at baseline	13
Subjects with 0 IM	13 (100.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	0

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing..
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX21-121-105

Table 2.1.5.1
Study VX21-121-105: Summary of Patients with Ongoing CF-related Medications at Baseline or at Week 24 non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline, N1	54
Subjects with 0 ongoing CF-related medications	1 (1.85)
Subjects with 1 ongoing CF-related medications	3 (5.56)
Subjects with 2 ongoing CF-related medications	2 (3.70)
Subjects with 3 ongoing CF-related medications	10 (18.52)
Subjects with 4 ongoing CF-related medications	12 (22.22)
Subjects with ≥5 ongoing CF-related medications	26 (48.15)
Week 24, N1	54
Subjects with 0 ongoing CF-related medications	1 (1.85)
Subjects with 1 ongoing CF-related medications	3 (5.56)
Subjects with 2 ongoing CF-related medications	4 (7.41)
Subjects with 3 ongoing CF-related medications	11 (20.37)
Subjects with 4 ongoing CF-related medications	12 (22.22)
Subjects with ≥5 ongoing CF-related medications	23 (42.59)

- CF-related medications: CF co-medications are defined as those medications with
o ATC level 2 names of "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES", "DIGESTIVES, INCL. ENZYMES", "ANTIBACTERIALS FOR SYSTEMIC USE", "DRUGS USED IN DIABETES", "BILE AND LIVER THERAPY", "GENERAL NUTRIENTS";
o or ATC level 3 names of "DRUGS FOR CONSTIPATION", "PROPULSIVES";
o or ATC level 4 names of "MUCOLYTICS".
In addition, the route of administration for "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES" and "MUCOLYTICS" requires to be "RESPIRATORY (INHALATION)" and the route for "ANTIBACTERIALS FOR SYSTEMIC USE" requires to be "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- The ongoing CF-related medications at baseline refer to those CF-related medications with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing CF-related medications at Week 24 refer to those CF-related medications with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX21-121-105

Table 2.2.1.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	53
Mean (SD)	102.11 (10.58)
Week 24	
n	50
Mean (SD)	101.07 (11.55)
Absolute Change at Week 24	
n	49
Mean (SD)	-1.83 (8.92)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	-0.91 (1.14)
95% CI of LS mean	(-3.20, 1.38)
P-value	0.4292

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	16.77 (2.14)
Week 24	
n	54
Mean (SD)	17.02 (2.45)
Absolute Change at Week 24	
n	54
Mean (SD)	0.24 (0.77)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	0.24 (0.10)
95% CI of LS mean	(0.04, 0.45)
P-value	0.0226

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 2.2.1.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	0.07 (0.86)
Week 24	
n	54
Mean (SD)	0.04 (0.93)
Absolute Change at Week 24	
n	54
Mean (SD)	-0.03 (0.31)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	-0.03 (0.04)
95% CI of LS mean	(-0.12, 0.05)
P-value	0.4250

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 2.2.1.4.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	35.22 (19.72)
Week 24	
n	52
Mean (SD)	27.88 (13.38)
Absolute Change at Week 24	
n	52
Mean (SD)	-7.53 (15.15)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	-7.87 (1.41)
95% CI of LS mean	(-10.70, -5.03)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.4.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Non-missing value at Week 24, N1	52
Number of subjects with missing value at Week 24	2
SwCl <60 mmol/L at Week 24, n (%)	51 (94.44)
95% CI for the proportion	(84.61, 98.84)

- N1: number of subjects with non-missing SwCl at Week 24
- n: number of subjects with SwCl <60 mmol/L
- 95% CI is based on the Clopper-Pearson method

Table 2.2.1.4.3
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Non-missing value at Week 24, N1	52
Number of subjects with missing value at Week 24	2
SwCl <30 mmol/L at Week 24, n (%)	33 (61.11)
95% CI for the proportion	(46.88, 74.08)

- N1: number of subjects with non-missing SwCl at Week 24
- n: number of subjects with SwCl <30 mmol/L
- 95% CI is based on the Clopper-Pearson method

Zusatzanalysen zur Studie VX21-121-105

Table 2.2.1.5
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	29.98 (8.23)
Week 24	
n	54
Mean (SD)	31.68 (9.01)
Absolute Change at Week 24	
n	54
Mean (SD)	1.70 (1.61)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	1.70 (0.21)
95% CI of LS mean	(1.28, 2.12)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 2.2.1.6
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	0.01 (0.91)
Week 24	
n	54
Mean (SD)	0.00 (0.96)
Absolute Change at Week 24	
n	54
Mean (SD)	-0.01 (0.23)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	-0.01 (0.03)
95% CI of LS mean	(-0.07, 0.05)
P-value	0.7305

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 2.2.1.7
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	132.36 (11.03)
Week 24	
n	54
Mean (SD)	135.05 (11.24)
Absolute Change at Week 24	
n	54
Mean (SD)	2.69 (1.08)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	2.69 (0.15)
95% CI of LS mean	(2.40, 2.98)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 2.2.1.8
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	-0.01 (0.96)
Week 24	
n	54
Mean (SD)	-0.01 (0.98)
Absolute Change at Week 24	
n	54
Mean (SD)	0.00 (0.18)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	0.00 (0.02)
95% CI of LS mean	(-0.05, 0.05)
P-value	0.9226

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.1.9
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	51
Mean (SD)	6.51 (0.53)
Week 24	
n	44
Mean (SD)	6.46 (0.52)
Absolute Change at Week 24	
n	42
Mean (SD)	-0.14 (0.52)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	-0.08 (0.06)
95% CI of LS mean	(-0.19, 0.04)
P-value	0.1827

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	82.53 (18.25)
Week 4 (MMRM)	
n	52
LS mean (SE)	83.33 (2.30)
95% CI of LS mean	(78.72, 87.95)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	0.80 (2.30)
95% CI of LS mean	(-3.82, 5.42)
Week 8 (MMRM)	
n	52
LS mean (SE)	85.10 (2.29)
95% CI of LS mean	(80.51, 89.69)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	2.56 (2.29)
95% CI of LS mean	(-2.03, 7.15)
Week 12 (MMRM)	
n	51
LS mean (SE)	89.85 (1.72)
95% CI of LS mean	(86.40, 93.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	7.32 (1.72)
95% CI of LS mean	(3.87, 10.77)
Week 16 (MMRM)	
n	52
LS mean (SE)	90.54 (1.76)
95% CI of LS mean	(87.01, 94.08)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	8.01 (1.76)
95% CI of LS mean	(4.48, 11.55)
Week 24	
n	54
Mean (SD)	84.26 (17.26)
Absolute Change at Week 24	
n	52
Mean (SD)	2.88 (21.32)
Week 24 (MMRM)	
n	54
LS mean (SE)	85.42 (2.21)
95% CI of LS mean	(80.99, 89.84)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	2.88 (2.21)
95% CI of LS mean	(-1.54, 7.31)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	5.45 (1.63)
95% CI of LS mean	(2.18, 8.71)
P-value	0.0015

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Respiration

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Body

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Digestion

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	51 (94.44)
Week 4	52 (96.30)
Absolute Change at Week 4	51 (94.44)
Week 8	52 (96.30)
Absolute Change at Week 8	51 (94.44)
Week 12	51 (94.44)
Absolute Change at Week 12	50 (92.59)
Week 16	52 (96.30)
Absolute Change at Week 16	51 (94.44)
Week 24	54 (100.00)
Absolute Change at Week 24	51 (94.44)
Through Week 24	54 (100.00)
Absolute Change through Week 24	51 (94.44)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Eat

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Emotion

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Physical

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Social

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	52 (96.30)
Week 4	52 (96.30)
Absolute Change at Week 4	52 (96.30)
Week 8	52 (96.30)
Absolute Change at Week 8	52 (96.30)
Week 12	51 (94.44)
Absolute Change at Week 12	51 (94.44)
Week 16	52 (96.30)
Absolute Change at Week 16	52 (96.30)
Week 24	54 (100.00)
Absolute Change at Week 24	52 (96.30)
Through Week 24	54 (100.00)
Absolute Change through Week 24	52 (96.30)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	85.51 (17.70)
Week 4 (MMRM)	
n	54
LS mean (SE)	85.08 (2.49)
95% CI of LS mean	(80.09, 90.07)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	-0.43 (2.49)
95% CI of LS mean	(-5.42, 4.56)
Week 8 (MMRM)	
n	54
LS mean (SE)	86.73 (2.09)
95% CI of LS mean	(82.54, 90.92)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	1.21 (2.09)
95% CI of LS mean	(-2.97, 5.40)
Week 12 (MMRM)	
n	53
LS mean (SE)	91.80 (1.72)
95% CI of LS mean	(88.36, 95.24)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	6.29 (1.72)
95% CI of LS mean	(2.84, 9.73)
Week 16 (MMRM)	
n	54
LS mean (SE)	91.11 (1.95)
95% CI of LS mean	(87.20, 95.02)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	5.60 (1.95)
95% CI of LS mean	(1.68, 9.51)
Week 24	
n	54
Mean (SD)	86.42 (17.19)
Absolute Change at Week 24	
n	54
Mean (SD)	0.91 (22.98)
Week 24 (MMRM)	
n	54
LS mean (SE)	86.42 (2.33)
95% CI of LS mean	(81.75, 91.09)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	0.91 (2.33)
95% CI of LS mean	(-3.76, 5.57)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	3.25 (1.75)
95% CI of LS mean	(-0.25, 6.75)
P-value	0.0682

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Respiration

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Body

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Digestion

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Eat

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Emotion

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Health Perception

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Physical

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: School

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Treatment Burden

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Vitality

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains) for non-(F/MF)
Full Analysis Set

Domain: Weight

	VNZ/TEZ/D-IVA N = 54 n (%)
Baseline	54 (100.00)
Week 4	54 (100.00)
Absolute Change at Week 4	54 (100.00)
Week 8	54 (100.00)
Absolute Change at Week 8	54 (100.00)
Week 12	53 (98.15)
Absolute Change at Week 12	53 (98.15)
Week 16	54 (100.00)
Absolute Change at Week 16	54 (100.00)
Week 24	54 (100.00)
Absolute Change at Week 24	54 (100.00)
Through Week 24	54 (100.00)
Absolute Change through Week 24	54 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	79.06 (25.34)
Week 4 (MMRM)	
n	52
LS mean (SE)	82.05 (2.78)
95% CI of LS mean	(76.47, 87.63)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	2.99 (2.78)
95% CI of LS mean	(-2.59, 8.57)
Week 8 (MMRM)	
n	52
LS mean (SE)	86.32 (2.50)
95% CI of LS mean	(81.30, 91.35)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	7.26 (2.50)
95% CI of LS mean	(2.24, 12.29)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Body

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	87.79 (2.23)
95% CI of LS mean	(83.31, 92.27)
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	8.73 (2.23)
95% CI of LS mean	(4.25, 13.21)
Week 16 (MMRM)	
n	52
LS mean (SE)	89.74 (2.02)
95% CI of LS mean	(85.68, 93.80)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	10.68 (2.02)
95% CI of LS mean	(6.62, 14.74)
Week 24	
n	54
Mean (SD)	85.19 (23.25)
Absolute Change at Week 24	
n	52
Mean (SD)	5.77 (27.35)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	84.83 (3.04)
95% CI of LS mean	(78.72, 90.93)
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	5.77 (3.04)
95% CI of LS mean	(-0.34, 11.87)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	8.23 (2.24)
95% CI of LS mean	(3.72, 12.73)
P-value	0.0006

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	51
Mean (SD)	79.08 (22.07)
Week 4 (MMRM)	
n	52
LS mean (SE)	71.90 (4.14)
95% CI of LS mean	(63.59, 80.20)
Absolute Change at Week 4 (MMRM)	
n	51
LS mean (SE)	-7.19 (4.14)
95% CI of LS mean	(-15.50, 1.12)
Week 8 (MMRM)	
n	52
LS mean (SE)	76.47 (3.38)
95% CI of LS mean	(69.67, 83.27)
Absolute Change at Week 8 (MMRM)	
n	51
LS mean (SE)	-2.61 (3.38)
95% CI of LS mean	(-9.41, 4.18)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Digestion

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	78.98 (2.87)
95% CI of LS mean	(73.22, 84.74)
Absolute Change at Week 12 (MMRM)	
n	50
LS mean (SE)	-0.10 (2.87)
95% CI of LS mean	(-5.87, 5.66)
Week 16 (MMRM)	
n	52
LS mean (SE)	82.35 (3.10)
95% CI of LS mean	(76.13, 88.58)
Absolute Change at Week 16 (MMRM)	
n	51
LS mean (SE)	3.27 (3.10)
95% CI of LS mean	(-2.96, 9.49)
Week 24	
n	54
Mean (SD)	83.33 (23.12)
Absolute Change at Week 24	
n	51
Mean (SD)	3.92 (25.51)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	83.01 (3.06)
95% CI of LS mean	(76.85, 89.16)
Absolute Change at Week 24 (MMRM)	
n	51
LS mean (SE)	3.92 (3.06)
95% CI of LS mean	(-2.23, 10.08)
Absolute Change through Week 24 (MMRM)	
n	51
LS mean (SE)	3.59 (2.64)
95% CI of LS mean	(-1.72, 8.91)
P-value	0.1800

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	78.21 (22.33)
Week 4 (MMRM)	
n	52
LS mean (SE)	79.27 (2.55)
95% CI of LS mean	(74.15, 84.40)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	1.07 (2.55)
95% CI of LS mean	(-4.05, 6.19)
Week 8 (MMRM)	
n	52
LS mean (SE)	76.92 (2.58)
95% CI of LS mean	(71.74, 82.11)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	-1.28 (2.58)
95% CI of LS mean	(-6.47, 3.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Eat

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	82.90 (2.68)
95% CI of LS mean	(77.52, 88.29)
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	4.70 (2.68)
95% CI of LS mean	(-0.69, 10.09)
Week 16 (MMRM)	
n	52
LS mean (SE)	84.19 (2.37)
95% CI of LS mean	(79.43, 88.94)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	5.98 (2.37)
95% CI of LS mean	(1.23, 10.74)
Week 24	
n	54
Mean (SD)	87.65 (18.65)
Absolute Change at Week 24	
n	52
Mean (SD)	9.40 (18.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	87.61 (2.09)
95% CI of LS mean	(83.41, 91.80)
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	9.40 (2.09)
95% CI of LS mean	(5.21, 13.60)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	7.69 (1.85)
95% CI of LS mean	(3.99, 11.40)
P-value	0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	73.00 (15.09)
Week 4 (MMRM)	
n	52
LS mean (SE)	73.34 (1.85)
95% CI of LS mean	(69.63, 77.05)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	0.34 (1.85)
95% CI of LS mean	(-3.36, 4.05)
Week 8 (MMRM)	
n	52
LS mean (SE)	75.64 (1.88)
95% CI of LS mean	(71.86, 79.43)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	2.64 (1.88)
95% CI of LS mean	(-1.14, 6.43)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Emotion

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	77.57 (1.91)
95% CI of LS mean	(73.73, 81.41)
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	4.57 (1.91)
95% CI of LS mean	(0.73, 8.41)
Week 16 (MMRM)	
n	52
LS mean (SE)	79.81 (1.94)
95% CI of LS mean	(75.91, 83.70)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	6.81 (1.94)
95% CI of LS mean	(2.92, 10.70)
Week 24	
n	54
Mean (SD)	78.47 (15.07)
Absolute Change at Week 24	
n	52
Mean (SD)	6.01 (12.77)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	79.01 (1.61)
95% CI of LS mean	(75.77, 82.24)
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	6.01 (1.61)
95% CI of LS mean	(2.77, 9.25)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	6.41 (1.58)
95% CI of LS mean	(3.24, 9.58)
P-value	0.0002

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	86.32 (12.90)
Week 4 (MMRM)	
n	52
LS mean (SE)	86.54 (1.84)
95% CI of LS mean	(82.84, 90.24)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	0.21 (1.84)
95% CI of LS mean	(-3.49, 3.92)
Week 8 (MMRM)	
n	52
LS mean (SE)	83.80 (2.30)
95% CI of LS mean	(79.19, 88.42)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	-2.52 (2.30)
95% CI of LS mean	(-7.13, 2.09)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Physical

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	85.53 (2.11)
95% CI of LS mean	(81.31, 89.76)
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	-0.79 (2.11)
95% CI of LS mean	(-5.02, 3.44)
Week 16 (MMRM)	
n	52
LS mean (SE)	89.00 (2.05)
95% CI of LS mean	(84.88, 93.11)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	2.67 (2.05)
95% CI of LS mean	(-1.45, 6.79)
Week 24	
n	54
Mean (SD)	89.61 (15.49)
Absolute Change at Week 24	
n	52
Mean (SD)	3.74 (16.01)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	90.06 (1.99)
95% CI of LS mean	(86.08, 94.05)
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	3.74 (1.99)
95% CI of LS mean	(-0.25, 7.73)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	3.21 (1.68)
95% CI of LS mean	(-0.16, 6.57)
P-value	0.0617

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	65.20 (20.52)
Week 4 (MMRM)	
n	52
LS mean (SE)	66.94 (1.99)
95% CI of LS mean	(62.93, 70.95)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	1.74 (1.99)
95% CI of LS mean	(-2.27, 5.75)
Week 8 (MMRM)	
n	52
LS mean (SE)	68.41 (2.23)
95% CI of LS mean	(63.93, 72.88)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	3.21 (2.23)
95% CI of LS mean	(-1.27, 7.68)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Social

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	72.64 (2.11)
95% CI of LS mean	(68.40, 76.87)
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	7.43 (2.11)
95% CI of LS mean	(3.20, 11.67)
Week 16 (MMRM)	
n	52
LS mean (SE)	72.53 (2.54)
95% CI of LS mean	(67.42, 77.63)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	7.33 (2.54)
95% CI of LS mean	(2.22, 12.43)
Week 24	
n	54
Mean (SD)	74.43 (15.49)
Absolute Change at Week 24	
n	52
Mean (SD)	10.26 (20.60)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	75.46 (1.97)
95% CI of LS mean	(71.49, 79.43)
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	10.26 (1.97)
95% CI of LS mean	(6.29, 14.23)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	8.79 (2.06)
95% CI of LS mean	(4.65, 12.94)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	52
Mean (SD)	75.21 (21.96)
Week 4 (MMRM)	
n	52
LS mean (SE)	78.21 (2.29)
95% CI of LS mean	(73.61, 82.80)
Absolute Change at Week 4 (MMRM)	
n	52
LS mean (SE)	2.99 (2.29)
95% CI of LS mean	(-1.60, 7.58)
Week 8 (MMRM)	
n	52
LS mean (SE)	77.67 (2.41)
95% CI of LS mean	(72.83, 82.52)
Absolute Change at Week 8 (MMRM)	
n	52
LS mean (SE)	2.46 (2.41)
95% CI of LS mean	(-2.39, 7.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Treatment Burden

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	51
LS mean (SE)	79.26 (2.55)
95% CI of LS mean	(74.14, 84.37)
Absolute Change at Week 12 (MMRM)	
n	51
LS mean (SE)	4.04 (2.55)
95% CI of LS mean	(-1.07, 9.16)
Week 16 (MMRM)	
n	52
LS mean (SE)	79.70 (2.83)
95% CI of LS mean	(74.01, 85.39)
Absolute Change at Week 16 (MMRM)	
n	52
LS mean (SE)	4.49 (2.83)
95% CI of LS mean	(-1.20, 10.18)
Week 24	
n	54
Mean (SD)	80.66 (21.93)
Absolute Change at Week 24	
n	52
Mean (SD)	5.34 (21.73)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	80.56 (2.67)
95% CI of LS mean	(75.20, 85.91)
Absolute Change at Week 24 (MMRM)	
n	52
LS mean (SE)	5.34 (2.67)
95% CI of LS mean	(-0.02, 10.70)
Absolute Change through Week 24 (MMRM)	
n	52
LS mean (SE)	4.91 (2.43)
95% CI of LS mean	(0.03, 9.79)
P-value	0.0484

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	79.12 (26.50)
Week 4 (MMRM)	
n	54
LS mean (SE)	81.69 (1.92)
95% CI of LS mean	(77.84, 85.54)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	2.57 (1.92)
95% CI of LS mean	(-1.28, 6.42)
Week 8 (MMRM)	
n	54
LS mean (SE)	81.28 (2.28)
95% CI of LS mean	(76.71, 85.84)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	2.16 (2.28)
95% CI of LS mean	(-2.41, 6.73)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	84.11 (2.01)
95% CI of LS mean	(80.07, 88.15)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	5.00 (2.01)
95% CI of LS mean	(0.96, 9.04)
Week 16 (MMRM)	
n	54
LS mean (SE)	85.80 (2.26)
95% CI of LS mean	(81.26, 90.35)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	6.69 (2.26)
95% CI of LS mean	(2.14, 11.23)
Week 24	
n	54
Mean (SD)	82.51 (19.85)
Absolute Change at Week 24	
n	54
Mean (SD)	3.40 (20.77)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	82.51 (2.12)
95% CI of LS mean	(78.26, 86.76)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	3.40 (2.12)
95% CI of LS mean	(-0.85, 7.64)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	5.04 (1.90)
95% CI of LS mean	(1.23, 8.85)
P-value	0.0106

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	82.51 (17.48)
Week 4 (MMRM)	
n	54
LS mean (SE)	83.13 (2.31)
95% CI of LS mean	(78.50, 87.76)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	0.62 (2.31)
95% CI of LS mean	(-4.01, 5.25)
Week 8 (MMRM)	
n	54
LS mean (SE)	82.51 (1.87)
95% CI of LS mean	(78.75, 86.27)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	0.00 (1.87)
95% CI of LS mean	(-3.76, 3.76)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	84.69 (1.89)
95% CI of LS mean	(80.90, 88.48)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	2.18 (1.89)
95% CI of LS mean	(-1.61, 5.97)
Week 16 (MMRM)	
n	54
LS mean (SE)	85.60 (1.61)
95% CI of LS mean	(82.37, 88.83)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	3.09 (1.61)
95% CI of LS mean	(-0.14, 6.32)
Week 24	
n	54
Mean (SD)	81.48 (14.80)
Absolute Change at Week 24	
n	54
Mean (SD)	-1.03 (17.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	81.48 (1.80)
95% CI of LS mean	(77.86, 85.10)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	-1.03 (1.80)
95% CI of LS mean	(-4.65, 2.59)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	1.03 (1.47)
95% CI of LS mean	(-1.92, 3.98)
P-value	0.4872

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	76.54 (26.01)
Week 4 (MMRM)	
n	54
LS mean (SE)	75.62 (2.29)
95% CI of LS mean	(71.02, 80.21)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	-0.93 (2.29)
95% CI of LS mean	(-5.52, 3.67)
Week 8 (MMRM)	
n	54
LS mean (SE)	75.31 (2.66)
95% CI of LS mean	(69.97, 80.65)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	-1.23 (2.66)
95% CI of LS mean	(-6.57, 4.10)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	75.56 (2.46)
95% CI of LS mean	(70.63, 80.49)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	-0.98 (2.46)
95% CI of LS mean	(-5.91, 3.95)
Week 16 (MMRM)	
n	54
LS mean (SE)	78.70 (1.83)
95% CI of LS mean	(75.04, 82.37)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	2.16 (1.83)
95% CI of LS mean	(-1.50, 5.82)
Week 24	
n	54
Mean (SD)	80.25 (22.68)
Absolute Change at Week 24	
n	54
Mean (SD)	3.70 (19.60)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	80.25 (2.26)
95% CI of LS mean	(75.71, 84.79)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	3.70 (2.26)
95% CI of LS mean	(-0.83, 8.24)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	2.93 (1.75)
95% CI of LS mean	(-0.57, 6.43)
P-value	0.0990

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	85.09 (14.10)
Week 4 (MMRM)	
n	54
LS mean (SE)	85.80 (1.22)
95% CI of LS mean	(83.36, 88.24)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	0.71 (1.22)
95% CI of LS mean	(-1.73, 3.15)
Week 8 (MMRM)	
n	54
LS mean (SE)	85.25 (1.22)
95% CI of LS mean	(82.81, 87.69)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	0.15 (1.22)
95% CI of LS mean	(-2.29, 2.60)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	88.38 (1.32)
95% CI of LS mean	(85.72, 91.03)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	3.28 (1.32)
95% CI of LS mean	(0.63, 5.94)
Week 16 (MMRM)	
n	54
LS mean (SE)	88.64 (1.31)
95% CI of LS mean	(86.01, 91.27)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	3.55 (1.31)
95% CI of LS mean	(0.92, 6.18)
Week 24	
n	54
Mean (SD)	88.64 (10.33)
Absolute Change at Week 24	
n	54
Mean (SD)	3.55 (12.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	88.64 (1.23)
95% CI of LS mean	(86.18, 91.11)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	3.55 (1.23)
95% CI of LS mean	(1.08, 6.02)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	3.55 (0.90)
95% CI of LS mean	(1.74, 5.36)
P-value	0.0003

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	86.63 (13.54)
Week 4 (MMRM)	
n	54
LS mean (SE)	83.33 (1.87)
95% CI of LS mean	(79.59, 87.08)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	-3.29 (1.87)
95% CI of LS mean	(-7.04, 0.45)
Week 8 (MMRM)	
n	54
LS mean (SE)	87.45 (1.50)
95% CI of LS mean	(84.44, 90.46)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	0.82 (1.50)
95% CI of LS mean	(-2.19, 3.83)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	87.00 (1.75)
95% CI of LS mean	(83.50, 90.50)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	0.37 (1.75)
95% CI of LS mean	(-3.13, 3.88)
Week 16 (MMRM)	
n	54
LS mean (SE)	89.30 (1.37)
95% CI of LS mean	(86.55, 92.05)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	2.67 (1.37)
95% CI of LS mean	(-0.08, 5.43)
Week 24	
n	54
Mean (SD)	87.04 (17.77)
Absolute Change at Week 24	
n	54
Mean (SD)	0.41 (18.31)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	87.04 (2.30)
95% CI of LS mean	(82.43, 91.65)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	0.41 (2.30)
95% CI of LS mean	(-4.20, 5.02)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	1.54 (1.50)
95% CI of LS mean	(-1.47, 4.56)
P-value	0.3089

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	90.66 (15.03)
Week 4 (MMRM)	
n	54
LS mean (SE)	91.13 (1.44)
95% CI of LS mean	(88.24, 94.02)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	0.46 (1.44)
95% CI of LS mean	(-2.43, 3.35)
Week 8 (MMRM)	
n	54
LS mean (SE)	90.60 (1.35)
95% CI of LS mean	(87.89, 93.30)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	-0.07 (1.35)
95% CI of LS mean	(-2.77, 2.64)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	94.03 (1.06)
95% CI of LS mean	(91.90, 96.16)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	3.37 (1.06)
95% CI of LS mean	(1.24, 5.49)
Week 16 (MMRM)	
n	54
LS mean (SE)	94.52 (1.35)
95% CI of LS mean	(91.80, 97.25)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	3.86 (1.35)
95% CI of LS mean	(1.13, 6.58)
Week 24	
n	54
Mean (SD)	91.59 (14.96)
Absolute Change at Week 24	
n	54
Mean (SD)	0.93 (12.00)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	91.59 (1.54)
95% CI of LS mean	(88.49, 94.69)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	0.93 (1.54)
95% CI of LS mean	(-2.17, 4.02)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	2.39 (1.02)
95% CI of LS mean	(0.34, 4.44)
P-value	0.0231

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	78.24 (18.34)
Week 4 (MMRM)	
n	54
LS mean (SE)	82.87 (1.79)
95% CI of LS mean	(79.28, 86.46)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	4.63 (1.79)
95% CI of LS mean	(1.04, 8.22)
Week 8 (MMRM)	
n	54
LS mean (SE)	81.64 (2.03)
95% CI of LS mean	(77.56, 85.71)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	3.40 (2.03)
95% CI of LS mean	(-0.68, 7.47)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	84.91 (1.65)
95% CI of LS mean	(81.60, 88.22)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	6.67 (1.65)
95% CI of LS mean	(3.36, 9.98)
Week 16 (MMRM)	
n	54
LS mean (SE)	83.80 (2.02)
95% CI of LS mean	(79.74, 87.85)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	5.56 (2.02)
95% CI of LS mean	(1.50, 9.61)
Week 24	
n	54
Mean (SD)	81.79 (16.27)
Absolute Change at Week 24	
n	54
Mean (SD)	3.55 (14.53)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	81.79 (1.69)
95% CI of LS mean	(78.40, 85.18)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	3.55 (1.69)
95% CI of LS mean	(0.16, 6.93)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	4.55 (1.54)
95% CI of LS mean	(1.47, 7.64)
P-value	0.0046

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	70.37 (20.13)
Week 4 (MMRM)	
n	54
LS mean (SE)	78.19 (1.67)
95% CI of LS mean	(74.84, 81.53)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	7.82 (1.67)
95% CI of LS mean	(4.47, 11.16)
Week 8 (MMRM)	
n	54
LS mean (SE)	79.42 (2.56)
95% CI of LS mean	(74.29, 84.56)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	9.05 (2.56)
95% CI of LS mean	(3.92, 14.19)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	77.57 (2.52)
95% CI of LS mean	(72.52, 82.61)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	7.20 (2.52)
95% CI of LS mean	(2.15, 12.24)
Week 16 (MMRM)	
n	54
LS mean (SE)	78.19 (1.99)
95% CI of LS mean	(74.20, 82.18)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	7.82 (1.99)
95% CI of LS mean	(3.83, 11.81)
Week 24	
n	54
Mean (SD)	80.45 (19.05)
Absolute Change at Week 24	
n	54
Mean (SD)	10.08 (19.46)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	80.45 (2.32)
95% CI of LS mean	(75.79, 85.11)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	10.08 (2.32)
95% CI of LS mean	(5.42, 14.74)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	8.95 (1.88)
95% CI of LS mean	(5.18, 12.72)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	75.43 (12.27)
Week 4 (MMRM)	
n	54
LS mean (SE)	73.09 (1.68)
95% CI of LS mean	(69.73, 76.45)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	-2.35 (1.68)
95% CI of LS mean	(-5.71, 1.02)
Week 8 (MMRM)	
n	54
LS mean (SE)	73.21 (1.35)
95% CI of LS mean	(70.51, 75.91)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	-2.22 (1.35)
95% CI of LS mean	(-4.93, 0.48)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	76.36 (1.43)
95% CI of LS mean	(73.48, 79.24)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	0.93 (1.43)
95% CI of LS mean	(-1.95, 3.81)
Week 16 (MMRM)	
n	54
LS mean (SE)	77.41 (1.35)
95% CI of LS mean	(74.71, 80.11)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	1.98 (1.35)
95% CI of LS mean	(-0.73, 4.68)
Week 24	
n	54
Mean (SD)	74.81 (13.56)
Absolute Change at Week 24	
n	54
Mean (SD)	-0.62 (14.72)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	74.81 (1.75)
95% CI of LS mean	(71.30, 78.33)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	-0.62 (1.75)
95% CI of LS mean	(-4.13, 2.89)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	0.68 (1.28)
95% CI of LS mean	(-1.89, 3.24)
P-value	0.5975

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Baseline	
n	54
Mean (SD)	71.60 (35.71)
Week 4 (MMRM)	
n	54
LS mean (SE)	70.37 (3.65)
95% CI of LS mean	(63.05, 77.69)
Absolute Change at Week 4 (MMRM)	
n	54
LS mean (SE)	-1.23 (3.65)
95% CI of LS mean	(-8.55, 6.08)
Week 8 (MMRM)	
n	54
LS mean (SE)	77.16 (3.19)
95% CI of LS mean	(70.76, 83.56)
Absolute Change at Week 8 (MMRM)	
n	54
LS mean (SE)	5.56 (3.19)
95% CI of LS mean	(-0.84, 11.95)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 54
Week 12 (MMRM)	
n	53
LS mean (SE)	75.26 (3.10)
95% CI of LS mean	(69.04, 81.48)
Absolute Change at Week 12 (MMRM)	
n	53
LS mean (SE)	3.65 (3.10)
95% CI of LS mean	(-2.57, 9.88)
Week 16 (MMRM)	
n	54
LS mean (SE)	77.78 (2.98)
95% CI of LS mean	(71.79, 83.76)
Absolute Change at Week 16 (MMRM)	
n	54
LS mean (SE)	6.17 (2.98)
95% CI of LS mean	(0.19, 12.16)
Week 24	
n	54
Mean (SD)	76.54 (30.80)
Absolute Change at Week 24	
n	54
Mean (SD)	4.94 (30.65)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 54
Week 24 (MMRM)	
n	54
LS mean (SE)	76.54 (3.43)
95% CI of LS mean	(69.66, 83.42)
Absolute Change at Week 24 (MMRM)	
n	54
LS mean (SE)	4.94 (3.43)
95% CI of LS mean	(-1.94, 11.82)
Absolute Change through Week 24 (MMRM)	
n	54
LS mean (SE)	5.56 (2.76)
95% CI of LS mean	(0.02, 11.09)
P-value	0.0493

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.1.13
Study VX21-121-105: Summary of Pulmonary Exacerbations through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54
Total number of days (years) of the PEx analysis period	9148 (27.2)
Pulmonary exacerbations	
Number of subjects with events, n (%)	4 (7.41)
Total number of events	4
Observed event rate per year	0.15
Pulmonary exacerbations requiring hospitalization	
Number of subjects with events, n (%)	1 (1.85)
Total number of events	1
Observed event rate per year	0.04
Pulmonary exacerbations requiring IV antibiotic therapy	
Number of subjects with events, n (%)	1 (1.85)
Total number of events	1
Observed event rate per year	0.04
Pulmonary exacerbations requiring hospitalization or IV antibiotic therapy	
Number of subjects with events, n (%)	1 (1.85)
Total number of events	1
Observed event rate per year	0.04

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Zusatzanalysen zur Studie VX21-121-105

Table 2.2.1.14.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Any Pulmonary Exacerbation	
Overall	
Subjects with Events	4 (7.41)
Subjects Censored	50 (92.59)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Zusatzanalysen zur Studie VX21-121-105

Table 2.2.1.15.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization	
Overall	
Subjects with Events	1 (1.85)
Subjects Censored	53 (98.15)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring hospitalization during the PEx analysis period were censored at the PEx analysis period end date.

Zusatzanalysen zur Studie VX21-121-105

Table 2.2.1.16.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24 non-(F/MF)
Full Analysis Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics	
Overall	
Subjects with Events	1 (1.85)
Subjects Censored	53 (98.15)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring IV antibiotics during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.4166
Region (North America vs. Rest of the World)	0.7840
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline $ppFEV_1$ as covariate.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	100.32 (10.87)
Week 24	
n	25
Mean (SD)	100.13 (12.23)
Absolute Change at Week 24	
n	25
Mean (SD)	-0.55 (10.22)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.31 (2.01)
95% CI of LS mean	(-3.82, 4.44)
P-value	0.8786

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	103.96 (10.14)
Week 24	
n	25
Mean (SD)	102.00 (11.00)
Absolute Change at Week 24	
n	24
Mean (SD)	-3.16 (7.31)
Absolute Change through Week 24 (MMRM)	
n	25
LS mean (SE)	-2.20 (1.02)
95% CI of LS mean	(-4.31, -0.10)
P-value	0.0410

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	100.90 (10.83)
Week 24	
n	34
Mean (SD)	99.65 (12.11)
Absolute Change at Week 24	
n	34
Mean (SD)	-1.55 (5.64)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	-0.21 (0.97)
95% CI of LS mean	(-2.18, 1.76)
P-value	0.8278

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	17
Mean (SD)	104.66 (9.85)
Week 24	
n	16
Mean (SD)	104.07 (9.96)
Absolute Change at Week 24	
n	15
Mean (SD)	-2.47 (14.04)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	-2.48 (3.60)
95% CI of LS mean	(-10.29, 5.32)
P-value	0.5028

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit, with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.2.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0484
Region (North America vs. Rest of the World)	0.5146
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline BMI as covariate.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	17.26 (2.44)
Week 24	
n	27
Mean (SD)	17.38 (2.77)
Absolute Change at Week 24	
n	27
Mean (SD)	0.12 (0.67)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.12 (0.12)
95% CI of LS mean	(-0.14, 0.37)
P-value	0.3559

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	16.29 (1.70)
Week 24	
n	27
Mean (SD)	16.65 (2.08)
Absolute Change at Week 24	
n	27
Mean (SD)	0.37 (0.86)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.37 (0.16)
95% CI of LS mean	(0.03, 0.70)
P-value	0.0321

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	17.16 (2.03)
Week 24	
n	36
Mean (SD)	17.57 (2.36)
Absolute Change at Week 24	
n	36
Mean (SD)	0.41 (0.87)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	0.41 (0.14)
95% CI of LS mean	(0.12, 0.70)
P-value	0.0077

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	16.01 (2.21)
Week 24	
n	18
Mean (SD)	15.92 (2.32)
Absolute Change at Week 24	
n	18
Mean (SD)	-0.09 (0.35)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-0.09 (0.08)
95% CI of LS mean	(-0.26, 0.09)
P-value	0.3027

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0363
Region (North America vs. Rest of the World)	0.0822
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline BMI z-score as covariate.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	0.28 (0.87)
Week 24	
n	27
Mean (SD)	0.18 (0.95)
Absolute Change at Week 24	
n	27
Mean (SD)	-0.09 (0.22)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-0.09 (0.04)
95% CI of LS mean	(-0.18, -0.01)
P-value	0.0342

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	-0.14 (0.80)
Week 24	
n	27
Mean (SD)	-0.11 (0.91)
Absolute Change at Week 24	
n	27
Mean (SD)	0.03 (0.37)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.03 (0.07)
95% CI of LS mean	(-0.12, 0.17)
P-value	0.7181

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	0.22 (0.73)
Week 24	
n	36
Mean (SD)	0.25 (0.78)
Absolute Change at Week 24	
n	36
Mean (SD)	0.03 (0.33)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	0.03 (0.06)
95% CI of LS mean	(-0.08, 0.15)
P-value	0.5607

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	-0.23 (1.02)
Week 24	
n	18
Mean (SD)	-0.40 (1.08)
Absolute Change at Week 24	
n	18
Mean (SD)	-0.17 (0.20)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-0.17 (0.05)
95% CI of LS mean	(-0.26, -0.07)
P-value	0.0022

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.4.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9397
Region (North America vs. Rest of the World)	0.1599
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline sweat chloride as covariate.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	36.28 (22.93)
Week 24	
n	26
Mean (SD)	29.06 (15.81)
Absolute Change at Week 24	
n	26
Mean (SD)	-7.58 (16.99)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-8.28 (2.64)
95% CI of LS mean	(-13.75, -2.80)
P-value	0.0047

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	34.17 (16.27)
Week 24	
n	26
Mean (SD)	26.69 (10.61)
Absolute Change at Week 24	
n	26
Mean (SD)	-7.48 (13.40)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-7.52 (1.29)
95% CI of LS mean	(-10.18, -4.87)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	37.40 (22.45)
Week 24	
n	35
Mean (SD)	30.04 (15.23)
Absolute Change at Week 24	
n	35
Mean (SD)	-7.46 (16.92)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	-8.25 (2.02)
95% CI of LS mean	(-12.37, -4.13)
P-value	0.0003

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	30.86 (12.05)
Week 24	
n	17
Mean (SD)	23.41 (6.79)
Absolute Change at Week 24	
n	17
Mean (SD)	-7.68 (11.12)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-7.21 (1.30)
95% CI of LS mean	(-9.96, -4.45)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.4.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 2.2.2.4.2.1
Study VX21-121-105: Subgroup Factor Test for
Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.5525
Region (North America vs. Rest of the World)	>0.9999
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Chi-square test.

Table 2.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Non-missing value at Week 24, N1	26
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	25 (92.59)
95% CI for the proportion	(75.71, 99.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 2.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Non-missing value at Week 24, N1	26
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	26 (96.30)
95% CI for the proportion	(81.03, 99.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 2.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Non-missing value at Week 24, N1	35
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	34 (94.44)
95% CI for the proportion	(81.34, 99.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 2.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Non-missing value at Week 24, N1	17
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	17 (94.44)
95% CI for the proportion	(72.71, 99.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 2.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 2.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 2.2.2.4.3.1
Study VX21-121-105: Subgroup Factor Test for
Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.7801
Region (North America vs. Rest of the World)	0.2363
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Chi-square test.

Table 2.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Non-missing value at Week 24, N1	26
Number of subjects with missing value at Week 24	1
SwCl <30 mmol/L at Week 24, n (%)	16 (59.26)
95% CI for the proportion	(38.80, 77.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 2.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Non-missing value at Week 24, N1	26
Number of subjects with missing value at Week 24	1
SwCl <30 mmol/L at Week 24, n (%)	17 (62.96)
95% CI for the proportion	(42.37, 80.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 2.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Non-missing value at Week 24, N1	35
Number of subjects with missing value at Week 24	1
SwCl <30 mmol/L at Week 24, n (%)	20 (55.56)
95% CI for the proportion	(38.10, 72.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 2.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Non-missing value at Week 24, N1	17
Number of subjects with missing value at Week 24	1
SwCl <30 mmol/L at Week 24, n (%)	13 (72.22)
95% CI for the proportion	(46.52, 90.31)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 2.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 2.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 2.2.2.5.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1199
Region (North America vs. Rest of the World)	0.5170
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline weight as covariate.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	30.81 (9.08)
Week 24	
n	27
Mean (SD)	32.31 (10.02)
Absolute Change at Week 24	
n	27
Mean (SD)	1.50 (1.63)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	1.50 (0.29)
95% CI of LS mean	(0.90, 2.09)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	29.14 (7.36)
Week 24	
n	27
Mean (SD)	31.05 (8.01)
Absolute Change at Week 24	
n	27
Mean (SD)	1.91 (1.59)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	1.91 (0.30)
95% CI of LS mean	(1.28, 2.53)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	31.21 (8.44)
Week 24	
n	36
Mean (SD)	33.12 (9.19)
Absolute Change at Week 24	
n	36
Mean (SD)	1.91 (1.82)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	1.91 (0.29)
95% CI of LS mean	(1.32, 2.51)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	27.52 (7.39)
Week 24	
n	18
Mean (SD)	28.80 (8.12)
Absolute Change at Week 24	
n	18
Mean (SD)	1.28 (1.00)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	1.28 (0.19)
95% CI of LS mean	(0.86, 1.70)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.6.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0354
Region (North America vs. Rest of the World)	0.5321
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline weight z-score as covariate.
- N/C: model does not converge.

Table 2.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	0.14 (0.93)
Week 24	
n	27
Mean (SD)	0.08 (1.01)
Absolute Change at Week 24	
n	27
Mean (SD)	-0.06 (0.19)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-0.06 (0.04)
95% CI of LS mean	(-0.13, 0.02)
P-value	0.1215

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	-0.13 (0.89)
Week 24	
n	27
Mean (SD)	-0.09 (0.92)
Absolute Change at Week 24	
n	27
Mean (SD)	0.04 (0.25)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.04 (0.05)
95% CI of LS mean	(-0.06, 0.14)
P-value	0.4684

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	0.06 (0.87)
Week 24	
n	36
Mean (SD)	0.08 (0.92)
Absolute Change at Week 24	
n	36
Mean (SD)	0.02 (0.26)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	0.02 (0.04)
95% CI of LS mean	(-0.07, 0.11)
P-value	0.6759

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	-0.10 (1.00)
Week 24	
n	18
Mean (SD)	-0.17 (1.04)
Absolute Change at Week 24	
n	18
Mean (SD)	-0.07 (0.14)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-0.07 (0.03)
95% CI of LS mean	(-0.14, 0.00)
P-value	0.0566

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.7.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.2332
Region (North America vs. Rest of the World)	0.2349
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline height as covariate.
- N/C: model does not converge.

Table 2.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	132.11 (10.56)
Week 24	
n	27
Mean (SD)	134.71 (10.61)
Absolute Change at Week 24	
n	27
Mean (SD)	2.60 (1.01)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	2.60 (0.20)
95% CI of LS mean	(2.20, 3.01)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	132.62 (11.68)
Week 24	
n	27
Mean (SD)	135.40 (12.03)
Absolute Change at Week 24	
n	27
Mean (SD)	2.78 (1.15)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	2.78 (0.22)
95% CI of LS mean	(2.33, 3.22)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	133.52 (11.51)
Week 24	
n	36
Mean (SD)	135.94 (11.67)
Absolute Change at Week 24	
n	36
Mean (SD)	2.42 (1.05)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	2.42 (0.17)
95% CI of LS mean	(2.07, 2.77)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	130.05 (9.91)
Week 24	
n	18
Mean (SD)	133.28 (10.40)
Absolute Change at Week 24	
n	18
Mean (SD)	3.23 (0.94)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	3.23 (0.22)
95% CI of LS mean	(2.75, 3.71)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.8.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.2884
Region (North America vs. Rest of the World)	0.3205
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and subgroup as fixed effect and baseline height z-score as covariate.
- N/C: model does not converge.

Table 2.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	-0.08 (0.94)
Week 24	
n	27
Mean (SD)	-0.07 (0.93)
Absolute Change at Week 24	
n	27
Mean (SD)	0.01 (0.18)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.01 (0.03)
95% CI of LS mean	(-0.06, 0.08)
P-value	0.7602

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	0.05 (0.99)
Week 24	
n	27
Mean (SD)	0.05 (1.05)
Absolute Change at Week 24	
n	27
Mean (SD)	-0.01 (0.19)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-0.01 (0.04)
95% CI of LS mean	(-0.08, 0.07)
P-value	0.8675

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	-0.07 (1.02)
Week 24	
n	36
Mean (SD)	-0.10 (1.05)
Absolute Change at Week 24	
n	36
Mean (SD)	-0.03 (0.18)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	-0.03 (0.03)
95% CI of LS mean	(-0.09, 0.03)
P-value	0.3505

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	0.10 (0.84)
Week 24	
n	18
Mean (SD)	0.17 (0.84)
Absolute Change at Week 24	
n	18
Mean (SD)	0.07 (0.16)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	0.07 (0.04)
95% CI of LS mean	(-0.02, 0.15)
P-value	0.1099

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect for visit, with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 2.2.2.9.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0004
Region (North America vs. Rest of the World)	0.8921
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline $LCI_{2.5}$ as covariate.
- N/C: model does not converge.

Table 2.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	25
Mean (SD)	6.47 (0.46)
Week 24	
n	21
Mean (SD)	6.31 (0.32)
Absolute Change at Week 24	
n	20
Mean (SD)	-0.28 (0.51)
Absolute Change through Week 24 (MMRM)	
n	20
LS mean (SE)	-0.23 (0.06)
95% CI of LS mean	(-0.36, -0.11)
P-value	0.0013

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	6.55 (0.60)
Week 24	
n	23
Mean (SD)	6.59 (0.64)
Absolute Change at Week 24	
n	22
Mean (SD)	-0.01 (0.50)
Absolute Change through Week 24 (MMRM)	
n	22
LS mean (SE)	0.08 (0.08)
95% CI of LS mean	(-0.09, 0.26)
P-value	0.3289

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	33
Mean (SD)	6.50 (0.54)
Week 24	
n	29
Mean (SD)	6.48 (0.54)
Absolute Change at Week 24	
n	27
Mean (SD)	-0.13 (0.52)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-0.07 (0.07)
95% CI of LS mean	(-0.22, 0.07)
P-value	0.3069

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	6.52 (0.52)
Week 24	
n	15
Mean (SD)	6.42 (0.52)
Absolute Change at Week 24	
n	15
Mean (SD)	-0.16 (0.54)
Absolute Change through Week 24 (MMRM)	
n	15
LS mean (SE)	-0.05 (0.11)
95% CI of LS mean	(-0.28, 0.18)
P-value	0.6513

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit, with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3174
Region (North America vs. Rest of the World)	0.1710
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Respiratory domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	82.37 (16.55)
Week 4 (MMRM)	
n	26
LS mean (SE)	82.37 (2.05)
95% CI of LS mean	(78.13, 86.62)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	0.00 (2.05)
95% CI of LS mean	(-4.25, 4.25)
Week 8 (MMRM)	
n	26
LS mean (SE)	83.65 (2.78)
95% CI of LS mean	(77.92, 89.39)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	1.28 (2.78)
95% CI of LS mean	(-4.45, 7.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	87.91 (2.26)
95% CI of LS mean	(83.26, 92.57)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	5.54 (2.26)
95% CI of LS mean	(0.88, 10.20)
Week 16 (MMRM)	
n	26
LS mean (SE)	88.78 (2.52)
95% CI of LS mean	(83.59, 93.97)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	6.41 (2.52)
95% CI of LS mean	(1.22, 11.60)
Week 24	
n	27
Mean (SD)	84.26 (17.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	2.56 (20.11)
Week 24 (MMRM)	
n	27
LS mean (SE)	84.94 (3.42)
95% CI of LS mean	(77.88, 91.99)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	2.56 (3.42)
95% CI of LS mean	(-4.49, 9.62)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	4.49 (2.38)
95% CI of LS mean	(-0.44, 9.42)
P-value	0.0725

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	82.69 (20.13)
Week 4 (MMRM)	
n	26
LS mean (SE)	84.29 (3.74)
95% CI of LS mean	(76.59, 92.00)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	1.60 (3.74)
95% CI of LS mean	(-6.11, 9.31)
Week 8 (MMRM)	
n	26
LS mean (SE)	86.54 (3.65)
95% CI of LS mean	(79.01, 94.07)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	3.85 (3.65)
95% CI of LS mean	(-3.68, 11.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	91.67 (2.16)
95% CI of LS mean	(87.22, 96.11)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	8.97 (2.16)
95% CI of LS mean	(4.53, 13.42)
Week 16 (MMRM)	
n	26
LS mean (SE)	92.31 (2.24)
95% CI of LS mean	(87.70, 96.92)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	9.62 (2.24)
95% CI of LS mean	(5.01, 14.23)
Week 24	
n	27
Mean (SD)	84.26 (17.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	3.21 (22.86)
Week 24 (MMRM)	
n	27
LS mean (SE)	85.90 (3.05)
95% CI of LS mean	(79.61, 92.18)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	3.21 (3.05)
95% CI of LS mean	(-3.08, 9.49)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	6.41 (2.25)
95% CI of LS mean	(1.78, 11.04)
P-value	0.0087

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	81.25 (19.25)
Week 4 (MMRM)	
n	36
LS mean (SE)	79.86 (2.91)
95% CI of LS mean	(73.95, 85.78)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-1.39 (2.91)
95% CI of LS mean	(-7.30, 4.53)
Week 8 (MMRM)	
n	36
LS mean (SE)	83.33 (2.86)
95% CI of LS mean	(77.53, 89.14)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	2.08 (2.86)
95% CI of LS mean	(-3.72, 7.89)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	88.89 (2.08)
95% CI of LS mean	(84.67, 93.11)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	7.64 (2.08)
95% CI of LS mean	(3.42, 11.86)
Week 16 (MMRM)	
n	36
LS mean (SE)	90.05 (2.04)
95% CI of LS mean	(85.90, 94.20)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	8.80 (2.04)
95% CI of LS mean	(4.65, 12.95)
Week 24	
n	36
Mean (SD)	83.10 (16.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	1.85 (21.56)
Week 24 (MMRM)	
n	36
LS mean (SE)	83.10 (2.67)
95% CI of LS mean	(77.69, 88.52)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	1.85 (2.67)
95% CI of LS mean	(-3.56, 7.27)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	5.32 (1.95)
95% CI of LS mean	(1.36, 9.29)
P-value	0.0100

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	85.42 (15.96)
Week 4 (MMRM)	
n	16
LS mean (SE)	91.15 (3.14)
95% CI of LS mean	(84.39, 97.91)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	5.73 (3.14)
95% CI of LS mean	(-1.03, 12.49)
Week 8 (MMRM)	
n	16
LS mean (SE)	89.06 (2.92)
95% CI of LS mean	(82.65, 95.48)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	3.65 (2.92)
95% CI of LS mean	(-2.77, 10.06)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	92.28 (3.37)
95% CI of LS mean	(85.02, 99.55)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	6.86 (3.37)
95% CI of LS mean	(-0.40, 14.13)
Week 16 (MMRM)	
n	16
LS mean (SE)	91.67 (4.08)
95% CI of LS mean	(82.81, 100.52)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	6.25 (4.08)
95% CI of LS mean	(-2.61, 15.11)
Week 24	
n	18
Mean (SD)	86.57 (18.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	5.21 (21.27)
Week 24 (MMRM)	
n	18
LS mean (SE)	90.63 (4.33)
95% CI of LS mean	(81.27, 99.98)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	5.21 (4.33)
95% CI of LS mean	(-4.14, 14.56)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	5.73 (3.59)
95% CI of LS mean	(-2.17, 13.63)
P-value	0.1389

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.6496
Region (North America vs. Rest of the World)	0.1402
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Respiratory domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	84.77 (16.20)
Week 4 (MMRM)	
n	27
LS mean (SE)	83.54 (3.18)
95% CI of LS mean	(77.01, 90.07)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-1.23 (3.18)
95% CI of LS mean	(-7.77, 5.30)
Week 8 (MMRM)	
n	27
LS mean (SE)	85.80 (2.91)
95% CI of LS mean	(79.82, 91.79)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	1.03 (2.91)
95% CI of LS mean	(-4.96, 7.02)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	92.33 (1.74)
95% CI of LS mean	(88.75, 95.91)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	7.56 (1.74)
95% CI of LS mean	(3.98, 11.14)
Week 16 (MMRM)	
n	27
LS mean (SE)	88.19 (3.28)
95% CI of LS mean	(81.44, 94.94)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	3.42 (3.28)
95% CI of LS mean	(-3.33, 10.16)
Week 24	
n	27
Mean (SD)	87.65 (15.59)
Absolute Change at Week 24	
n	27
Mean (SD)	2.88 (18.39)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 24 (MMRM)	
n	27
LS mean (SE)	87.65 (2.85)
95% CI of LS mean	(81.80, 93.51)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	2.88 (2.85)
95% CI of LS mean	(-2.97, 8.74)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	3.15 (2.47)
95% CI of LS mean	(-1.93, 8.22)
P-value	0.2135

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	86.26 (19.36)
Week 4 (MMRM)	
n	27
LS mean (SE)	86.63 (3.82)
95% CI of LS mean	(78.77, 94.49)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	0.37 (3.82)
95% CI of LS mean	(-7.49, 8.23)
Week 8 (MMRM)	
n	27
LS mean (SE)	87.65 (3.01)
95% CI of LS mean	(81.47, 93.84)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	1.40 (3.01)
95% CI of LS mean	(-4.79, 7.58)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	91.15 (2.90)
95% CI of LS mean	(85.19, 97.12)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	4.90 (2.90)
95% CI of LS mean	(-1.07, 10.86)
Week 16 (MMRM)	
n	27
LS mean (SE)	94.03 (2.00)
95% CI of LS mean	(89.92, 98.15)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	7.78 (2.00)
95% CI of LS mean	(3.66, 11.90)
Week 24	
n	27
Mean (SD)	85.19 (18.87)
Absolute Change at Week 24	
n	27
Mean (SD)	-1.07 (27.02)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 24 (MMRM)	
n	27
LS mean (SE)	85.19 (3.66)
95% CI of LS mean	(77.65, 92.72)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	-1.07 (3.66)
95% CI of LS mean	(-8.61, 6.47)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	3.35 (2.46)
95% CI of LS mean	(-1.70, 8.41)
P-value	0.1839

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	84.29 (19.11)
Week 4 (MMRM)	
n	36
LS mean (SE)	84.26 (2.71)
95% CI of LS mean	(78.77, 89.75)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-0.03 (2.71)
95% CI of LS mean	(-5.53, 5.46)
Week 8 (MMRM)	
n	36
LS mean (SE)	86.27 (2.39)
95% CI of LS mean	(81.41, 91.13)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	1.98 (2.39)
95% CI of LS mean	(-2.88, 6.84)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	92.90 (2.06)
95% CI of LS mean	(88.72, 97.08)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	8.61 (2.06)
95% CI of LS mean	(4.43, 12.79)
Week 16 (MMRM)	
n	36
LS mean (SE)	93.83 (1.45)
95% CI of LS mean	(90.89, 96.77)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	9.54 (1.45)
95% CI of LS mean	(6.60, 12.48)
Week 24	
n	36
Mean (SD)	87.35 (16.46)
Absolute Change at Week 24	
n	36
Mean (SD)	3.06 (21.17)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 24 (MMRM)	
n	36
LS mean (SE)	87.35 (2.67)
95% CI of LS mean	(81.93, 92.76)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	3.06 (2.67)
95% CI of LS mean	(-2.36, 8.47)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	6.30 (1.61)
95% CI of LS mean	(3.03, 9.57)
P-value	0.0004

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	87.96 (14.67)
Week 4 (MMRM)	
n	18
LS mean (SE)	86.73 (5.60)
95% CI of LS mean	(74.86, 98.60)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	-1.23 (5.60)
95% CI of LS mean	(-13.10, 10.64)
Week 8 (MMRM)	
n	18
LS mean (SE)	87.65 (3.08)
95% CI of LS mean	(81.13, 94.18)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	-0.31 (3.08)
95% CI of LS mean	(-6.84, 6.22)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	89.74 (3.39)
95% CI of LS mean	(82.38, 97.10)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	1.78 (3.39)
95% CI of LS mean	(-5.59, 9.14)
Week 16 (MMRM)	
n	18
LS mean (SE)	85.68 (5.17)
95% CI of LS mean	(74.70, 96.66)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	-2.28 (5.17)
95% CI of LS mean	(-13.26, 8.69)
Week 24	
n	18
Mean (SD)	84.57 (18.92)
Absolute Change at Week 24	
n	18
Mean (SD)	-3.40 (26.34)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 24 (MMRM)	
n	18
LS mean (SE)	84.57 (5.80)
95% CI of LS mean	(72.12, 97.02)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-3.40 (5.80)
95% CI of LS mean	(-15.84, 9.05)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-2.84 (4.92)
95% CI of LS mean	(-13.40, 7.72)
P-value	0.5729

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Body

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.7671
Region (North America vs. Rest of the World)	0.4673
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Body domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Digestion

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.6414
Region (North America vs. Rest of the World)	0.4330
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Digestion domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Eat

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3103
Region (North America vs. Rest of the World)	0.3122
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Eat domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Emotion

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9606
Region (North America vs. Rest of the World)	0.1873
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Emotion domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Physical

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.5530
Region (North America vs. Rest of the World)	0.1474
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Physical domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Social

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.8639
Region (North America vs. Rest of the World)	0.8423
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Social domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Treatment Burden

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.7027
Region (North America vs. Rest of the World)	0.0046
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Treatment Burden domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	81.20 (24.90)
Week 4 (MMRM)	
n	26
LS mean (SE)	85.47 (4.40)
95% CI of LS mean	(76.41, 94.53)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	4.27 (4.40)
95% CI of LS mean	(-4.79, 13.34)
Week 8 (MMRM)	
n	26
LS mean (SE)	88.46 (3.88)
95% CI of LS mean	(80.37, 96.55)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	7.26 (3.88)
95% CI of LS mean	(-0.83, 15.36)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	88.27 (2.95)
95% CI of LS mean	(82.11, 94.42)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	7.07 (2.95)
95% CI of LS mean	(0.92, 13.22)
Week 16 (MMRM)	
n	26
LS mean (SE)	90.60 (2.60)
95% CI of LS mean	(85.23, 95.97)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	9.40 (2.60)
95% CI of LS mean	(4.03, 14.77)
Week 24	
n	27
Mean (SD)	87.24 (22.79)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	5.56 (30.83)
Week 24 (MMRM)	
n	27
LS mean (SE)	86.75 (4.48)
95% CI of LS mean	(77.51, 95.99)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	5.56 (4.48)
95% CI of LS mean	(-3.68, 14.79)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	7.48 (3.01)
95% CI of LS mean	(1.27, 13.69)
P-value	0.0203

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	76.92 (26.09)
Week 4 (MMRM)	
n	26
LS mean (SE)	78.63 (2.95)
95% CI of LS mean	(72.50, 84.77)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	1.71 (2.95)
95% CI of LS mean	(-4.43, 7.85)
Week 8 (MMRM)	
n	26
LS mean (SE)	84.19 (3.45)
95% CI of LS mean	(77.09, 91.29)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	7.26 (3.45)
95% CI of LS mean	(0.17, 14.36)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	87.18 (3.68)
95% CI of LS mean	(79.58, 94.78)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	10.26 (3.68)
95% CI of LS mean	(2.65, 17.86)
Week 16 (MMRM)	
n	26
LS mean (SE)	88.89 (3.05)
95% CI of LS mean	(82.60, 95.18)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	11.97 (3.05)
95% CI of LS mean	(5.67, 18.26)
Week 24	
n	27
Mean (SD)	83.13 (23.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	5.98 (23.98)
Week 24 (MMRM)	
n	27
LS mean (SE)	82.91 (4.01)
95% CI of LS mean	(74.64, 91.17)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	5.98 (4.01)
95% CI of LS mean	(-2.29, 14.25)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	8.97 (3.22)
95% CI of LS mean	(2.33, 15.62)
P-value	0.0102

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	76.23 (26.04)
Week 4 (MMRM)	
n	36
LS mean (SE)	80.86 (3.74)
95% CI of LS mean	(73.27, 88.46)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	4.63 (3.74)
95% CI of LS mean	(-2.96, 12.22)
Week 8 (MMRM)	
n	36
LS mean (SE)	82.72 (3.53)
95% CI of LS mean	(75.54, 89.89)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	6.48 (3.53)
95% CI of LS mean	(-0.69, 13.65)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	88.27 (2.42)
95% CI of LS mean	(83.36, 93.18)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	12.04 (2.42)
95% CI of LS mean	(7.13, 16.95)
Week 16 (MMRM)	
n	36
LS mean (SE)	89.20 (2.74)
95% CI of LS mean	(83.63, 94.76)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	12.96 (2.74)
95% CI of LS mean	(7.40, 18.53)
Week 24	
n	36
Mean (SD)	82.10 (26.73)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	5.86 (30.92)
Week 24 (MMRM)	
n	36
LS mean (SE)	82.10 (4.24)
95% CI of LS mean	(73.48, 90.72)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	5.86 (4.24)
95% CI of LS mean	(-2.75, 14.48)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	9.41 (3.16)
95% CI of LS mean	(2.99, 15.84)
P-value	0.0053

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	85.42 (23.21)
Week 4 (MMRM)	
n	16
LS mean (SE)	84.72 (3.47)
95% CI of LS mean	(77.26, 92.19)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	-0.69 (3.47)
95% CI of LS mean	(-8.16, 6.77)
Week 8 (MMRM)	
n	16
LS mean (SE)	94.44 (1.30)
95% CI of LS mean	(91.63, 97.26)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	9.03 (1.30)
95% CI of LS mean	(6.21, 11.84)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	86.89 (4.93)
95% CI of LS mean	(76.38, 97.41)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	1.48 (4.93)
95% CI of LS mean	(-9.04, 11.99)
Week 16 (MMRM)	
n	16
LS mean (SE)	90.97 (2.39)
95% CI of LS mean	(85.83, 96.11)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	5.56 (2.39)
95% CI of LS mean	(0.41, 10.70)
Week 24	
n	18
Mean (SD)	91.36 (12.38)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	5.56 (17.68)
Week 24 (MMRM)	
n	18
LS mean (SE)	90.97 (2.47)
95% CI of LS mean	(85.71, 96.24)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	5.56 (2.47)
95% CI of LS mean	(0.29, 10.82)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	5.56 (1.68)
95% CI of LS mean	(1.93, 9.18)
P-value	0.0055

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	25
Mean (SD)	77.33 (23.01)
Week 4 (MMRM)	
n	26
LS mean (SE)	70.67 (5.47)
95% CI of LS mean	(59.36, 81.97)
Absolute Change at Week 4 (MMRM)	
n	25
LS mean (SE)	-6.67 (5.47)
95% CI of LS mean	(-17.97, 4.64)
Week 8 (MMRM)	
n	26
LS mean (SE)	72.00 (5.18)
95% CI of LS mean	(61.31, 82.69)
Absolute Change at Week 8 (MMRM)	
n	25
LS mean (SE)	-5.33 (5.18)
95% CI of LS mean	(-16.02, 5.36)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	81.32 (4.38)
95% CI of LS mean	(72.25, 90.38)
Absolute Change at Week 12 (MMRM)	
n	24
LS mean (SE)	3.98 (4.38)
95% CI of LS mean	(-5.09, 13.05)
Week 16 (MMRM)	
n	26
LS mean (SE)	84.00 (4.13)
95% CI of LS mean	(75.47, 92.53)
Absolute Change at Week 16 (MMRM)	
n	25
LS mean (SE)	6.67 (4.13)
95% CI of LS mean	(-1.87, 15.20)
Week 24	
n	27
Mean (SD)	83.95 (23.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	25
Mean (SD)	6.67 (25.46)
Week 24 (MMRM)	
n	27
LS mean (SE)	84.00 (4.48)
95% CI of LS mean	(74.71, 93.29)
Absolute Change at Week 24 (MMRM)	
n	25
LS mean (SE)	6.67 (4.48)
95% CI of LS mean	(-2.62, 15.95)
Absolute Change through Week 24 (MMRM)	
n	25
LS mean (SE)	6.67 (3.85)
95% CI of LS mean	(-1.30, 14.64)
P-value	0.0970

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	80.77 (21.44)
Week 4 (MMRM)	
n	26
LS mean (SE)	73.08 (6.00)
95% CI of LS mean	(60.71, 85.44)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	-7.69 (6.00)
95% CI of LS mean	(-20.06, 4.67)
Week 8 (MMRM)	
n	26
LS mean (SE)	80.77 (4.32)
95% CI of LS mean	(71.86, 89.68)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	0.00 (4.32)
95% CI of LS mean	(-8.91, 8.91)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	76.92 (3.81)
95% CI of LS mean	(69.06, 84.78)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	-3.85 (3.81)
95% CI of LS mean	(-11.71, 4.01)
Week 16 (MMRM)	
n	26
LS mean (SE)	80.77 (4.35)
95% CI of LS mean	(71.78, 89.76)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	0.00 (4.35)
95% CI of LS mean	(-8.99, 8.99)
Week 24	
n	27
Mean (SD)	82.72 (23.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	1.28 (25.79)
Week 24 (MMRM)	
n	27
LS mean (SE)	82.05 (4.39)
95% CI of LS mean	(73.01, 91.09)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	1.28 (4.39)
95% CI of LS mean	(-7.76, 10.33)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	0.64 (3.57)
95% CI of LS mean	(-6.71, 7.99)
P-value	0.8588

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	80.56 (23.06)
Week 4 (MMRM)	
n	36
LS mean (SE)	73.15 (5.19)
95% CI of LS mean	(62.61, 83.69)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-7.41 (5.19)
95% CI of LS mean	(-17.94, 3.13)
Week 8 (MMRM)	
n	36
LS mean (SE)	76.85 (4.18)
95% CI of LS mean	(68.37, 85.33)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	-3.70 (4.18)
95% CI of LS mean	(-12.18, 4.78)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	79.63 (3.58)
95% CI of LS mean	(72.35, 86.91)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	-0.93 (3.58)
95% CI of LS mean	(-8.20, 6.35)
Week 16 (MMRM)	
n	36
LS mean (SE)	78.70 (3.89)
95% CI of LS mean	(70.81, 86.60)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	-1.85 (3.89)
95% CI of LS mean	(-9.74, 6.04)
Week 24	
n	36
Mean (SD)	81.48 (24.49)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	0.93 (24.54)
Week 24 (MMRM)	
n	36
LS mean (SE)	81.48 (3.65)
95% CI of LS mean	(74.07, 88.89)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	0.93 (3.65)
95% CI of LS mean	(-6.48, 8.34)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	-0.46 (3.31)
95% CI of LS mean	(-7.19, 6.26)
P-value	0.8896

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	15
Mean (SD)	75.56 (19.79)
Week 4 (MMRM)	
n	16
LS mean (SE)	68.89 (7.14)
95% CI of LS mean	(53.44, 84.34)
Absolute Change at Week 4 (MMRM)	
n	15
LS mean (SE)	-6.67 (7.14)
95% CI of LS mean	(-22.12, 8.79)
Week 8 (MMRM)	
n	16
LS mean (SE)	75.56 (6.32)
95% CI of LS mean	(61.77, 89.34)
Absolute Change at Week 8 (MMRM)	
n	15
LS mean (SE)	0.00 (6.32)
95% CI of LS mean	(-13.79, 13.79)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	76.36 (4.92)
95% CI of LS mean	(65.73, 86.98)
Absolute Change at Week 12 (MMRM)	
n	14
LS mean (SE)	0.80 (4.92)
95% CI of LS mean	(-9.82, 11.42)
Week 16 (MMRM)	
n	16
LS mean (SE)	91.11 (3.86)
95% CI of LS mean	(82.81, 99.41)
Absolute Change at Week 16 (MMRM)	
n	15
LS mean (SE)	15.56 (3.86)
95% CI of LS mean	(7.26, 23.85)
Week 24	
n	18
Mean (SD)	87.04 (20.26)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	15
Mean (SD)	11.11 (27.22)
Week 24 (MMRM)	
n	18
LS mean (SE)	86.67 (5.49)
95% CI of LS mean	(74.88, 98.45)
Absolute Change at Week 24 (MMRM)	
n	15
LS mean (SE)	11.11 (5.49)
95% CI of LS mean	(-0.67, 22.90)
Absolute Change through Week 24 (MMRM)	
n	15
LS mean (SE)	13.33 (3.50)
95% CI of LS mean	(5.78, 20.88)
P-value	0.0021

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	76.07 (24.68)
Week 4 (MMRM)	
n	26
LS mean (SE)	82.48 (2.84)
95% CI of LS mean	(76.61, 88.35)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	6.41 (2.84)
95% CI of LS mean	(0.54, 12.28)
Week 8 (MMRM)	
n	26
LS mean (SE)	76.07 (4.02)
95% CI of LS mean	(67.76, 84.38)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	0.00 (4.02)
95% CI of LS mean	(-8.31, 8.31)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	83.34 (4.54)
95% CI of LS mean	(74.00, 92.68)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	7.27 (4.54)
95% CI of LS mean	(-2.07, 16.61)
Week 16 (MMRM)	
n	26
LS mean (SE)	83.33 (3.71)
95% CI of LS mean	(75.70, 90.97)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	7.26 (3.71)
95% CI of LS mean	(-0.37, 14.90)
Week 24	
n	27
Mean (SD)	86.83 (20.22)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	10.26 (18.03)
Week 24 (MMRM)	
n	27
LS mean (SE)	86.32 (2.95)
95% CI of LS mean	(80.23, 92.42)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	10.26 (2.95)
95% CI of LS mean	(4.16, 16.35)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	8.76 (2.68)
95% CI of LS mean	(3.24, 14.28)
P-value	0.0032

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	80.34 (19.95)
Week 4 (MMRM)	
n	26
LS mean (SE)	76.07 (4.04)
95% CI of LS mean	(67.75, 84.39)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	-4.27 (4.04)
95% CI of LS mean	(-12.59, 4.04)
Week 8 (MMRM)	
n	26
LS mean (SE)	77.78 (3.16)
95% CI of LS mean	(71.24, 84.32)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	-2.56 (3.16)
95% CI of LS mean	(-9.10, 3.98)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	82.48 (3.03)
95% CI of LS mean	(76.23, 88.73)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	2.14 (3.03)
95% CI of LS mean	(-4.11, 8.38)
Week 16 (MMRM)	
n	26
LS mean (SE)	85.04 (2.93)
95% CI of LS mean	(79.00, 91.08)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	4.70 (2.93)
95% CI of LS mean	(-1.34, 10.74)
Week 24	
n	27
Mean (SD)	88.48 (17.29)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	8.55 (18.94)
Week 24 (MMRM)	
n	27
LS mean (SE)	88.89 (3.03)
95% CI of LS mean	(82.65, 95.13)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	8.55 (3.03)
95% CI of LS mean	(2.31, 14.79)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	6.62 (2.55)
95% CI of LS mean	(1.36, 11.88)
P-value	0.0157

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	76.54 (24.02)
Week 4 (MMRM)	
n	36
LS mean (SE)	78.09 (2.75)
95% CI of LS mean	(72.49, 83.69)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	1.54 (2.75)
95% CI of LS mean	(-4.06, 7.14)
Week 8 (MMRM)	
n	36
LS mean (SE)	77.47 (3.22)
95% CI of LS mean	(70.91, 84.02)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	0.93 (3.22)
95% CI of LS mean	(-5.63, 7.48)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	82.72 (3.47)
95% CI of LS mean	(75.68, 89.75)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	6.17 (3.47)
95% CI of LS mean	(-0.86, 13.21)
Week 16 (MMRM)	
n	36
LS mean (SE)	83.02 (3.23)
95% CI of LS mean	(76.45, 89.60)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	6.48 (3.23)
95% CI of LS mean	(-0.09, 13.05)
Week 24	
n	36
Mean (SD)	88.58 (18.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	12.04 (19.22)
Week 24 (MMRM)	
n	36
LS mean (SE)	88.58 (2.43)
95% CI of LS mean	(83.63, 93.53)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	12.04 (2.43)
95% CI of LS mean	(7.09, 16.98)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	9.26 (2.40)
95% CI of LS mean	(4.38, 14.14)
P-value	0.0005

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	81.94 (18.09)
Week 4 (MMRM)	
n	16
LS mean (SE)	81.94 (5.75)
95% CI of LS mean	(69.67, 94.22)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	0.00 (5.75)
95% CI of LS mean	(-12.28, 12.28)
Week 8 (MMRM)	
n	16
LS mean (SE)	75.69 (4.31)
95% CI of LS mean	(66.08, 85.31)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	-6.25 (4.31)
95% CI of LS mean	(-15.86, 3.36)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	83.02 (4.09)
95% CI of LS mean	(74.24, 91.79)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	1.07 (4.09)
95% CI of LS mean	(-7.70, 9.85)
Week 16 (MMRM)	
n	16
LS mean (SE)	86.81 (2.80)
95% CI of LS mean	(80.83, 92.78)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	4.86 (2.80)
95% CI of LS mean	(-1.12, 10.84)
Week 24	
n	18
Mean (SD)	85.80 (20.10)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	3.47 (15.03)
Week 24 (MMRM)	
n	18
LS mean (SE)	85.42 (3.84)
95% CI of LS mean	(77.15, 93.69)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	3.47 (3.84)
95% CI of LS mean	(-4.80, 11.74)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	4.17 (2.68)
95% CI of LS mean	(-1.64, 9.97)
P-value	0.1449

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	75.96 (13.66)
Week 4 (MMRM)	
n	26
LS mean (SE)	75.16 (2.75)
95% CI of LS mean	(69.49, 80.83)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	-0.80 (2.75)
95% CI of LS mean	(-6.47, 4.87)
Week 8 (MMRM)	
n	26
LS mean (SE)	78.85 (2.52)
95% CI of LS mean	(73.65, 84.05)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	2.88 (2.52)
95% CI of LS mean	(-2.31, 8.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	80.76 (3.15)
95% CI of LS mean	(74.28, 87.25)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	4.80 (3.15)
95% CI of LS mean	(-1.69, 11.28)
Week 16 (MMRM)	
n	26
LS mean (SE)	84.29 (3.16)
95% CI of LS mean	(77.76, 90.82)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	8.33 (3.16)
95% CI of LS mean	(1.80, 14.86)
Week 24	
n	27
Mean (SD)	79.63 (15.86)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	4.49 (12.80)
Week 24 (MMRM)	
n	27
LS mean (SE)	80.45 (2.45)
95% CI of LS mean	(75.38, 85.51)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	4.49 (2.45)
95% CI of LS mean	(-0.58, 9.55)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	6.41 (2.55)
95% CI of LS mean	(1.13, 11.69)
P-value	0.0194

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	70.03 (16.12)
Week 4 (MMRM)	
n	26
LS mean (SE)	71.52 (2.36)
95% CI of LS mean	(66.66, 76.38)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	1.49 (2.36)
95% CI of LS mean	(-3.37, 6.35)
Week 8 (MMRM)	
n	26
LS mean (SE)	72.44 (2.69)
95% CI of LS mean	(66.90, 77.98)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	2.40 (2.69)
95% CI of LS mean	(-3.14, 7.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	74.36 (2.24)
95% CI of LS mean	(69.74, 78.98)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	4.33 (2.24)
95% CI of LS mean	(-0.29, 8.95)
Week 16 (MMRM)	
n	26
LS mean (SE)	75.32 (2.35)
95% CI of LS mean	(70.45, 80.19)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	5.29 (2.35)
95% CI of LS mean	(0.42, 10.15)
Week 24	
n	27
Mean (SD)	77.31 (14.45)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	7.53 (12.80)
Week 24 (MMRM)	
n	27
LS mean (SE)	77.56 (2.20)
95% CI of LS mean	(73.04, 82.09)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	7.53 (2.20)
95% CI of LS mean	(3.00, 12.06)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	6.41 (2.01)
95% CI of LS mean	(2.25, 10.57)
P-value	0.0040

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	70.95 (15.12)
Week 4 (MMRM)	
n	36
LS mean (SE)	69.94 (2.33)
95% CI of LS mean	(65.21, 74.67)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-1.01 (2.33)
95% CI of LS mean	(-5.74, 3.73)
Week 8 (MMRM)	
n	36
LS mean (SE)	73.73 (2.35)
95% CI of LS mean	(68.95, 78.51)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	2.78 (2.35)
95% CI of LS mean	(-2.00, 7.56)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	75.93 (2.29)
95% CI of LS mean	(71.27, 80.58)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	4.98 (2.29)
95% CI of LS mean	(0.32, 9.63)
Week 16 (MMRM)	
n	36
LS mean (SE)	77.89 (2.53)
95% CI of LS mean	(72.76, 83.03)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	6.94 (2.53)
95% CI of LS mean	(1.81, 12.08)
Week 24	
n	36
Mean (SD)	76.85 (15.92)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	5.90 (13.08)
Week 24 (MMRM)	
n	36
LS mean (SE)	76.85 (2.05)
95% CI of LS mean	(72.70, 81.01)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	5.90 (2.05)
95% CI of LS mean	(1.75, 10.06)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	6.42 (2.08)
95% CI of LS mean	(2.20, 10.65)
P-value	0.0040

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	77.60 (14.42)
Week 4 (MMRM)	
n	16
LS mean (SE)	80.99 (2.78)
95% CI of LS mean	(75.01, 86.97)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	3.39 (2.78)
95% CI of LS mean	(-2.59, 9.36)
Week 8 (MMRM)	
n	16
LS mean (SE)	79.95 (3.16)
95% CI of LS mean	(73.22, 86.68)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	2.34 (3.16)
95% CI of LS mean	(-4.39, 9.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	81.38 (3.54)
95% CI of LS mean	(73.83, 88.94)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	3.78 (3.54)
95% CI of LS mean	(-3.78, 11.33)
Week 16 (MMRM)	
n	16
LS mean (SE)	84.11 (2.89)
95% CI of LS mean	(77.94, 90.29)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	6.51 (2.89)
95% CI of LS mean	(0.33, 12.69)
Week 24	
n	18
Mean (SD)	81.71 (13.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	6.25 (12.45)
Week 24 (MMRM)	
n	18
LS mean (SE)	83.85 (2.51)
95% CI of LS mean	(78.48, 89.23)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	6.25 (2.51)
95% CI of LS mean	(0.88, 11.62)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	6.38 (2.18)
95% CI of LS mean	(1.71, 11.05)
P-value	0.0109

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	89.10 (10.60)
Week 4 (MMRM)	
n	26
LS mean (SE)	87.61 (2.56)
95% CI of LS mean	(82.34, 92.88)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	-1.50 (2.56)
95% CI of LS mean	(-6.77, 3.78)
Week 8 (MMRM)	
n	26
LS mean (SE)	83.12 (3.39)
95% CI of LS mean	(76.13, 90.11)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	-5.98 (3.39)
95% CI of LS mean	(-12.97, 1.01)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	85.23 (2.84)
95% CI of LS mean	(79.38, 91.09)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	-3.87 (2.84)
95% CI of LS mean	(-9.72, 1.99)
Week 16 (MMRM)	
n	26
LS mean (SE)	88.68 (3.23)
95% CI of LS mean	(82.01, 95.34)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	-0.43 (3.23)
95% CI of LS mean	(-7.09, 6.24)
Week 24	
n	27
Mean (SD)	90.33 (17.68)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	1.07 (18.26)
Week 24 (MMRM)	
n	27
LS mean (SE)	90.17 (3.43)
95% CI of LS mean	(83.10, 97.24)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	1.07 (3.43)
95% CI of LS mean	(-6.00, 8.14)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	0.32 (2.60)
95% CI of LS mean	(-5.04, 5.68)
P-value	0.9029

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	83.55 (14.53)
Week 4 (MMRM)	
n	26
LS mean (SE)	85.47 (2.75)
95% CI of LS mean	(79.78, 91.16)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	1.92 (2.75)
95% CI of LS mean	(-3.76, 7.61)
Week 8 (MMRM)	
n	26
LS mean (SE)	84.49 (3.15)
95% CI of LS mean	(77.98, 90.99)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	0.94 (3.15)
95% CI of LS mean	(-5.56, 7.44)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	85.90 (3.11)
95% CI of LS mean	(79.48, 92.31)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	2.35 (3.11)
95% CI of LS mean	(-4.07, 8.77)
Week 16 (MMRM)	
n	26
LS mean (SE)	89.32 (2.57)
95% CI of LS mean	(84.02, 94.61)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	5.77 (2.57)
95% CI of LS mean	(0.47, 11.06)
Week 24	
n	27
Mean (SD)	88.89 (13.25)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	6.41 (13.21)
Week 24 (MMRM)	
n	27
LS mean (SE)	89.96 (2.08)
95% CI of LS mean	(85.67, 94.25)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	6.41 (2.08)
95% CI of LS mean	(2.12, 10.70)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	6.09 (2.16)
95% CI of LS mean	(1.63, 10.55)
P-value	0.0094

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	85.34 (12.11)
Week 4 (MMRM)	
n	36
LS mean (SE)	83.95 (2.34)
95% CI of LS mean	(79.19, 88.71)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-1.39 (2.34)
95% CI of LS mean	(-6.15, 3.37)
Week 8 (MMRM)	
n	36
LS mean (SE)	82.93 (2.69)
95% CI of LS mean	(77.47, 88.40)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	-2.41 (2.69)
95% CI of LS mean	(-7.87, 3.06)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	85.34 (2.73)
95% CI of LS mean	(79.80, 90.88)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	0.00 (2.73)
95% CI of LS mean	(-5.54, 5.54)
Week 16 (MMRM)	
n	36
LS mean (SE)	89.81 (2.46)
95% CI of LS mean	(84.81, 94.82)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	4.48 (2.46)
95% CI of LS mean	(-0.53, 9.49)
Week 24	
n	36
Mean (SD)	88.12 (17.22)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	2.78 (17.99)
Week 24 (MMRM)	
n	36
LS mean (SE)	88.12 (2.80)
95% CI of LS mean	(82.42, 93.82)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	2.78 (2.80)
95% CI of LS mean	(-2.92, 8.48)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	3.63 (2.22)
95% CI of LS mean	(-0.89, 8.15)
P-value	0.1122

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	88.54 (14.69)
Week 4 (MMRM)	
n	16
LS mean (SE)	92.36 (2.04)
95% CI of LS mean	(87.99, 96.73)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	3.82 (2.04)
95% CI of LS mean	(-0.55, 8.19)
Week 8 (MMRM)	
n	16
LS mean (SE)	85.76 (4.42)
95% CI of LS mean	(76.33, 95.20)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	-2.78 (4.42)
95% CI of LS mean	(-12.21, 6.66)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	87.01 (3.25)
95% CI of LS mean	(79.98, 94.04)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	-1.53 (3.25)
95% CI of LS mean	(-8.57, 5.50)
Week 16 (MMRM)	
n	16
LS mean (SE)	87.15 (3.81)
95% CI of LS mean	(79.02, 95.28)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	-1.39 (3.81)
95% CI of LS mean	(-9.52, 6.74)
Week 24	
n	18
Mean (SD)	92.59 (11.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	5.90 (10.44)
Week 24 (MMRM)	
n	18
LS mean (SE)	94.44 (1.50)
95% CI of LS mean	(91.23, 97.66)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	5.90 (1.50)
95% CI of LS mean	(2.69, 9.12)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	2.26 (2.46)
95% CI of LS mean	(-2.98, 7.50)
P-value	0.3729

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	65.93 (17.85)
Week 4 (MMRM)	
n	26
LS mean (SE)	68.68 (2.67)
95% CI of LS mean	(63.17, 74.19)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	2.75 (2.67)
95% CI of LS mean	(-2.76, 8.25)
Week 8 (MMRM)	
n	26
LS mean (SE)	66.85 (2.59)
95% CI of LS mean	(61.51, 72.19)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	0.92 (2.59)
95% CI of LS mean	(-4.42, 6.26)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	73.23 (2.81)
95% CI of LS mean	(67.43, 79.03)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	7.30 (2.81)
95% CI of LS mean	(1.50, 13.09)
Week 16 (MMRM)	
n	26
LS mean (SE)	76.19 (2.87)
95% CI of LS mean	(70.28, 82.10)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	10.26 (2.87)
95% CI of LS mean	(4.34, 16.17)
Week 24	
n	27
Mean (SD)	77.07 (15.40)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	11.90 (17.93)
Week 24 (MMRM)	
n	27
LS mean (SE)	77.84 (2.76)
95% CI of LS mean	(72.14, 83.54)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	11.90 (2.76)
95% CI of LS mean	(6.20, 17.61)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	11.08 (2.65)
95% CI of LS mean	(5.61, 16.55)
P-value	0.0003

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	64.47 (23.22)
Week 4 (MMRM)	
n	26
LS mean (SE)	65.20 (3.01)
95% CI of LS mean	(58.98, 71.43)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	0.73 (3.01)
95% CI of LS mean	(-5.49, 6.96)
Week 8 (MMRM)	
n	26
LS mean (SE)	69.96 (3.63)
95% CI of LS mean	(62.49, 77.44)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	5.49 (3.63)
95% CI of LS mean	(-1.98, 12.97)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	71.98 (3.18)
95% CI of LS mean	(65.42, 78.54)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	7.51 (3.18)
95% CI of LS mean	(0.95, 14.07)
Week 16 (MMRM)	
n	26
LS mean (SE)	68.86 (4.15)
95% CI of LS mean	(60.31, 77.42)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	4.40 (4.15)
95% CI of LS mean	(-4.16, 12.95)
Week 24	
n	27
Mean (SD)	71.78 (15.40)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	8.61 (23.21)
Week 24 (MMRM)	
n	27
LS mean (SE)	73.08 (2.82)
95% CI of LS mean	(67.22, 78.93)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	8.61 (2.82)
95% CI of LS mean	(2.75, 14.46)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	6.50 (3.12)
95% CI of LS mean	(0.05, 12.95)
P-value	0.0484

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	64.02 (21.25)
Week 4 (MMRM)	
n	36
LS mean (SE)	67.20 (2.32)
95% CI of LS mean	(62.48, 71.92)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	3.17 (2.32)
95% CI of LS mean	(-1.55, 7.89)
Week 8 (MMRM)	
n	36
LS mean (SE)	67.86 (3.02)
95% CI of LS mean	(61.73, 73.99)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	3.84 (3.02)
95% CI of LS mean	(-2.30, 9.97)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	72.49 (2.71)
95% CI of LS mean	(66.99, 77.98)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	8.47 (2.71)
95% CI of LS mean	(2.97, 13.96)
Week 16 (MMRM)	
n	36
LS mean (SE)	73.15 (3.27)
95% CI of LS mean	(66.50, 79.79)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	9.13 (3.27)
95% CI of LS mean	(2.48, 15.77)
Week 24	
n	36
Mean (SD)	75.40 (14.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	11.38 (21.43)
Week 24 (MMRM)	
n	36
LS mean (SE)	75.40 (2.40)
95% CI of LS mean	(70.50, 80.30)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	11.38 (2.40)
95% CI of LS mean	(6.47, 16.28)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	10.25 (2.61)
95% CI of LS mean	(4.93, 15.57)
P-value	0.0004

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	67.86 (19.17)
Week 4 (MMRM)	
n	16
LS mean (SE)	66.37 (3.92)
95% CI of LS mean	(57.94, 74.79)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	-1.49 (3.92)
95% CI of LS mean	(-9.91, 6.94)
Week 8 (MMRM)	
n	16
LS mean (SE)	69.64 (2.74)
95% CI of LS mean	(63.79, 75.49)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	1.79 (2.74)
95% CI of LS mean	(-4.06, 7.64)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	72.98 (3.28)
95% CI of LS mean	(65.89, 80.07)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	5.12 (3.28)
95% CI of LS mean	(-1.97, 12.21)
Week 16 (MMRM)	
n	16
LS mean (SE)	71.13 (3.91)
95% CI of LS mean	(62.78, 79.48)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	3.27 (3.91)
95% CI of LS mean	(-5.07, 11.62)
Week 24	
n	18
Mean (SD)	72.49 (17.86)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	7.74 (19.04)
Week 24 (MMRM)	
n	18
LS mean (SE)	75.60 (3.67)
95% CI of LS mean	(67.76, 83.43)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	7.74 (3.67)
95% CI of LS mean	(-0.10, 15.57)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	5.51 (3.41)
95% CI of LS mean	(-1.77, 12.78)
P-value	0.1274

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	77.35 (22.55)
Week 4 (MMRM)	
n	26
LS mean (SE)	77.78 (2.62)
95% CI of LS mean	(72.38, 83.18)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	0.43 (2.62)
95% CI of LS mean	(-4.97, 5.83)
Week 8 (MMRM)	
n	26
LS mean (SE)	78.63 (3.44)
95% CI of LS mean	(71.53, 85.73)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	1.28 (3.44)
95% CI of LS mean	(-5.82, 8.38)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	25
LS mean (SE)	80.49 (4.39)
95% CI of LS mean	(71.45, 89.52)
Absolute Change at Week 12 (MMRM)	
n	25
LS mean (SE)	3.14 (4.39)
95% CI of LS mean	(-5.90, 12.17)
Week 16 (MMRM)	
n	26
LS mean (SE)	80.77 (4.41)
95% CI of LS mean	(71.69, 89.84)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	3.42 (4.41)
95% CI of LS mean	(-5.66, 12.49)
Week 24	
n	27
Mean (SD)	82.72 (22.92)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	5.56 (25.39)
Week 24 (MMRM)	
n	27
LS mean (SE)	82.91 (4.39)
95% CI of LS mean	(73.85, 91.96)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	5.56 (4.39)
95% CI of LS mean	(-3.50, 14.61)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	4.49 (4.02)
95% CI of LS mean	(-3.81, 12.79)
P-value	0.2757

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	26
Mean (SD)	73.08 (21.58)
Week 4 (MMRM)	
n	26
LS mean (SE)	78.63 (3.98)
95% CI of LS mean	(70.40, 86.87)
Absolute Change at Week 4 (MMRM)	
n	26
LS mean (SE)	5.56 (3.98)
95% CI of LS mean	(-2.68, 13.79)
Week 8 (MMRM)	
n	26
LS mean (SE)	76.71 (3.47)
95% CI of LS mean	(69.56, 83.86)
Absolute Change at Week 8 (MMRM)	
n	26
LS mean (SE)	3.63 (3.47)
95% CI of LS mean	(-3.52, 10.79)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	78.21 (2.59)
95% CI of LS mean	(72.85, 83.56)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	5.13 (2.59)
95% CI of LS mean	(-0.23, 10.48)
Week 16 (MMRM)	
n	26
LS mean (SE)	78.63 (3.67)
95% CI of LS mean	(71.07, 86.19)
Absolute Change at Week 16 (MMRM)	
n	26
LS mean (SE)	5.56 (3.67)
95% CI of LS mean	(-2.00, 13.12)
Week 24	
n	27
Mean (SD)	78.60 (21.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	26
Mean (SD)	5.13 (17.84)
Week 24 (MMRM)	
n	27
LS mean (SE)	78.21 (3.24)
95% CI of LS mean	(71.53, 84.88)
Absolute Change at Week 24 (MMRM)	
n	26
LS mean (SE)	5.13 (3.24)
95% CI of LS mean	(-1.55, 11.81)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	5.34 (2.88)
95% CI of LS mean	(-0.61, 11.29)
P-value	0.0763

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	74.38 (22.51)
Week 4 (MMRM)	
n	36
LS mean (SE)	73.46 (2.74)
95% CI of LS mean	(67.88, 79.03)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-0.93 (2.74)
95% CI of LS mean	(-6.50, 4.65)
Week 8 (MMRM)	
n	36
LS mean (SE)	73.61 (2.91)
95% CI of LS mean	(67.69, 79.53)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	-0.77 (2.91)
95% CI of LS mean	(-6.69, 5.15)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	76.23 (3.04)
95% CI of LS mean	(70.05, 82.42)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	1.85 (3.04)
95% CI of LS mean	(-4.33, 8.04)
Week 16 (MMRM)	
n	36
LS mean (SE)	79.63 (3.47)
95% CI of LS mean	(72.59, 86.67)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	5.25 (3.47)
95% CI of LS mean	(-1.79, 12.28)
Week 24	
n	36
Mean (SD)	77.47 (24.70)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	3.09 (20.85)
Week 24 (MMRM)	
n	36
LS mean (SE)	77.47 (3.27)
95% CI of LS mean	(70.82, 84.11)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	3.09 (3.27)
95% CI of LS mean	(-3.56, 9.73)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	4.17 (2.98)
95% CI of LS mean	(-1.88, 10.22)
P-value	0.1707

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	16
Mean (SD)	77.08 (21.26)
Week 4 (MMRM)	
n	16
LS mean (SE)	88.89 (2.59)
95% CI of LS mean	(83.34, 94.44)
Absolute Change at Week 4 (MMRM)	
n	16
LS mean (SE)	11.81 (2.59)
95% CI of LS mean	(6.26, 17.35)
Week 8 (MMRM)	
n	16
LS mean (SE)	86.81 (3.92)
95% CI of LS mean	(78.35, 95.27)
Absolute Change at Week 8 (MMRM)	
n	16
LS mean (SE)	9.72 (3.92)
95% CI of LS mean	(1.26, 18.18)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	15
LS mean (SE)	86.13 (4.14)
95% CI of LS mean	(77.29, 94.97)
Absolute Change at Week 12 (MMRM)	
n	15
LS mean (SE)	9.05 (4.14)
95% CI of LS mean	(0.21, 17.89)
Week 16 (MMRM)	
n	16
LS mean (SE)	79.86 (4.93)
95% CI of LS mean	(69.33, 90.39)
Absolute Change at Week 16 (MMRM)	
n	16
LS mean (SE)	2.78 (4.93)
95% CI of LS mean	(-7.75, 13.31)
Week 24	
n	18
Mean (SD)	87.04 (13.34)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	16
Mean (SD)	10.42 (23.47)
Week 24 (MMRM)	
n	18
LS mean (SE)	87.50 (3.59)
95% CI of LS mean	(79.80, 95.20)
Absolute Change at Week 24 (MMRM)	
n	16
LS mean (SE)	10.42 (3.59)
95% CI of LS mean	(2.72, 18.11)
Absolute Change through Week 24 (MMRM)	
n	16
LS mean (SE)	6.60 (3.78)
95% CI of LS mean	(-1.47, 14.66)
P-value	0.1017

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0462
Region (North America vs. Rest of the World)	0.1403
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Body (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9881
Region (North America vs. Rest of the World)	0.2890
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Digestion (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0852
Region (North America vs. Rest of the World)	0.7233
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Eat (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.4944
Region (North America vs. Rest of the World)	0.8943
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Emotion (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.6048
Region (North America vs. Rest of the World)	0.1919
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Health Perceptions (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3077
Region (North America vs. Rest of the World)	0.5926
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Physical (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9604
Region (North America vs. Rest of the World)	0.4461
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R School (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.4092
Region (North America vs. Rest of the World)	0.8400
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Treatment Burden (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.5284
Region (North America vs. Rest of the World)	0.4631
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Vitality (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.5107
Region (North America vs. Rest of the World)	0.1630
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit as fixed effect and baseline CFQ-R Weight (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	79.42 (27.16)
Week 4 (MMRM)	
n	27
LS mean (SE)	86.01 (2.37)
95% CI of LS mean	(81.13, 90.89)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	6.58 (2.37)
95% CI of LS mean	(1.70, 11.47)
Week 8 (MMRM)	
n	27
LS mean (SE)	80.66 (3.08)
95% CI of LS mean	(74.32, 87.00)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	1.23 (3.08)
95% CI of LS mean	(-5.11, 7.57)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	85.89 (2.29)
95% CI of LS mean	(81.17, 90.60)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	6.46 (2.29)
95% CI of LS mean	(1.75, 11.18)
Week 16 (MMRM)	
n	27
LS mean (SE)	90.12 (3.38)
95% CI of LS mean	(83.12, 97.13)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	10.70 (3.38)
95% CI of LS mean	(3.69, 17.71)
Week 24	
n	27
Mean (SD)	88.07 (18.98)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	8.64 (18.58)
Week 24 (MMRM)	
n	27
LS mean (SE)	88.07 (2.53)
95% CI of LS mean	(82.86, 93.27)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	8.64 (2.53)
95% CI of LS mean	(3.44, 13.85)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	9.67 (2.61)
95% CI of LS mean	(4.27, 15.07)
P-value	0.0012

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	78.81 (26.33)
Week 4 (MMRM)	
n	27
LS mean (SE)	77.37 (2.79)
95% CI of LS mean	(71.58, 83.15)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-1.44 (2.79)
95% CI of LS mean	(-7.22, 4.34)
Week 8 (MMRM)	
n	27
LS mean (SE)	81.89 (3.49)
95% CI of LS mean	(74.66, 89.12)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	3.09 (3.49)
95% CI of LS mean	(-4.14, 10.32)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	82.30 (3.36)
95% CI of LS mean	(75.38, 89.23)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	3.50 (3.36)
95% CI of LS mean	(-3.43, 10.42)
Week 16 (MMRM)	
n	27
LS mean (SE)	81.48 (2.93)
95% CI of LS mean	(75.46, 87.50)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	2.67 (2.93)
95% CI of LS mean	(-3.34, 8.69)
Week 24	
n	27
Mean (SD)	76.95 (19.47)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	-1.85 (21.85)
Week 24 (MMRM)	
n	27
LS mean (SE)	76.95 (3.17)
95% CI of LS mean	(70.41, 83.50)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	-1.85 (3.17)
95% CI of LS mean	(-8.40, 4.70)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.41 (2.56)
95% CI of LS mean	(-4.87, 5.70)
P-value	0.8738

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	77.47 (26.36)
Week 4 (MMRM)	
n	36
LS mean (SE)	80.56 (2.40)
95% CI of LS mean	(75.68, 85.44)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	3.09 (2.40)
95% CI of LS mean	(-1.79, 7.97)
Week 8 (MMRM)	
n	36
LS mean (SE)	78.40 (2.34)
95% CI of LS mean	(73.64, 83.15)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	0.93 (2.34)
95% CI of LS mean	(-3.83, 5.68)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	80.86 (2.75)
95% CI of LS mean	(75.27, 86.45)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	3.40 (2.75)
95% CI of LS mean	(-2.20, 8.99)
Week 16 (MMRM)	
n	36
LS mean (SE)	85.80 (3.08)
95% CI of LS mean	(79.54, 92.07)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	8.33 (3.08)
95% CI of LS mean	(2.07, 14.60)
Week 24	
n	36
Mean (SD)	79.63 (21.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	2.16 (20.88)
Week 24 (MMRM)	
n	36
LS mean (SE)	79.63 (2.78)
95% CI of LS mean	(73.99, 85.27)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	2.16 (2.78)
95% CI of LS mean	(-3.48, 7.80)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	5.25 (2.65)
95% CI of LS mean	(-0.14, 10.63)
P-value	0.0557

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	82.41 (27.23)
Week 4 (MMRM)	
n	18
LS mean (SE)	83.95 (3.11)
95% CI of LS mean	(77.32, 90.58)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	1.54 (3.11)
95% CI of LS mean	(-5.09, 8.17)
Week 8 (MMRM)	
n	18
LS mean (SE)	87.04 (5.13)
95% CI of LS mean	(76.14, 97.94)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	4.63 (5.13)
95% CI of LS mean	(-6.27, 15.53)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	90.69 (2.19)
95% CI of LS mean	(85.94, 95.45)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	8.29 (2.19)
95% CI of LS mean	(3.53, 13.04)
Week 16 (MMRM)	
n	18
LS mean (SE)	85.80 (3.17)
95% CI of LS mean	(79.11, 92.50)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	3.40 (3.17)
95% CI of LS mean	(-3.30, 10.09)
Week 24	
n	18
Mean (SD)	88.27 (15.47)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	5.86 (20.92)
Week 24 (MMRM)	
n	18
LS mean (SE)	88.27 (3.16)
95% CI of LS mean	(81.56, 94.98)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	5.86 (3.16)
95% CI of LS mean	(-0.85, 12.58)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	4.63 (2.46)
95% CI of LS mean	(-0.62, 9.88)
P-value	0.0798

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	80.66 (16.76)
Week 4 (MMRM)	
n	27
LS mean (SE)	78.19 (4.11)
95% CI of LS mean	(69.74, 86.64)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-2.47 (4.11)
95% CI of LS mean	(-10.92, 5.98)
Week 8 (MMRM)	
n	27
LS mean (SE)	81.89 (2.84)
95% CI of LS mean	(76.05, 87.74)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	1.23 (2.84)
95% CI of LS mean	(-4.61, 7.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	83.37 (3.03)
95% CI of LS mean	(77.13, 89.61)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	2.72 (3.03)
95% CI of LS mean	(-3.53, 8.96)
Week 16 (MMRM)	
n	27
LS mean (SE)	86.01 (2.27)
95% CI of LS mean	(81.35, 90.67)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	5.35 (2.27)
95% CI of LS mean	(0.69, 10.01)
Week 24	
n	27
Mean (SD)	81.89 (14.17)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	1.23 (16.11)
Week 24 (MMRM)	
n	27
LS mean (SE)	81.89 (2.44)
95% CI of LS mean	(76.87, 86.91)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	1.23 (2.44)
95% CI of LS mean	(-3.79, 6.25)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	3.29 (2.07)
95% CI of LS mean	(-0.98, 7.56)
P-value	0.1248

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	84.36 (18.30)
Week 4 (MMRM)	
n	27
LS mean (SE)	88.07 (1.89)
95% CI of LS mean	(84.17, 91.97)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	3.70 (1.89)
95% CI of LS mean	(-0.20, 7.60)
Week 8 (MMRM)	
n	27
LS mean (SE)	83.13 (2.52)
95% CI of LS mean	(77.95, 88.30)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	-1.23 (2.52)
95% CI of LS mean	(-6.41, 3.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	86.01 (2.31)
95% CI of LS mean	(81.26, 90.76)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	1.65 (2.31)
95% CI of LS mean	(-3.10, 6.40)
Week 16 (MMRM)	
n	27
LS mean (SE)	85.19 (2.32)
95% CI of LS mean	(80.41, 89.96)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	0.82 (2.32)
95% CI of LS mean	(-3.95, 5.60)
Week 24	
n	27
Mean (SD)	81.07 (15.66)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	-3.29 (17.92)
Week 24 (MMRM)	
n	27
LS mean (SE)	81.07 (2.71)
95% CI of LS mean	(75.51, 86.63)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	-3.29 (2.71)
95% CI of LS mean	(-8.86, 2.27)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-1.23 (2.12)
95% CI of LS mean	(-5.60, 3.13)
P-value	0.5655

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	82.10 (18.65)
Week 4 (MMRM)	
n	36
LS mean (SE)	85.80 (1.98)
95% CI of LS mean	(81.77, 89.83)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	3.70 (1.98)
95% CI of LS mean	(-0.33, 7.73)
Week 8 (MMRM)	
n	36
LS mean (SE)	82.41 (2.28)
95% CI of LS mean	(77.77, 87.04)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	0.31 (2.28)
95% CI of LS mean	(-4.32, 4.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	83.64 (2.28)
95% CI of LS mean	(79.00, 88.29)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	1.54 (2.28)
95% CI of LS mean	(-3.10, 6.19)
Week 16 (MMRM)	
n	36
LS mean (SE)	86.42 (1.89)
95% CI of LS mean	(82.57, 90.27)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	4.32 (1.89)
95% CI of LS mean	(0.47, 8.17)
Week 24	
n	36
Mean (SD)	81.48 (14.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	-0.62 (17.41)
Week 24 (MMRM)	
n	36
LS mean (SE)	81.48 (2.13)
95% CI of LS mean	(77.16, 85.80)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	-0.62 (2.13)
95% CI of LS mean	(-4.94, 3.71)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	1.85 (1.75)
95% CI of LS mean	(-1.70, 5.40)
P-value	0.2968

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	83.33 (15.36)
Week 4 (MMRM)	
n	18
LS mean (SE)	77.78 (5.60)
95% CI of LS mean	(65.96, 89.60)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	-5.56 (5.60)
95% CI of LS mean	(-17.38, 6.27)
Week 8 (MMRM)	
n	18
LS mean (SE)	82.72 (3.30)
95% CI of LS mean	(75.68, 89.75)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	-0.62 (3.30)
95% CI of LS mean	(-7.65, 6.42)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	87.15 (3.35)
95% CI of LS mean	(80.01, 94.29)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	3.82 (3.35)
95% CI of LS mean	(-3.32, 10.96)
Week 16 (MMRM)	
n	18
LS mean (SE)	83.95 (3.03)
95% CI of LS mean	(77.54, 90.36)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	0.62 (3.03)
95% CI of LS mean	(-5.80, 7.03)
Week 24	
n	18
Mean (SD)	81.48 (16.17)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-1.85 (16.72)
Week 24 (MMRM)	
n	18
LS mean (SE)	81.48 (3.55)
95% CI of LS mean	(73.96, 89.00)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-1.85 (3.55)
95% CI of LS mean	(-9.37, 5.67)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-0.62 (2.82)
95% CI of LS mean	(-6.60, 5.37)
P-value	0.8295

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	76.54 (24.57)
Week 4 (MMRM)	
n	27
LS mean (SE)	79.01 (3.24)
95% CI of LS mean	(72.34, 85.69)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	2.47 (3.24)
95% CI of LS mean	(-4.20, 9.14)
Week 8 (MMRM)	
n	27
LS mean (SE)	76.54 (4.17)
95% CI of LS mean	(67.95, 85.14)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	0.00 (4.17)
95% CI of LS mean	(-8.59, 8.59)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	79.71 (3.59)
95% CI of LS mean	(72.29, 87.14)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	3.17 (3.59)
95% CI of LS mean	(-4.25, 10.60)
Week 16 (MMRM)	
n	27
LS mean (SE)	80.25 (2.77)
95% CI of LS mean	(74.56, 85.94)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	3.70 (2.77)
95% CI of LS mean	(-1.99, 9.39)
Week 24	
n	27
Mean (SD)	82.10 (20.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	5.56 (19.61)
Week 24 (MMRM)	
n	27
LS mean (SE)	82.10 (3.04)
95% CI of LS mean	(75.84, 88.36)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	5.56 (3.04)
95% CI of LS mean	(-0.71, 11.82)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	4.63 (2.41)
95% CI of LS mean	(-0.34, 9.60)
P-value	0.0664

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	76.54 (27.83)
Week 4 (MMRM)	
n	27
LS mean (SE)	72.22 (3.21)
95% CI of LS mean	(65.63, 78.81)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-4.32 (3.21)
95% CI of LS mean	(-10.91, 2.27)
Week 8 (MMRM)	
n	27
LS mean (SE)	74.07 (3.43)
95% CI of LS mean	(67.03, 81.12)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	-2.47 (3.43)
95% CI of LS mean	(-9.51, 4.57)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	71.60 (3.33)
95% CI of LS mean	(64.75, 78.46)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	-4.94 (3.33)
95% CI of LS mean	(-11.79, 1.92)
Week 16 (MMRM)	
n	27
LS mean (SE)	77.16 (2.43)
95% CI of LS mean	(72.16, 82.16)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	0.62 (2.43)
95% CI of LS mean	(-4.38, 5.62)
Week 24	
n	27
Mean (SD)	78.40 (25.24)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	1.85 (19.79)
Week 24 (MMRM)	
n	27
LS mean (SE)	78.40 (3.37)
95% CI of LS mean	(71.46, 85.33)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	1.85 (3.37)
95% CI of LS mean	(-5.08, 8.78)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	1.23 (2.54)
95% CI of LS mean	(-4.00, 6.46)
P-value	0.6314

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	74.54 (26.27)
Week 4 (MMRM)	
n	36
LS mean (SE)	74.54 (2.84)
95% CI of LS mean	(68.77, 80.31)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	0.00 (2.84)
95% CI of LS mean	(-5.77, 5.77)
Week 8 (MMRM)	
n	36
LS mean (SE)	75.46 (3.00)
95% CI of LS mean	(69.37, 81.55)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	0.93 (3.00)
95% CI of LS mean	(-5.16, 7.01)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	74.07 (2.55)
95% CI of LS mean	(68.88, 79.27)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	-0.46 (2.55)
95% CI of LS mean	(-5.66, 4.73)
Week 16 (MMRM)	
n	36
LS mean (SE)	78.24 (2.11)
95% CI of LS mean	(73.95, 82.53)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	3.70 (2.11)
95% CI of LS mean	(-0.59, 8.00)
Week 24	
n	36
Mean (SD)	81.48 (21.00)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	6.94 (17.98)
Week 24 (MMRM)	
n	36
LS mean (SE)	81.48 (2.42)
95% CI of LS mean	(76.57, 86.40)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	6.94 (2.42)
95% CI of LS mean	(2.03, 11.86)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	5.32 (1.94)
95% CI of LS mean	(1.39, 9.26)
P-value	0.0095

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	80.56 (25.72)
Week 4 (MMRM)	
n	18
LS mean (SE)	77.78 (3.87)
95% CI of LS mean	(69.61, 85.94)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	-2.78 (3.87)
95% CI of LS mean	(-10.94, 5.39)
Week 8 (MMRM)	
n	18
LS mean (SE)	75.00 (5.41)
95% CI of LS mean	(63.56, 86.44)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	-5.56 (5.41)
95% CI of LS mean	(-16.99, 5.88)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	79.29 (5.55)
95% CI of LS mean	(67.55, 91.02)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	-1.27 (5.55)
95% CI of LS mean	(-13.01, 10.47)
Week 16 (MMRM)	
n	18
LS mean (SE)	79.63 (3.77)
95% CI of LS mean	(71.64, 87.62)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	-0.93 (3.77)
95% CI of LS mean	(-8.92, 7.06)
Week 24	
n	18
Mean (SD)	77.78 (26.20)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-2.78 (21.58)
Week 24 (MMRM)	
n	18
LS mean (SE)	77.78 (4.70)
95% CI of LS mean	(67.86, 87.69)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-2.78 (4.70)
95% CI of LS mean	(-12.69, 7.14)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-1.85 (3.64)
95% CI of LS mean	(-9.54, 5.83)
P-value	0.6172

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	85.68 (13.80)
Week 4 (MMRM)	
n	27
LS mean (SE)	86.91 (1.58)
95% CI of LS mean	(83.64, 90.19)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	1.23 (1.58)
95% CI of LS mean	(-2.04, 4.51)
Week 8 (MMRM)	
n	27
LS mean (SE)	85.93 (2.01)
95% CI of LS mean	(81.79, 90.06)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	0.25 (2.01)
95% CI of LS mean	(-3.89, 4.38)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	89.06 (1.88)
95% CI of LS mean	(85.19, 92.94)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	3.39 (1.88)
95% CI of LS mean	(-0.49, 7.26)
Week 16 (MMRM)	
n	27
LS mean (SE)	88.64 (2.26)
95% CI of LS mean	(84.00, 93.28)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	2.96 (2.26)
95% CI of LS mean	(-1.68, 7.60)
Week 24	
n	27
Mean (SD)	89.88 (9.31)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	4.20 (13.22)
Week 24 (MMRM)	
n	27
LS mean (SE)	89.88 (1.74)
95% CI of LS mean	(86.27, 93.48)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	4.20 (1.74)
95% CI of LS mean	(0.60, 7.80)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	3.58 (1.45)
95% CI of LS mean	(0.60, 6.56)
P-value	0.0206

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	84.51 (14.63)
Week 4 (MMRM)	
n	27
LS mean (SE)	84.69 (1.89)
95% CI of LS mean	(80.80, 88.59)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	0.19 (1.89)
95% CI of LS mean	(-3.71, 4.08)
Week 8 (MMRM)	
n	27
LS mean (SE)	84.57 (1.32)
95% CI of LS mean	(81.86, 87.28)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	0.06 (1.32)
95% CI of LS mean	(-2.65, 2.77)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	87.65 (1.91)
95% CI of LS mean	(83.73, 91.58)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	3.15 (1.91)
95% CI of LS mean	(-0.77, 7.07)
Week 16 (MMRM)	
n	27
LS mean (SE)	88.64 (1.41)
95% CI of LS mean	(85.74, 91.54)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	4.14 (1.41)
95% CI of LS mean	(1.24, 7.03)
Week 24	
n	27
Mean (SD)	87.41 (11.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	2.90 (11.58)
Week 24 (MMRM)	
n	27
LS mean (SE)	87.41 (1.73)
95% CI of LS mean	(83.84, 90.97)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	2.90 (1.73)
95% CI of LS mean	(-0.66, 6.47)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	3.52 (1.11)
95% CI of LS mean	(1.24, 5.80)
P-value	0.0040

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	85.60 (14.61)
Week 4 (MMRM)	
n	36
LS mean (SE)	86.11 (1.40)
95% CI of LS mean	(83.26, 88.97)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	0.51 (1.40)
95% CI of LS mean	(-2.35, 3.36)
Week 8 (MMRM)	
n	36
LS mean (SE)	85.28 (1.40)
95% CI of LS mean	(82.43, 88.12)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	-0.32 (1.40)
95% CI of LS mean	(-3.17, 2.52)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	88.15 (1.47)
95% CI of LS mean	(85.15, 91.14)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	2.55 (1.47)
95% CI of LS mean	(-0.45, 5.54)
Week 16 (MMRM)	
n	36
LS mean (SE)	90.19 (1.33)
95% CI of LS mean	(87.48, 92.90)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	4.58 (1.33)
95% CI of LS mean	(1.87, 7.29)
Week 24	
n	36
Mean (SD)	88.70 (9.93)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	3.10 (10.62)
Week 24 (MMRM)	
n	36
LS mean (SE)	88.70 (1.21)
95% CI of LS mean	(86.24, 91.17)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	3.10 (1.21)
95% CI of LS mean	(0.64, 5.57)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	3.84 (1.07)
95% CI of LS mean	(1.66, 6.02)
P-value	0.0011

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	84.07 (13.36)
Week 4 (MMRM)	
n	18
LS mean (SE)	85.19 (2.42)
95% CI of LS mean	(80.07, 90.30)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	1.11 (2.42)
95% CI of LS mean	(-4.00, 6.22)
Week 8 (MMRM)	
n	18
LS mean (SE)	85.19 (2.36)
95% CI of LS mean	(80.16, 90.21)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	1.11 (2.36)
95% CI of LS mean	(-3.91, 6.13)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	88.69 (2.80)
95% CI of LS mean	(82.77, 94.61)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	4.62 (2.80)
95% CI of LS mean	(-1.31, 10.54)
Week 16 (MMRM)	
n	18
LS mean (SE)	85.56 (2.81)
95% CI of LS mean	(79.58, 91.53)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	1.48 (2.81)
95% CI of LS mean	(-4.49, 7.46)
Week 24	
n	18
Mean (SD)	88.52 (11.39)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	4.44 (15.51)
Week 24 (MMRM)	
n	18
LS mean (SE)	88.52 (2.90)
95% CI of LS mean	(82.34, 94.70)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	4.44 (2.90)
95% CI of LS mean	(-1.73, 10.62)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	2.96 (1.68)
95% CI of LS mean	(-0.60, 6.53)
P-value	0.0971

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	86.01 (14.65)
Week 4 (MMRM)	
n	27
LS mean (SE)	83.13 (2.94)
95% CI of LS mean	(77.08, 89.17)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-2.88 (2.94)
95% CI of LS mean	(-8.92, 3.16)
Week 8 (MMRM)	
n	27
LS mean (SE)	85.60 (2.52)
95% CI of LS mean	(80.42, 90.77)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	-0.41 (2.52)
95% CI of LS mean	(-5.59, 4.76)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	87.89 (2.01)
95% CI of LS mean	(83.77, 92.02)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	1.88 (2.01)
95% CI of LS mean	(-2.24, 6.01)
Week 16 (MMRM)	
n	27
LS mean (SE)	90.12 (2.13)
95% CI of LS mean	(85.74, 94.51)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	4.12 (2.13)
95% CI of LS mean	(-0.27, 8.50)
Week 24	
n	27
Mean (SD)	90.12 (14.89)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	4.12 (14.83)
Week 24 (MMRM)	
n	27
LS mean (SE)	90.12 (2.51)
95% CI of LS mean	(84.96, 95.29)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	4.12 (2.51)
95% CI of LS mean	(-1.05, 9.28)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	4.12 (1.85)
95% CI of LS mean	(0.32, 7.92)
P-value	0.0349

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	87.24 (12.59)
Week 4 (MMRM)	
n	27
LS mean (SE)	83.54 (2.39)
95% CI of LS mean	(78.62, 88.46)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-3.70 (2.39)
95% CI of LS mean	(-8.62, 1.21)
Week 8 (MMRM)	
n	27
LS mean (SE)	89.30 (1.68)
95% CI of LS mean	(85.85, 92.75)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	2.06 (1.68)
95% CI of LS mean	(-1.39, 5.51)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	86.01 (2.84)
95% CI of LS mean	(80.17, 91.84)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	-1.23 (2.84)
95% CI of LS mean	(-7.07, 4.60)
Week 16 (MMRM)	
n	27
LS mean (SE)	88.48 (1.73)
95% CI of LS mean	(84.91, 92.04)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	1.23 (1.73)
95% CI of LS mean	(-2.33, 4.80)
Week 24	
n	27
Mean (SD)	83.95 (20.05)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	-3.29 (20.86)
Week 24 (MMRM)	
n	27
LS mean (SE)	83.95 (3.81)
95% CI of LS mean	(76.13, 91.78)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	-3.29 (3.81)
95% CI of LS mean	(-11.12, 4.53)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	-1.03 (2.34)
95% CI of LS mean	(-5.84, 3.78)
P-value	0.6636

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	86.73 (12.41)
Week 4 (MMRM)	
n	36
LS mean (SE)	83.33 (2.34)
95% CI of LS mean	(78.58, 88.09)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-3.40 (2.34)
95% CI of LS mean	(-8.15, 1.36)
Week 8 (MMRM)	
n	36
LS mean (SE)	87.35 (1.87)
95% CI of LS mean	(83.54, 91.15)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	0.62 (1.87)
95% CI of LS mean	(-3.19, 4.42)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	87.65 (2.12)
95% CI of LS mean	(83.36, 91.95)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	0.93 (2.12)
95% CI of LS mean	(-3.37, 5.22)
Week 16 (MMRM)	
n	36
LS mean (SE)	91.36 (1.52)
95% CI of LS mean	(88.27, 94.45)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	4.63 (1.52)
95% CI of LS mean	(1.54, 7.72)
Week 24	
n	36
Mean (SD)	90.43 (15.29)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	3.70 (14.55)
Week 24 (MMRM)	
n	36
LS mean (SE)	90.43 (2.27)
95% CI of LS mean	(85.83, 95.04)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	3.70 (2.27)
95% CI of LS mean	(-0.90, 8.31)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	4.17 (1.56)
95% CI of LS mean	(1.00, 7.34)
P-value	0.0115

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	86.42 (15.97)
Week 4 (MMRM)	
n	18
LS mean (SE)	83.33 (3.24)
95% CI of LS mean	(76.48, 90.18)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	-3.09 (3.24)
95% CI of LS mean	(-9.93, 3.76)
Week 8 (MMRM)	
n	18
LS mean (SE)	87.65 (2.62)
95% CI of LS mean	(82.12, 93.19)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	1.23 (2.62)
95% CI of LS mean	(-4.30, 6.77)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	85.64 (3.19)
95% CI of LS mean	(78.90, 92.38)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	-0.78 (3.19)
95% CI of LS mean	(-7.52, 5.96)
Week 16 (MMRM)	
n	18
LS mean (SE)	85.19 (2.60)
95% CI of LS mean	(79.68, 90.69)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	-1.23 (2.60)
95% CI of LS mean	(-6.74, 4.27)
Week 24	
n	18
Mean (SD)	80.25 (20.72)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-6.17 (23.25)
Week 24 (MMRM)	
n	18
LS mean (SE)	80.25 (4.91)
95% CI of LS mean	(69.89, 90.61)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-6.17 (4.91)
95% CI of LS mean	(-16.53, 4.19)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-3.70 (2.92)
95% CI of LS mean	(-9.87, 2.46)
P-value	0.2219

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	91.51 (11.87)
Week 4 (MMRM)	
n	27
LS mean (SE)	92.75 (1.72)
95% CI of LS mean	(89.19, 96.30)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	1.23 (1.72)
95% CI of LS mean	(-2.32, 4.79)
Week 8 (MMRM)	
n	27
LS mean (SE)	89.81 (1.99)
95% CI of LS mean	(85.72, 93.91)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	-1.70 (1.99)
95% CI of LS mean	(-5.80, 2.40)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	92.22 (1.88)
95% CI of LS mean	(88.34, 96.10)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	0.71 (1.88)
95% CI of LS mean	(-3.17, 4.59)
Week 16 (MMRM)	
n	27
LS mean (SE)	93.98 (2.26)
95% CI of LS mean	(89.29, 98.68)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	2.47 (2.26)
95% CI of LS mean	(-2.22, 7.16)
Week 24	
n	27
Mean (SD)	92.28 (14.70)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	0.77 (9.81)
Week 24 (MMRM)	
n	27
LS mean (SE)	92.28 (1.95)
95% CI of LS mean	(88.27, 96.30)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	0.77 (1.95)
95% CI of LS mean	(-3.24, 4.79)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	1.62 (1.55)
95% CI of LS mean	(-1.58, 4.82)
P-value	0.3065

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	89.81 (17.84)
Week 4 (MMRM)	
n	27
LS mean (SE)	89.51 (2.67)
95% CI of LS mean	(84.01, 95.00)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-0.31 (2.67)
95% CI of LS mean	(-5.80, 5.18)
Week 8 (MMRM)	
n	27
LS mean (SE)	91.38 (2.10)
95% CI of LS mean	(87.05, 95.71)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	1.57 (2.10)
95% CI of LS mean	(-2.77, 5.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	95.68 (0.83)
95% CI of LS mean	(93.97, 97.39)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	5.86 (0.83)
95% CI of LS mean	(4.15, 7.58)
Week 16 (MMRM)	
n	27
LS mean (SE)	95.06 (1.67)
95% CI of LS mean	(91.63, 98.50)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	5.25 (1.67)
95% CI of LS mean	(1.81, 8.68)
Week 24	
n	27
Mean (SD)	90.90 (15.46)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	1.08 (14.04)
Week 24 (MMRM)	
n	27
LS mean (SE)	90.90 (2.48)
95% CI of LS mean	(85.78, 96.01)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	1.08 (2.48)
95% CI of LS mean	(-4.03, 6.19)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	3.16 (1.49)
95% CI of LS mean	(0.09, 6.24)
P-value	0.0443

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	90.63 (15.73)
Week 4 (MMRM)	
n	36
LS mean (SE)	90.74 (1.78)
95% CI of LS mean	(87.12, 94.36)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	0.12 (1.78)
95% CI of LS mean	(-3.50, 3.74)
Week 8 (MMRM)	
n	36
LS mean (SE)	90.18 (1.89)
95% CI of LS mean	(86.33, 94.03)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	-0.45 (1.89)
95% CI of LS mean	(-4.29, 3.40)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	94.21 (1.11)
95% CI of LS mean	(91.97, 96.46)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	3.59 (1.11)
95% CI of LS mean	(1.34, 5.83)
Week 16 (MMRM)	
n	36
LS mean (SE)	96.06 (0.96)
95% CI of LS mean	(94.10, 98.03)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	5.44 (0.96)
95% CI of LS mean	(3.47, 7.41)
Week 24	
n	36
Mean (SD)	92.13 (15.42)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	1.50 (9.35)
Week 24 (MMRM)	
n	36
LS mean (SE)	92.13 (1.67)
95% CI of LS mean	(88.72, 95.54)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	1.50 (1.67)
95% CI of LS mean	(-1.90, 4.91)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	3.47 (0.98)
95% CI of LS mean	(1.48, 5.46)
P-value	0.0012

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	90.74 (13.97)
Week 4 (MMRM)	
n	18
LS mean (SE)	91.90 (2.31)
95% CI of LS mean	(87.02, 96.77)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	1.16 (2.31)
95% CI of LS mean	(-3.72, 6.03)
Week 8 (MMRM)	
n	18
LS mean (SE)	91.44 (1.22)
95% CI of LS mean	(88.86, 94.01)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	0.69 (1.22)
95% CI of LS mean	(-1.88, 3.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	93.68 (2.20)
95% CI of LS mean	(89.03, 98.34)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	2.94 (2.20)
95% CI of LS mean	(-1.71, 7.59)
Week 16 (MMRM)	
n	18
LS mean (SE)	91.44 (3.34)
95% CI of LS mean	(84.39, 98.48)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	0.69 (3.34)
95% CI of LS mean	(-6.35, 7.74)
Week 24	
n	18
Mean (SD)	90.51 (14.35)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-0.23 (16.32)
Week 24 (MMRM)	
n	18
LS mean (SE)	90.51 (3.20)
95% CI of LS mean	(83.76, 97.26)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-0.23 (3.20)
95% CI of LS mean	(-6.98, 6.52)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	0.23 (2.12)
95% CI of LS mean	(-4.25, 4.71)
P-value	0.9144

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	81.79 (19.20)
Week 4 (MMRM)	
n	27
LS mean (SE)	84.57 (2.45)
95% CI of LS mean	(79.53, 89.60)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	2.78 (2.45)
95% CI of LS mean	(-2.26, 7.81)
Week 8 (MMRM)	
n	27
LS mean (SE)	82.72 (2.98)
95% CI of LS mean	(76.60, 88.84)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	0.93 (2.98)
95% CI of LS mean	(-5.19, 7.05)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	85.79 (2.17)
95% CI of LS mean	(81.32, 90.26)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	4.00 (2.17)
95% CI of LS mean	(-0.47, 8.47)
Week 16 (MMRM)	
n	27
LS mean (SE)	83.33 (3.09)
95% CI of LS mean	(76.98, 89.68)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	1.54 (3.09)
95% CI of LS mean	(-4.81, 7.89)
Week 24	
n	27
Mean (SD)	85.49 (16.92)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	3.70 (14.68)
Week 24 (MMRM)	
n	27
LS mean (SE)	85.49 (2.43)
95% CI of LS mean	(80.50, 90.49)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	3.70 (2.43)
95% CI of LS mean	(-1.29, 8.70)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	2.62 (2.33)
95% CI of LS mean	(-2.19, 7.43)
P-value	0.2718

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	74.69 (17.06)
Week 4 (MMRM)	
n	27
LS mean (SE)	81.17 (2.53)
95% CI of LS mean	(75.96, 86.39)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	6.48 (2.53)
95% CI of LS mean	(1.27, 11.70)
Week 8 (MMRM)	
n	27
LS mean (SE)	80.56 (3.05)
95% CI of LS mean	(74.21, 86.90)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	5.86 (3.05)
95% CI of LS mean	(-0.48, 12.21)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	83.95 (2.45)
95% CI of LS mean	(78.91, 88.99)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	9.26 (2.45)
95% CI of LS mean	(4.22, 14.30)
Week 16 (MMRM)	
n	27
LS mean (SE)	84.26 (2.67)
95% CI of LS mean	(78.77, 89.75)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	9.57 (2.67)
95% CI of LS mean	(4.08, 15.06)
Week 24	
n	27
Mean (SD)	78.09 (15.01)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	3.40 (14.66)
Week 24 (MMRM)	
n	27
LS mean (SE)	78.09 (2.42)
95% CI of LS mean	(73.10, 83.08)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	3.40 (2.42)
95% CI of LS mean	(-1.60, 8.39)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	6.48 (2.14)
95% CI of LS mean	(2.06, 10.90)
P-value	0.0059

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	76.85 (19.43)
Week 4 (MMRM)	
n	36
LS mean (SE)	82.64 (1.94)
95% CI of LS mean	(78.68, 86.59)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	5.79 (1.94)
95% CI of LS mean	(1.83, 9.74)
Week 8 (MMRM)	
n	36
LS mean (SE)	80.32 (2.80)
95% CI of LS mean	(74.63, 86.02)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	3.47 (2.80)
95% CI of LS mean	(-2.22, 9.16)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	84.95 (1.94)
95% CI of LS mean	(81.00, 88.91)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	8.10 (1.94)
95% CI of LS mean	(4.15, 12.06)
Week 16 (MMRM)	
n	36
LS mean (SE)	84.49 (2.37)
95% CI of LS mean	(79.67, 89.31)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	7.64 (2.37)
95% CI of LS mean	(2.82, 12.46)
Week 24	
n	36
Mean (SD)	82.41 (16.64)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	5.56 (13.66)
Week 24 (MMRM)	
n	36
LS mean (SE)	82.41 (1.93)
95% CI of LS mean	(78.48, 86.33)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	5.56 (1.93)
95% CI of LS mean	(1.63, 9.48)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	6.60 (1.97)
95% CI of LS mean	(2.59, 10.61)
P-value	0.0020

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	81.02 (16.12)
Week 4 (MMRM)	
n	18
LS mean (SE)	83.33 (3.90)
95% CI of LS mean	(75.09, 91.58)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	2.31 (3.90)
95% CI of LS mean	(-5.93, 10.56)
Week 8 (MMRM)	
n	18
LS mean (SE)	84.26 (2.53)
95% CI of LS mean	(78.73, 89.79)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	3.24 (2.53)
95% CI of LS mean	(-2.29, 8.77)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	85.34 (3.09)
95% CI of LS mean	(78.73, 91.96)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	4.33 (3.09)
95% CI of LS mean	(-2.29, 10.95)
Week 16 (MMRM)	
n	18
LS mean (SE)	82.41 (3.83)
95% CI of LS mean	(74.27, 90.55)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	1.39 (3.83)
95% CI of LS mean	(-6.75, 9.53)
Week 24	
n	18
Mean (SD)	80.56 (15.91)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-0.46 (15.78)
Week 24 (MMRM)	
n	18
LS mean (SE)	80.56 (3.25)
95% CI of LS mean	(73.69, 87.42)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-0.46 (3.25)
95% CI of LS mean	(-7.33, 6.40)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	0.46 (2.35)
95% CI of LS mean	(-4.59, 5.51)
P-value	0.8468

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	74.07 (20.90)
Week 4 (MMRM)	
n	27
LS mean (SE)	81.89 (2.14)
95% CI of LS mean	(77.42, 86.36)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	7.82 (2.14)
95% CI of LS mean	(3.35, 12.29)
Week 8 (MMRM)	
n	27
LS mean (SE)	86.42 (3.58)
95% CI of LS mean	(78.99, 93.85)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	12.35 (3.58)
95% CI of LS mean	(4.92, 19.78)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	82.93 (3.45)
95% CI of LS mean	(75.82, 90.04)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	8.86 (3.45)
95% CI of LS mean	(1.74, 15.97)
Week 16 (MMRM)	
n	27
LS mean (SE)	82.30 (2.85)
95% CI of LS mean	(76.42, 88.19)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	8.23 (2.85)
95% CI of LS mean	(2.34, 14.12)
Week 24	
n	27
Mean (SD)	86.83 (14.79)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	12.76 (21.73)
Week 24 (MMRM)	
n	27
LS mean (SE)	86.83 (3.49)
95% CI of LS mean	(79.52, 94.14)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	12.76 (3.49)
95% CI of LS mean	(5.44, 20.07)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	10.49 (2.67)
95% CI of LS mean	(4.87, 16.12)
P-value	0.0010

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	66.67 (19.00)
Week 4 (MMRM)	
n	27
LS mean (SE)	74.49 (2.64)
95% CI of LS mean	(69.04, 79.93)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	7.82 (2.64)
95% CI of LS mean	(2.38, 13.26)
Week 8 (MMRM)	
n	27
LS mean (SE)	72.43 (3.63)
95% CI of LS mean	(64.95, 79.91)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	5.76 (3.63)
95% CI of LS mean	(-1.72, 13.24)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	72.02 (3.69)
95% CI of LS mean	(64.44, 79.60)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	5.35 (3.69)
95% CI of LS mean	(-2.23, 12.93)
Week 16 (MMRM)	
n	27
LS mean (SE)	74.07 (2.89)
95% CI of LS mean	(68.13, 80.02)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	7.41 (2.89)
95% CI of LS mean	(1.46, 13.36)
Week 24	
n	27
Mean (SD)	74.07 (20.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	7.41 (16.88)
Week 24 (MMRM)	
n	27
LS mean (SE)	74.07 (3.11)
95% CI of LS mean	(67.68, 80.47)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	7.41 (3.11)
95% CI of LS mean	(1.01, 13.80)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	7.41 (2.72)
95% CI of LS mean	(1.80, 13.02)
P-value	0.0117

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	70.37 (21.25)
Week 4 (MMRM)	
n	36
LS mean (SE)	77.16 (2.09)
95% CI of LS mean	(72.91, 81.41)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	6.79 (2.09)
95% CI of LS mean	(2.54, 11.04)
Week 8 (MMRM)	
n	36
LS mean (SE)	79.01 (3.12)
95% CI of LS mean	(72.68, 85.35)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	8.64 (3.12)
95% CI of LS mean	(2.31, 14.98)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	75.00 (2.97)
95% CI of LS mean	(68.97, 81.03)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	4.63 (2.97)
95% CI of LS mean	(-1.40, 10.66)
Week 16 (MMRM)	
n	36
LS mean (SE)	80.86 (2.46)
95% CI of LS mean	(75.87, 85.86)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	10.49 (2.46)
95% CI of LS mean	(5.50, 15.49)
Week 24	
n	36
Mean (SD)	79.94 (19.12)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	9.57 (19.73)
Week 24 (MMRM)	
n	36
LS mean (SE)	79.94 (2.78)
95% CI of LS mean	(74.29, 85.59)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	9.57 (2.78)
95% CI of LS mean	(3.91, 15.22)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	10.03 (2.34)
95% CI of LS mean	(5.26, 14.80)
P-value	0.0002

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	70.37 (18.28)
Week 4 (MMRM)	
n	18
LS mean (SE)	80.25 (2.71)
95% CI of LS mean	(74.50, 86.00)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	9.88 (2.71)
95% CI of LS mean	(4.13, 15.63)
Week 8 (MMRM)	
n	18
LS mean (SE)	80.25 (4.82)
95% CI of LS mean	(70.01, 90.48)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	9.88 (4.82)
95% CI of LS mean	(-0.36, 20.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	82.96 (4.80)
95% CI of LS mean	(72.80, 93.12)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	12.59 (4.80)
95% CI of LS mean	(2.43, 22.75)
Week 16 (MMRM)	
n	18
LS mean (SE)	72.84 (2.95)
95% CI of LS mean	(66.60, 79.08)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	2.47 (2.95)
95% CI of LS mean	(-3.77, 8.71)
Week 24	
n	18
Mean (SD)	81.48 (19.43)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	11.11 (19.43)
Week 24 (MMRM)	
n	18
LS mean (SE)	81.48 (4.57)
95% CI of LS mean	(71.75, 91.22)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	11.11 (4.57)
95% CI of LS mean	(1.38, 20.85)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	6.79 (3.26)
95% CI of LS mean	(-0.19, 13.77)
P-value	0.0559

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	77.78 (11.84)
Week 4 (MMRM)	
n	27
LS mean (SE)	74.07 (1.98)
95% CI of LS mean	(69.99, 78.16)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-3.70 (1.98)
95% CI of LS mean	(-7.78, 0.38)
Week 8 (MMRM)	
n	27
LS mean (SE)	75.06 (2.23)
95% CI of LS mean	(70.47, 79.65)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	-2.72 (2.23)
95% CI of LS mean	(-7.30, 1.87)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	77.84 (1.56)
95% CI of LS mean	(74.63, 81.06)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	0.07 (1.56)
95% CI of LS mean	(-3.14, 3.28)
Week 16 (MMRM)	
n	27
LS mean (SE)	79.26 (1.84)
95% CI of LS mean	(75.47, 83.05)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	1.48 (1.84)
95% CI of LS mean	(-2.30, 5.27)
Week 24	
n	27
Mean (SD)	79.01 (12.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	1.23 (13.47)
Week 24 (MMRM)	
n	27
LS mean (SE)	79.01 (2.30)
95% CI of LS mean	(74.28, 83.74)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	1.23 (2.30)
95% CI of LS mean	(-3.50, 5.97)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	1.36 (1.66)
95% CI of LS mean	(-2.05, 4.76)
P-value	0.4196

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	73.09 (12.47)
Week 4 (MMRM)	
n	27
LS mean (SE)	72.10 (2.74)
95% CI of LS mean	(66.47, 77.73)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-0.99 (2.74)
95% CI of LS mean	(-6.62, 4.64)
Week 8 (MMRM)	
n	27
LS mean (SE)	71.36 (1.59)
95% CI of LS mean	(68.08, 74.64)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	-1.73 (1.59)
95% CI of LS mean	(-5.01, 1.55)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	74.81 (2.45)
95% CI of LS mean	(69.77, 79.86)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	1.73 (2.45)
95% CI of LS mean	(-3.32, 6.77)
Week 16 (MMRM)	
n	27
LS mean (SE)	75.56 (1.99)
95% CI of LS mean	(71.46, 79.65)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	2.47 (1.99)
95% CI of LS mean	(-1.62, 6.56)
Week 24	
n	27
Mean (SD)	70.62 (13.11)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	-2.47 (15.92)
Week 24 (MMRM)	
n	27
LS mean (SE)	70.62 (2.62)
95% CI of LS mean	(65.21, 76.02)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	-2.47 (2.62)
95% CI of LS mean	(-7.87, 2.93)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	0.00 (1.96)
95% CI of LS mean	(-4.04, 4.04)
P-value	>0.9999

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	74.63 (13.41)
Week 4 (MMRM)	
n	36
LS mean (SE)	74.07 (2.16)
95% CI of LS mean	(69.69, 78.46)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-0.56 (2.16)
95% CI of LS mean	(-4.94, 3.83)
Week 8 (MMRM)	
n	36
LS mean (SE)	73.15 (1.65)
95% CI of LS mean	(69.79, 76.50)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	-1.48 (1.65)
95% CI of LS mean	(-4.84, 1.87)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	75.37 (1.68)
95% CI of LS mean	(71.97, 78.77)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	0.74 (1.68)
95% CI of LS mean	(-2.66, 4.14)
Week 16 (MMRM)	
n	36
LS mean (SE)	77.96 (1.41)
95% CI of LS mean	(75.09, 80.83)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	3.33 (1.41)
95% CI of LS mean	(0.46, 6.20)
Week 24	
n	36
Mean (SD)	75.00 (12.28)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	0.37 (12.24)
Week 24 (MMRM)	
n	36
LS mean (SE)	75.00 (1.72)
95% CI of LS mean	(71.51, 78.49)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	0.37 (1.72)
95% CI of LS mean	(-3.12, 3.86)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	1.85 (1.26)
95% CI of LS mean	(-0.71, 4.41)
P-value	0.1509

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	77.04 (9.76)
Week 4 (MMRM)	
n	18
LS mean (SE)	71.11 (2.50)
95% CI of LS mean	(65.82, 76.40)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	-5.93 (2.50)
95% CI of LS mean	(-11.21, -0.64)
Week 8 (MMRM)	
n	18
LS mean (SE)	73.33 (2.40)
95% CI of LS mean	(68.26, 78.41)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	-3.70 (2.40)
95% CI of LS mean	(-8.78, 1.37)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	78.51 (2.83)
95% CI of LS mean	(72.52, 84.50)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	1.47 (2.83)
95% CI of LS mean	(-4.52, 7.46)
Week 16 (MMRM)	
n	18
LS mean (SE)	76.30 (2.82)
95% CI of LS mean	(70.30, 82.29)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	-0.74 (2.82)
95% CI of LS mean	(-6.74, 5.26)
Week 24	
n	18
Mean (SD)	74.44 (16.21)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-2.59 (19.01)
Week 24 (MMRM)	
n	18
LS mean (SE)	74.44 (4.18)
95% CI of LS mean	(65.56, 83.33)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-2.59 (4.18)
95% CI of LS mean	(-11.48, 6.30)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-1.67 (2.98)
95% CI of LS mean	(-7.97, 4.64)
P-value	0.5834

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	72.84 (34.64)
Week 4 (MMRM)	
n	27
LS mean (SE)	69.14 (4.86)
95% CI of LS mean	(59.15, 79.12)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	-3.70 (4.86)
95% CI of LS mean	(-13.69, 6.29)
Week 8 (MMRM)	
n	27
LS mean (SE)	79.01 (4.44)
95% CI of LS mean	(69.85, 88.18)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	6.17 (4.44)
95% CI of LS mean	(-2.99, 15.34)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	26
LS mean (SE)	74.08 (3.95)
95% CI of LS mean	(65.96, 82.20)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	1.24 (3.95)
95% CI of LS mean	(-6.88, 9.36)
Week 16 (MMRM)	
n	27
LS mean (SE)	76.54 (3.91)
95% CI of LS mean	(68.50, 84.58)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	3.70 (3.91)
95% CI of LS mean	(-4.34, 11.74)
Week 24	
n	27
Mean (SD)	71.60 (31.63)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	-1.23 (21.64)
Week 24 (MMRM)	
n	27
LS mean (SE)	71.60 (3.77)
95% CI of LS mean	(63.85, 79.36)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	-1.23 (3.77)
95% CI of LS mean	(-8.99, 6.52)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	1.23 (2.80)
95% CI of LS mean	(-4.54, 7.01)
P-value	0.6635

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Baseline	
n	27
Mean (SD)	70.37 (37.36)
Week 4 (MMRM)	
n	27
LS mean (SE)	71.60 (5.39)
95% CI of LS mean	(60.52, 82.69)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	1.23 (5.39)
95% CI of LS mean	(-9.85, 12.32)
Week 8 (MMRM)	
n	27
LS mean (SE)	75.31 (4.76)
95% CI of LS mean	(65.50, 85.11)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	4.94 (4.76)
95% CI of LS mean	(-4.87, 14.74)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Week 12 (MMRM)	
n	27
LS mean (SE)	76.54 (4.73)
95% CI of LS mean	(66.80, 86.29)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	6.17 (4.73)
95% CI of LS mean	(-3.57, 15.92)
Week 16 (MMRM)	
n	27
LS mean (SE)	79.01 (4.52)
95% CI of LS mean	(69.71, 88.32)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	8.64 (4.52)
95% CI of LS mean	(-0.66, 17.95)
Week 24	
n	27
Mean (SD)	81.48 (29.72)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 27
Absolute Change at Week 24	
n	27
Mean (SD)	11.11 (36.98)
Week 24 (MMRM)	
n	27
LS mean (SE)	81.48 (5.37)
95% CI of LS mean	(70.41, 92.55)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	11.11 (5.37)
95% CI of LS mean	(0.04, 22.18)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	9.88 (4.56)
95% CI of LS mean	(0.49, 19.26)
P-value	0.0399

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Baseline	
n	36
Mean (SD)	71.30 (37.50)
Week 4 (MMRM)	
n	36
LS mean (SE)	70.37 (5.00)
95% CI of LS mean	(60.21, 80.53)
Absolute Change at Week 4 (MMRM)	
n	36
LS mean (SE)	-0.93 (5.00)
95% CI of LS mean	(-11.09, 9.24)
Week 8 (MMRM)	
n	36
LS mean (SE)	78.70 (4.01)
95% CI of LS mean	(70.55, 86.85)
Absolute Change at Week 8 (MMRM)	
n	36
LS mean (SE)	7.41 (4.01)
95% CI of LS mean	(-0.74, 15.56)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Week 12 (MMRM)	
n	36
LS mean (SE)	76.85 (3.85)
95% CI of LS mean	(69.03, 84.68)
Absolute Change at Week 12 (MMRM)	
n	36
LS mean (SE)	5.56 (3.85)
95% CI of LS mean	(-2.27, 13.38)
Week 16 (MMRM)	
n	36
LS mean (SE)	81.48 (3.70)
95% CI of LS mean	(73.97, 89.00)
Absolute Change at Week 16 (MMRM)	
n	36
LS mean (SE)	10.19 (3.70)
95% CI of LS mean	(2.67, 17.70)
Week 24	
n	36
Mean (SD)	80.56 (28.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 36
Absolute Change at Week 24	
n	36
Mean (SD)	9.26 (31.48)
Week 24 (MMRM)	
n	36
LS mean (SE)	80.56 (3.88)
95% CI of LS mean	(72.68, 88.43)
Absolute Change at Week 24 (MMRM)	
n	36
LS mean (SE)	9.26 (3.88)
95% CI of LS mean	(1.38, 17.14)
Absolute Change through Week 24 (MMRM)	
n	36
LS mean (SE)	9.72 (3.12)
95% CI of LS mean	(3.38, 16.06)
P-value	0.0037

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Baseline	
n	18
Mean (SD)	72.22 (32.84)
Week 4 (MMRM)	
n	18
LS mean (SE)	70.37 (3.41)
95% CI of LS mean	(63.12, 77.62)
Absolute Change at Week 4 (MMRM)	
n	18
LS mean (SE)	-1.85 (3.41)
95% CI of LS mean	(-9.11, 5.40)
Week 8 (MMRM)	
n	18
LS mean (SE)	74.07 (5.24)
95% CI of LS mean	(62.94, 85.21)
Absolute Change at Week 8 (MMRM)	
n	18
LS mean (SE)	1.85 (5.24)
95% CI of LS mean	(-9.28, 12.99)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Week 12 (MMRM)	
n	17
LS mean (SE)	72.34 (5.28)
95% CI of LS mean	(61.19, 83.49)
Absolute Change at Week 12 (MMRM)	
n	17
LS mean (SE)	0.12 (5.28)
95% CI of LS mean	(-11.03, 11.27)
Week 16 (MMRM)	
n	18
LS mean (SE)	70.37 (4.66)
95% CI of LS mean	(60.50, 80.25)
Absolute Change at Week 16 (MMRM)	
n	18
LS mean (SE)	-1.85 (4.66)
95% CI of LS mean	(-11.73, 8.02)
Week 24	
n	18
Mean (SD)	68.52 (35.19)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 18
Absolute Change at Week 24	
n	18
Mean (SD)	-3.70 (27.75)
Week 24 (MMRM)	
n	18
LS mean (SE)	68.52 (6.28)
95% CI of LS mean	(55.25, 81.79)
Absolute Change at Week 24 (MMRM)	
n	18
LS mean (SE)	-3.70 (6.28)
95% CI of LS mean	(-16.97, 9.56)
Absolute Change through Week 24 (MMRM)	
n	18
LS mean (SE)	-2.78 (4.93)
95% CI of LS mean	(-13.21, 7.65)
P-value	0.5806

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups non-(F/MF)
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 2.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Any Pulmonary Exacerbation	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 2.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring Hospitalization	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 2.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring IV Antibiotic Therapy	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 2.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring Hospitalization or IV Antibiotic Therapy	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 2.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 2.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 2.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 2.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 2.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 2.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 2.2.2.14.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 2.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.15.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 2.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)
Subgroup criteria are not met for this subgroup factor.	

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.16.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period non-(F/MF)
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 2.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 2.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups non-(F/MF)
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Zusatzanalysen zur Studie VX21-121-105

Table 2.3.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any TEAEs	50 (92.59)
Respiratory, thoracic and mediastinal disorders	34 (62.96)
Cough	25 (46.30)
Oropharyngeal pain	10 (18.52)
Rhinorrhoea	9 (16.67)
Infections and infestations	22 (40.74)
Gastrointestinal disorders	17 (31.48)
Abdominal pain	8 (14.81)
Vomiting	6 (11.11)
Investigations	16 (29.63)
General disorders and administration site conditions	15 (27.78)
Pyrexia	12 (22.22)
Nervous system disorders	13 (24.07)
Headache	11 (20.37)
Injury, poisoning and procedural complications	8 (14.81)
Skin and subcutaneous tissue disorders	7 (12.96)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any TEAEs	50 (92.59)
Grade 1/Mild	32 (59.26)
Grade 2/Moderate	18 (33.33)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Respiratory, thoracic and mediastinal disorders	34 (62.96)
Grade 1/Mild	27 (50.00)
Grade 2/Moderate	7 (12.96)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Cough	25 (46.30)
Grade 1/Mild	20 (37.04)
Grade 2/Moderate	5 (9.26)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Oropharyngeal pain	10 (18.52)
Grade 1/Mild	10 (18.52)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 54 n (%)
Rhinorrhoea	9 (16.67)
Grade 1/Mild	9 (16.67)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Infections and infestations	22 (40.74)
Grade 1/Mild	15 (27.78)
Grade 2/Moderate	7 (12.96)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Gastrointestinal disorders	17 (31.48)
Grade 1/Mild	15 (27.78)
Grade 2/Moderate	2 (3.70)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Abdominal pain	8 (14.81)
Grade 1/Mild	7 (12.96)
Grade 2/Moderate	1 (1.85)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 54 n (%)
Vomiting	6 (11.11)
Grade 1/Mild	4 (7.41)
Grade 2/Moderate	2 (3.70)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Investigations	16 (29.63)
Grade 1/Mild	12 (22.22)
Grade 2/Moderate	4 (7.41)
Grade 3/Severe	0
Grade 4/Life Threatening	0
General disorders and administration site conditions	15 (27.78)
Grade 1/Mild	13 (24.07)
Grade 2/Moderate	2 (3.70)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Pyrexia	12 (22.22)
Grade 1/Mild	10 (18.52)
Grade 2/Moderate	2 (3.70)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 54 n (%)
Nervous system disorders	13 (24.07)
Grade 1/Mild	9 (16.67)
Grade 2/Moderate	4 (7.41)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Headache	11 (20.37)
Grade 1/Mild	9 (16.67)
Grade 2/Moderate	2 (3.70)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Injury, poisoning and procedural complications	8 (14.81)
Grade 1/Mild	8 (14.81)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Skin and subcutaneous tissue disorders	7 (12.96)
Grade 1/Mild	7 (12.96)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Zusatzanalysen zur Studie VX21-121-105

Table 2.3.1.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 54 n (%)

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Zusatzanalysen zur Studie VX21-121-105

Table 2.3.1.3
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any Serious TEAEs	4 (7.41)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Zusatzanalysen zur Studie VX21-121-105

Table 2.3.1.4
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any TEAEs leading to treatment discontinuation	1 (1.85)
General disorders and administration site conditions	1 (1.85)
Fatigue	1 (1.85)
Respiratory, thoracic and mediastinal disorders	1 (1.85)
Cough	1 (1.85)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.1.11
Study VX21-121-105: Summary of Death non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.

Zusatzanalysen zur Studie VX21-121-105

Table 2.3.1.12
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events non-(F/MF)
Safety Set

	VNZ/TEZ/D-IVA N = 54 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	10 (18.52)
Subjects with non-severe events (Maximum Grade 1/2)	10 (18.52)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	2 (3.70)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 2.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Subjects with any TEAEs	
Sex (Male vs. Female)	>0.9999
Region (North America vs. Rest of the World)	0.1416
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-
Respiratory, thoracic and mediastinal disorders	
Sex (Male vs. Female)	0.5730
Region (North America vs. Rest of the World)	0.6902
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Cough	
Sex (Male vs. Female)	0.7849
Region (North America vs. Rest of the World)	0.4402
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-
Infections and infestations	
Sex (Male vs. Female)	0.2679
Region (North America vs. Rest of the World)	0.6953
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Investigations	
Sex (Male vs. Female)	0.0738
Region (North America vs. Rest of the World)	0.6734
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-
General disorders and administration site conditions	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	>0.9999
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)
Subjects with any TEAEs	25 (92.59)
Respiratory, thoracic and mediastinal disorders	18 (66.67)
Cough	12 (44.44)
Infections and infestations	13 (48.15)
Investigations	11 (40.74)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)
Subjects with any TEAEs	25 (92.59)
Respiratory, thoracic and mediastinal disorders	16 (59.26)
Cough	13 (48.15)
Infections and infestations	9 (33.33)
Investigations	5 (18.52)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 36 n (%)
Subjects with any TEAEs	32 (88.89)
Respiratory, thoracic and mediastinal disorders	22 (61.11)
Cough	18 (50.00)
Infections and infestations	14 (38.89)
General disorders and administration site conditions	10 (27.78)
Investigations	10 (27.78)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 18 n (%)
Subjects with any TEAEs	18 (100.00)
Respiratory, thoracic and mediastinal disorders	12 (66.67)
Cough	7 (38.89)
Infections and infestations	8 (44.44)
Investigations	6 (33.33)
General disorders and administration site conditions	5 (27.78)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.2.1
Study VX21-121-105: Subgroup Factor Test for Grade 3/4/5 TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.3.1
Study VX21-121-105: Subgroup Factor Test for Serious TEAEs by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.1
Study VX21-121-105: Subgroup Factor Test for TEAEs Leading to Treatment Discontinuation by SOC and PT non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor non-(F/MF)
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 2.3.2.11.1
Study VX21-121-105: Subgroup Factor Test for Death non-(F/MF)
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.1
Study VX21-121-105: Subgroup Factor Test for Treatment-emergent Infective Pulmonary Exacerbation Events non-(F/MF)
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 27 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 36 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 18 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 47 n (%)
Subgroup criteria are not met for this subgroup factor.	

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 2.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor non-(F/MF)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 4 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 78
Overall Study Observation Time	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
$ppFEV_1$ (percentage points)	
n	77
Mean (SD)	23.30 (2.74)
Median	24.14
Min, Max	12.00, 25.57
BMI (kg/m^2)	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
BMI z-score	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
Sweat Chloride (mmol/L)	
n	78
Mean (SD)	23.74 (1.83)
Median	24.14
Min, Max	16.14, 25.57

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 3.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 78
Weight (kg)	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
Weight z-score	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
Height (cm)	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
Height z-score	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
CFQ-R	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Table 3.1.1.1
Study VX21-121-105: Summary of Duration of Observation (Weeks) per Endpoint
Full Analysis Set

Duration of observation (weeks)	VNZ/TEZ/D-IVA N = 78
Pulmonary Exacerbation	
n	78
Mean (SD)	24.15 (0.48)
Median	24.14
Min, Max	23.14, 25.57
$LCI_{2.5}$	
n	76
Mean (SD)	22.19 (5.01)
Median	24.14
Min, Max	3.86, 25.57
Safety	
n	78
Mean (SD)	23.98 (1.64)
Median	24.14
Min, Max	10.29, 25.57

- Observation duration [weeks] is defined as (date of last observation - first date of study drug in the Treatment Period +1)/7
- For $ppFEV_1$, observation duration is derived from dates of accepted results. For sweat chloride, observation duration is derived from dates of evaluable results. For $LCI_{2.5}$, observation duration is derived from dates of accepted multiple breath washout results.

Zusatzanalysen zur Studie VX21-121-105

Table 3.1.2.1
Study VX21-121-105: Summary of Patients with Ongoing Antibiotic Medications at Baseline or at Week 24
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline, N1	78
Subjects with 0 ongoing AB	63 (80.77)
Subjects with 1 ongoing AB	12 (15.38)
Subjects with ≥ 2 ongoing AB	3 (3.85)
Subjects with ≥ 1 ongoing IV AB	0
Week 24, N1	78
Subjects with 0 ongoing AB	66 (84.62)
Subjects with 1 ongoing AB	10 (12.82)
Subjects with ≥ 2 ongoing AB	2 (2.56)
Subjects with ≥ 1 ongoing IV AB	0

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- The ongoing antibiotic medications at baseline refer to those with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing antibiotic medications at Week 24 refer to those with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 3.1.2.2
Study VX21-121-105: Summary of Patients with Antibiotic Medications during the Study Treatment Period
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
All subjects	78
Subjects with 0 AB	27 (34.62)
Subjects with 1-3 AB	44 (56.41)
Subjects with ≥ 4 AB	7 (8.97)
Subjects with 0 IV AB	73 (93.59)
Subjects with 1 IV AB	3 (3.85)
Subjects with ≥ 2 IV AB	2 (2.56)
Subjects with 0 ongoing antibiotic medication at baseline	63
Subjects with 0 AB	27 (42.86)
Subjects with 1-3 AB	34 (53.97)
Subjects with ≥ 4 AB	2 (3.17)
Subjects with 0 IV AB	59 (93.65)
Subjects with 1 IV AB	3 (4.76)
Subjects with ≥ 2 IV AB	1 (1.59)

- AB: Antibiotic medications are defined as those medications with the ATC level 2 names of "ANTIBACTERIALS FOR SYSTEMIC USE" and "ANTIMYCOBACTERIALS".
- Antibiotic medications included in this summary refer to those with route being "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- IV antibiotic medications refer to those with route being "INTRAVENOUS" or "INTRAVENOUS BOLUS".
- Antibiotic medications during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX21-121-105

Table 3.1.3.1
Study VX21-121-105: Summary of Patients with Ongoing Physiotherapies at Baseline or at Week 24
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline, N1	78
Subjects with 0 ongoing PT	21 (26.92)
Subjects with 1 ongoing PT	50 (64.10)
Subjects with ≥ 2 ongoing PT	7 (8.97)
Week 24, N1	78
Subjects with 0 ongoing PT	21 (26.92)
Subjects with 1 ongoing PT	49 (62.82)
Subjects with ≥ 2 ongoing PT	8 (10.26)

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- The ongoing physiotherapy at baseline is defined as a physiotherapy whose start date is prior to first dose date of study drug in the Treatment Period and the end date is ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing physiotherapy at Week 24 is defined as a physiotherapy whose start date is prior to Week 24 visit date and the end date is ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 3.1.3.2
Study VX21-121-105: Summary of Patients with Physiotherapies during the Study Treatment Period
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
All subjects	78
Subjects with 0 PT	21 (26.92)
Subjects with 1 PT	49 (62.82)
Subjects with ≥ 2 PT	8 (10.26)
Subjects with 0 ongoing physiotherapies at baseline	21
Subjects with 0 PT	21 (100.00)
Subjects with 1 PT	0
Subjects with ≥ 2 PT	0

- PT: Physiotherapies refer to the non-pharmacological treatments with preferred names of "Positive expiratory pressure therapy", "Airway secretion clearance therapy", "Positive end-expiratory pressure", or "Physiotherapy chest".
- Physiotherapies during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period, and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX21-121-105

Table 3.1.4.1
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications at Baseline or at Week 24
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline, N1	78
Subjects with 0 ongoing IM	6 (7.69)
Subjects with 1 ongoing IM	6 (7.69)
Subjects with ≥ 2 ongoing IM	66 (84.62)
Week 24, N1	78
Subjects with 0 ongoing IM	6 (7.69)
Subjects with 1 ongoing IM	6 (7.69)
Subjects with ≥ 2 ongoing IM	66 (84.62)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX21-121-105

Table 3.1.4.2
Study VX21-121-105: Summary of Patients with Inhaled Medications during the Study Treatment Period
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
All subjects	78
Subjects with 0 IM	5 (6.41)
Subjects with 1 IM	6 (7.69)
Subjects with ≥ 2 IM	67 (85.90)
Subjects with 0 ongoing inhaled medication at baseline	6
Subjects with 0 IM	5 (83.33)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	1 (16.67)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB) and for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX21-121-105

Table 3.1.4.3
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications for Mucolytics at Baseline or at Week 24
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline, N1	78
Subjects with 0 ongoing IM	11 (14.10)
Subjects with 1 ongoing IM	26 (33.33)
Subjects with ≥ 2 ongoing IM	41 (52.56)
Week 24, N1	78
Subjects with 0 ongoing IM	11 (14.10)
Subjects with 1 ongoing IM	26 (33.33)
Subjects with ≥ 2 ongoing IM	41 (52.56)

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 3.1.4.4
Study VX21-121-105: Summary of Patients with Inhaled Medications for Mucolytics during the Study Treatment Period
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
All subjects	78
Subjects with 0 IM	11 (14.10)
Subjects with 1 IM	26 (33.33)
Subjects with ≥ 2 IM	41 (52.56)
Subjects with 0 ongoing inhaled medication at baseline	11
Subjects with 0 IM	11 (100.00)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	0

- IM: Inhaled medications refer to those medications for mucolytics (defined as the ATC codes of R05CB or B05CB). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The percentages in this table are calculated based on the number of subjects under each category.

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Table 3.1.4.5
Study VX21-121-105: Summary of Patients with Ongoing Inhaled Medications for Obstructive Airway Disease at Baseline or at Week 24
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline, N1	78
Subjects with 0 ongoing IM	18 (23.08)
Subjects with 1 ongoing IM	35 (44.87)
Subjects with ≥ 2 ongoing IM	25 (32.05)
Week 24, N1	78
Subjects with 0 ongoing IM	18 (23.08)
Subjects with 1 ongoing IM	35 (44.87)
Subjects with ≥ 2 ongoing IM	25 (32.05)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- The ongoing IMs at baseline refer to those IMs with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing IMs at Week 24 refer to those IMs with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Table 3.1.4.6
Study VX21-121-105: Summary of Patients with Inhaled Medications for Obstructive Airway Disease during the Study Treatment Period
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
All subjects	78
Subjects with 0 IM	17 (21.79)
Subjects with 1 IM	34 (43.59)
Subjects with ≥ 2 IM	27 (34.62)
Subjects with 0 ongoing inhaled medication at baseline	18
Subjects with 0 IM	17 (94.44)
Subjects with 1 IM	0
Subjects with ≥ 2 IM	1 (5.56)

- IM: Inhaled medications refer to those medications for obstructive airway disease (defined as the ATC code of R03xx). It also requires the route of administration to be "RESPIRATORY (INHALATION)".
- IMs during study refer to those with start date ≤ end date of treatment-emergent period of the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing..
- The percentages in this table are calculated based on the number of subjects under each category.

Zusatzanalysen zur Studie VX21-121-105

Table 3.1.5.1
Study VX21-121-105: Summary of Patients with Ongoing CF-related Medications at Baseline or at Week 24
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline, N1	78
Subjects with 0 ongoing CF-related medications	1 (1.28)
Subjects with 1 ongoing CF-related medications	4 (5.13)
Subjects with 2 ongoing CF-related medications	2 (2.56)
Subjects with 3 ongoing CF-related medications	13 (16.67)
Subjects with 4 ongoing CF-related medications	16 (20.51)
Subjects with ≥5 ongoing CF-related medications	42 (53.85)
Week 24, N1	78
Subjects with 0 ongoing CF-related medications	1 (1.28)
Subjects with 1 ongoing CF-related medications	4 (5.13)
Subjects with 2 ongoing CF-related medications	4 (5.13)
Subjects with 3 ongoing CF-related medications	14 (17.95)
Subjects with 4 ongoing CF-related medications	15 (19.23)
Subjects with ≥5 ongoing CF-related medications	40 (51.28)

- CF-related medications: CF co-medications are defined as those medications with
o ATC level 2 names of "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES", "DIGESTIVES, INCL. ENZYMES", "ANTIBACTERIALS FOR SYSTEMIC USE", "DRUGS USED IN DIABETES", "BILE AND LIVER THERAPY", "GENERAL NUTRIENTS";
o or ATC level 3 names of "DRUGS FOR CONSTIPATION", "PROPULSIVES";
o or ATC level 4 names of "MUCOLYTICS".
In addition, the route of administration for "DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES" and "MUCOLYTICS" requires to be "RESPIRATORY (INHALATION)" and the route for "ANTIBACTERIALS FOR SYSTEMIC USE" requires to be "INTRAMUSCULAR", "INTRAVENOUS", "INTRAVENOUS BOLUS", "NASAL", "ORAL", or "RESPIRATORY (INHALATION)".
- The ongoing CF-related medications at baseline refer to those CF-related medications with start date < first dose date of study drug in the Treatment Period and end date ≥ first dose date of study drug in the Treatment Period or end date is missing.
- The ongoing CF-related medications at Week 24 refer to those CF-related medications with start date < Week 24 visit date and the end date ≥ Week 24 visit date or end date is missing.
- N1 refers to the number of subjects with a Day 1 visit and the number of subjects with a Week 24 visit, respectively. The percentages in this table are calculated based on N1.

Zusatzanalysen zur Studie VX21-121-105

Table 3.2.1.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	77
Mean (SD)	99.66 (15.07)
Week 24	
n	70
Mean (SD)	99.97 (13.56)
Absolute Change at Week 24	
n	69
Mean (SD)	-1.19 (8.45)
Absolute Change through Week 24 (MMRM)	
n	74
LS mean (SE)	-0.07 (0.99)
95% CI of LS mean	(-2.05, 1.90)
P-value	0.9421

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 3.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	16.83 (2.13)
Week 24	
n	78
Mean (SD)	17.05 (2.43)
Absolute Change at Week 24	
n	78
Mean (SD)	0.22 (0.73)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	0.22 (0.08)
95% CI of LS mean	(0.05, 0.38)
P-value	0.0097

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 3.2.1.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	0.07 (0.87)
Week 24	
n	78
Mean (SD)	0.02 (0.96)
Absolute Change at Week 24	
n	78
Mean (SD)	-0.05 (0.31)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	-0.05 (0.03)
95% CI of LS mean	(-0.12, 0.02)
P-value	0.1533

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 3.2.1.4.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	77
Mean (SD)	40.41 (20.94)
Week 24	
n	74
Mean (SD)	32.14 (15.49)
Absolute Change at Week 24	
n	74
Mean (SD)	-8.72 (13.95)
Absolute Change through Week 24 (MMRM)	
n	77
LS mean (SE)	-8.65 (1.17)
95% CI of LS mean	(-10.98, -6.32)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects visit and genotype group (F/MF vs rest), with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.4.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Non-missing value at Week 24, N1	74
Number of subjects with missing value at Week 24	4
SwCl <60 mmol/L at Week 24, n (%)	69 (88.46)
95% CI for the proportion	(79.22, 94.59)

- N1: number of subjects with non-missing SwCl at Week 24
- n: number of subjects with SwCl <60 mmol/L
- 95% CI is based on the Clopper-Pearson method

Table 3.2.1.4.3
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Non-missing value at Week 24, N1	74
Number of subjects with missing value at Week 24	4
SwCl <30 mmol/L at Week 24, n (%)	38 (48.72)
95% CI for the proportion	(37.23, 60.31)

- N1: number of subjects with non-missing SwCl at Week 24
- n: number of subjects with SwCl <30 mmol/L
- 95% CI is based on the Clopper-Pearson method

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Table 3.2.1.5
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	30.21 (7.48)
Week 24	
n	78
Mean (SD)	31.88 (8.21)
Absolute Change at Week 24	
n	78
Mean (SD)	1.67 (1.51)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	1.67 (0.17)
95% CI of LS mean	(1.34, 2.00)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 3.2.1.6
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	0.00 (0.89)
Week 24	
n	78
Mean (SD)	-0.01 (0.95)
Absolute Change at Week 24	
n	78
Mean (SD)	-0.02 (0.22)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	-0.02 (0.03)
95% CI of LS mean	(-0.07, 0.03)
P-value	0.4704

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.1.7
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	132.96 (10.51)
Week 24	
n	78
Mean (SD)	135.69 (10.71)
Absolute Change at Week 24	
n	78
Mean (SD)	2.73 (1.05)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	2.73 (0.12)
95% CI of LS mean	(2.50, 2.97)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

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Table 3.2.1.8
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	-0.03 (0.94)
Week 24	
n	78
Mean (SD)	-0.02 (0.96)
Absolute Change at Week 24	
n	78
Mean (SD)	0.01 (0.17)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	0.01 (0.02)
95% CI of LS mean	(-0.03, 0.05)
P-value	0.5430

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.1.9
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	72
Mean (SD)	6.63 (0.74)
Week 24	
n	61
Mean (SD)	6.46 (0.54)
Absolute Change at Week 24	
n	58
Mean (SD)	-0.17 (0.54)
Absolute Change through Week 24 (MMRM)	
n	58
LS mean (SE)	-0.09 (0.05)
95% CI of LS mean	(-0.19, 0.01)
P-value	0.0832

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

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	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	84.78 (16.12)
Week 4 (MMRM)	
n	75
LS mean (SE)	85.44 (1.70)
95% CI of LS mean	(82.05, 88.83)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	0.67 (1.70)
95% CI of LS mean	(-2.72, 4.06)
Week 8 (MMRM)	
n	75
LS mean (SE)	86.44 (1.74)
95% CI of LS mean	(82.97, 89.91)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	1.67 (1.74)
95% CI of LS mean	(-1.80, 5.14)
Week 12 (MMRM)	
n	74
LS mean (SE)	90.40 (1.31)
95% CI of LS mean	(87.79, 93.00)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	5.62 (1.31)
95% CI of LS mean	(3.02, 8.23)
Week 16 (MMRM)	
n	75
LS mean (SE)	90.89 (1.34)
95% CI of LS mean	(88.22, 93.55)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	6.11 (1.34)
95% CI of LS mean	(3.45, 8.78)
Week 24	
n	78
Mean (SD)	85.79 (15.61)
Absolute Change at Week 24	
n	75
Mean (SD)	1.78 (18.70)
Week 24 (MMRM)	
n	78
LS mean (SE)	86.56 (1.66)
95% CI of LS mean	(83.25, 89.86)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.1
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	1.78 (1.66)
95% CI of LS mean	(-1.52, 5.08)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	3.94 (1.21)
95% CI of LS mean	(1.53, 6.36)
P-value	0.0017

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Respiration

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

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	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Body

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Digestion

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	74 (94.87)
Week 4	75 (96.15)
Absolute Change at Week 4	74 (94.87)
Week 8	75 (96.15)
Absolute Change at Week 8	74 (94.87)
Week 12	74 (94.87)
Absolute Change at Week 12	73 (93.59)
Week 16	75 (96.15)
Absolute Change at Week 16	74 (94.87)
Week 24	78 (100.00)
Absolute Change at Week 24	74 (94.87)
Through Week 24	78 (100.00)
Absolute Change through Week 24	74 (94.87)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Eat

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Emotion

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Physical

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Social

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.1.1
Study VX21-121-105: Compliance Rate for CFQ-R (Child's Version) by Visit (All Domains)
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	75 (96.15)
Week 4	75 (96.15)
Absolute Change at Week 4	75 (96.15)
Week 8	75 (96.15)
Absolute Change at Week 8	75 (96.15)
Week 12	74 (94.87)
Absolute Change at Week 12	74 (94.87)
Week 16	75 (96.15)
Absolute Change at Week 16	75 (96.15)
Week 24	78 (100.00)
Absolute Change at Week 24	75 (96.15)
Through Week 24	78 (100.00)
Absolute Change through Week 24	75 (96.15)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	87.39 (15.81)
Week 4 (MMRM)	
n	78
LS mean (SE)	84.62 (1.98)
95% CI of LS mean	(80.67, 88.56)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	-2.78 (1.98)
95% CI of LS mean	(-6.72, 1.16)
Week 8 (MMRM)	
n	78
LS mean (SE)	86.75 (1.83)
95% CI of LS mean	(83.11, 90.39)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	-0.64 (1.83)
95% CI of LS mean	(-4.28, 3.00)
Week 12 (MMRM)	
n	77
LS mean (SE)	92.18 (1.27)
95% CI of LS mean	(89.65, 94.71)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	4.79 (1.27)
95% CI of LS mean	(2.26, 7.32)
Week 16 (MMRM)	
n	78
LS mean (SE)	91.35 (1.53)
95% CI of LS mean	(88.31, 94.39)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	3.96 (1.53)
95% CI of LS mean	(0.92, 7.00)
Week 24	
n	78
Mean (SD)	87.04 (16.08)
Absolute Change at Week 24	
n	78
Mean (SD)	-0.36 (21.01)
Week 24 (MMRM)	
n	78
LS mean (SE)	87.04 (1.81)
95% CI of LS mean	(83.42, 90.65)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	-0.36 (1.81)
95% CI of LS mean	(-3.97, 3.26)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	1.80 (1.31)
95% CI of LS mean	(-0.81, 4.41)
P-value	0.1732

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Respiration

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Body

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Digestion

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Eat

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Emotion

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Health Perception

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Physical

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: School

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Treatment Burden

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Vitality

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.2.1
Study VX21-121-105: Compliance Rate for CFQ-R (Parent's Version) by Visit (All Domains)
Full Analysis Set

Domain: Weight

	VNZ/TEZ/D-IVA N = 78 n (%)
Baseline	78 (100.00)
Week 4	78 (100.00)
Absolute Change at Week 4	78 (100.00)
Week 8	78 (100.00)
Absolute Change at Week 8	78 (100.00)
Week 12	77 (98.72)
Absolute Change at Week 12	77 (98.72)
Week 16	78 (100.00)
Absolute Change at Week 16	78 (100.00)
Week 24	78 (100.00)
Absolute Change at Week 24	78 (100.00)
Through Week 24	78 (100.00)
Absolute Change through Week 24	78 (100.00)

- n (%): For "Through Week 24", n is the number of patients for whom the average between Week 16 and Week 24 can be calculated, i.e. for whom at least one of Week 16 or Week 24 is non-missing. For "Change at Week X" or "Change through Week 24", n is the number of patients for which the stated change is calculable, i.e. for whom both Baseline and the given post-Baseline visit (or through Week 24 average) are non-missing. Otherwise, n is the number of patients with non-missing values at the given visits.
- % is the compliance rate = n expressed as a percentage of N.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	82.67 (23.48)
Week 4 (MMRM)	
n	75
LS mean (SE)	84.89 (2.18)
95% CI of LS mean	(80.55, 89.23)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	2.22 (2.18)
95% CI of LS mean	(-2.12, 6.56)
Week 8 (MMRM)	
n	75
LS mean (SE)	87.56 (2.03)
95% CI of LS mean	(83.51, 91.60)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	4.89 (2.03)
95% CI of LS mean	(0.84, 8.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Body

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	88.56 (1.74)
95% CI of LS mean	(85.09, 92.03)
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	5.89 (1.74)
95% CI of LS mean	(2.42, 9.36)
Week 16 (MMRM)	
n	75
LS mean (SE)	91.26 (1.51)
95% CI of LS mean	(88.25, 94.27)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	8.59 (1.51)
95% CI of LS mean	(5.59, 11.60)
Week 24	
n	78
Mean (SD)	88.03 (20.87)
Absolute Change at Week 24	
n	75
Mean (SD)	5.63 (24.19)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Body

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	88.30 (2.21)
95% CI of LS mean	(83.89, 92.71)
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	5.63 (2.21)
95% CI of LS mean	(1.22, 10.04)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	7.11 (1.65)
95% CI of LS mean	(3.81, 10.41)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	74
Mean (SD)	79.73 (21.24)
Week 4 (MMRM)	
n	75
LS mean (SE)	77.48 (3.00)
95% CI of LS mean	(71.49, 83.46)
Absolute Change at Week 4 (MMRM)	
n	74
LS mean (SE)	-2.25 (3.00)
95% CI of LS mean	(-8.24, 3.73)
Week 8 (MMRM)	
n	75
LS mean (SE)	79.73 (2.67)
95% CI of LS mean	(74.40, 85.06)
Absolute Change at Week 8 (MMRM)	
n	74
LS mean (SE)	0.00 (2.67)
95% CI of LS mean	(-5.33, 5.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Digestion

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	80.07 (2.20)
95% CI of LS mean	(75.68, 84.47)
Absolute Change at Week 12 (MMRM)	
n	73
LS mean (SE)	0.34 (2.20)
95% CI of LS mean	(-4.05, 4.74)
Week 16 (MMRM)	
n	75
LS mean (SE)	83.78 (2.46)
95% CI of LS mean	(78.88, 88.69)
Absolute Change at Week 16 (MMRM)	
n	74
LS mean (SE)	4.05 (2.46)
95% CI of LS mean	(-0.85, 8.96)
Week 24	
n	78
Mean (SD)	84.62 (21.95)
Absolute Change at Week 24	
n	74
Mean (SD)	4.95 (26.28)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Digestion

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	84.68 (2.50)
95% CI of LS mean	(79.69, 89.68)
Absolute Change at Week 24 (MMRM)	
n	74
LS mean (SE)	4.95 (2.50)
95% CI of LS mean	(-0.04, 9.95)
Absolute Change through Week 24 (MMRM)	
n	74
LS mean (SE)	4.50 (2.05)
95% CI of LS mean	(0.41, 8.59)
P-value	0.0314

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	81.48 (21.41)
Week 4 (MMRM)	
n	75
LS mean (SE)	81.78 (2.05)
95% CI of LS mean	(77.69, 85.87)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	0.30 (2.05)
95% CI of LS mean	(-3.79, 4.39)
Week 8 (MMRM)	
n	75
LS mean (SE)	79.85 (2.23)
95% CI of LS mean	(75.41, 84.29)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	-1.63 (2.23)
95% CI of LS mean	(-6.07, 2.81)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Eat

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	83.38 (2.24)
95% CI of LS mean	(78.92, 87.85)
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	1.90 (2.24)
95% CI of LS mean	(-2.57, 6.37)
Week 16 (MMRM)	
n	75
LS mean (SE)	84.44 (2.17)
95% CI of LS mean	(80.12, 88.77)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	2.96 (2.17)
95% CI of LS mean	(-1.37, 7.29)
Week 24	
n	78
Mean (SD)	88.89 (18.17)
Absolute Change at Week 24	
n	75
Mean (SD)	7.26 (17.18)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Eat

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	88.74 (1.67)
95% CI of LS mean	(85.42, 92.06)
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	7.26 (1.67)
95% CI of LS mean	(3.94, 10.58)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	5.11 (1.63)
95% CI of LS mean	(1.87, 8.35)
P-value	0.0024

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	76.50 (14.67)
Week 4 (MMRM)	
n	75
LS mean (SE)	76.52 (1.49)
95% CI of LS mean	(73.54, 79.49)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	0.02 (1.49)
95% CI of LS mean	(-2.96, 2.99)
Week 8 (MMRM)	
n	75
LS mean (SE)	77.94 (1.49)
95% CI of LS mean	(74.98, 80.91)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	1.44 (1.49)
95% CI of LS mean	(-1.52, 4.41)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Emotion

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	79.58 (1.63)
95% CI of LS mean	(76.33, 82.83)
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	3.08 (1.63)
95% CI of LS mean	(-0.17, 6.33)
Week 16 (MMRM)	
n	75
LS mean (SE)	80.22 (1.66)
95% CI of LS mean	(76.91, 83.53)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	3.72 (1.66)
95% CI of LS mean	(0.41, 7.03)
Week 24	
n	78
Mean (SD)	79.81 (15.02)
Absolute Change at Week 24	
n	75
Mean (SD)	3.78 (12.37)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Emotion

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	80.28 (1.32)
95% CI of LS mean	(77.65, 82.91)
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	3.78 (1.32)
95% CI of LS mean	(1.15, 6.41)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	3.75 (1.34)
95% CI of LS mean	(1.08, 6.42)
P-value	0.0065

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	87.26 (13.01)
Week 4 (MMRM)	
n	75
LS mean (SE)	86.96 (1.39)
95% CI of LS mean	(84.19, 89.74)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	-0.30 (1.39)
95% CI of LS mean	(-3.07, 2.48)
Week 8 (MMRM)	
n	75
LS mean (SE)	85.51 (1.81)
95% CI of LS mean	(81.91, 89.11)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	-1.75 (1.81)
95% CI of LS mean	(-5.35, 1.85)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Physical

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	86.31 (1.85)
95% CI of LS mean	(82.63, 89.99)
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	-0.95 (1.85)
95% CI of LS mean	(-4.63, 2.73)
Week 16 (MMRM)	
n	75
LS mean (SE)	88.52 (1.67)
95% CI of LS mean	(85.19, 91.85)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	1.26 (1.67)
95% CI of LS mean	(-2.07, 4.59)
Week 24	
n	78
Mean (SD)	90.38 (14.43)
Absolute Change at Week 24	
n	75
Mean (SD)	3.33 (14.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Physical

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	90.59 (1.48)
95% CI of LS mean	(87.63, 93.55)
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	3.33 (1.48)
95% CI of LS mean	(0.37, 6.29)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	2.30 (1.32)
95% CI of LS mean	(-0.34, 4.94)
P-value	0.0871

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	66.98 (19.25)
Week 4 (MMRM)	
n	75
LS mean (SE)	68.13 (1.60)
95% CI of LS mean	(64.93, 71.32)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	1.14 (1.60)
95% CI of LS mean	(-2.05, 4.34)
Week 8 (MMRM)	
n	75
LS mean (SE)	69.02 (1.83)
95% CI of LS mean	(65.37, 72.66)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	2.03 (1.83)
95% CI of LS mean	(-1.62, 5.68)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Social

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	72.38 (1.70)
95% CI of LS mean	(68.99, 75.77)
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	5.39 (1.70)
95% CI of LS mean	(2.00, 8.78)
Week 16 (MMRM)	
n	75
LS mean (SE)	72.70 (2.00)
95% CI of LS mean	(68.72, 76.68)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	5.71 (2.00)
95% CI of LS mean	(1.73, 9.70)
Week 24	
n	78
Mean (SD)	74.88 (15.34)
Absolute Change at Week 24	
n	75
Mean (SD)	8.67 (19.80)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Social

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	75.65 (1.66)
95% CI of LS mean	(72.34, 78.96)
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	8.67 (1.66)
95% CI of LS mean	(5.35, 11.98)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	7.19 (1.67)
95% CI of LS mean	(3.86, 10.52)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	75
Mean (SD)	76.37 (21.19)
Week 4 (MMRM)	
n	75
LS mean (SE)	79.11 (1.95)
95% CI of LS mean	(75.23, 82.99)
Absolute Change at Week 4 (MMRM)	
n	75
LS mean (SE)	2.74 (1.95)
95% CI of LS mean	(-1.14, 6.62)
Week 8 (MMRM)	
n	75
LS mean (SE)	79.63 (1.85)
95% CI of LS mean	(75.94, 83.32)
Absolute Change at Week 8 (MMRM)	
n	75
LS mean (SE)	3.26 (1.85)
95% CI of LS mean	(-0.44, 6.95)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Treatment Burden

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	74
LS mean (SE)	80.88 (1.92)
95% CI of LS mean	(77.05, 84.70)
Absolute Change at Week 12 (MMRM)	
n	74
LS mean (SE)	4.51 (1.92)
95% CI of LS mean	(0.68, 8.33)
Week 16 (MMRM)	
n	75
LS mean (SE)	79.56 (2.43)
95% CI of LS mean	(74.70, 84.41)
Absolute Change at Week 16 (MMRM)	
n	75
LS mean (SE)	3.19 (2.43)
95% CI of LS mean	(-1.67, 8.04)
Week 24	
n	78
Mean (SD)	81.77 (21.34)
Absolute Change at Week 24	
n	75
Mean (SD)	5.41 (19.82)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.3
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Domain: Treatment Burden

	VNZ/TEZ/D-IVA N = 78
Week 24 (MMRM)	
n	78
LS mean (SE)	81.78 (2.07)
95% CI of LS mean	(77.65, 85.91)
Absolute Change at Week 24 (MMRM)	
n	75
LS mean (SE)	5.41 (2.07)
95% CI of LS mean	(1.28, 9.54)
Absolute Change through Week 24 (MMRM)	
n	75
LS mean (SE)	4.30 (1.90)
95% CI of LS mean	(0.52, 8.08)
P-value	0.0265

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	80.13 (26.10)
Week 4 (MMRM)	
n	78
LS mean (SE)	81.34 (1.68)
95% CI of LS mean	(78.00, 84.68)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	1.21 (1.68)
95% CI of LS mean	(-2.13, 4.55)
Week 8 (MMRM)	
n	78
LS mean (SE)	82.48 (1.82)
95% CI of LS mean	(78.85, 86.11)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	2.35 (1.82)
95% CI of LS mean	(-1.28, 5.98)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	84.17 (1.75)
95% CI of LS mean	(80.68, 87.66)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	4.04 (1.75)
95% CI of LS mean	(0.56, 7.53)
Week 16 (MMRM)	
n	78
LS mean (SE)	85.90 (1.85)
95% CI of LS mean	(82.21, 89.59)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	5.77 (1.85)
95% CI of LS mean	(2.08, 9.46)
Week 24	
n	78
Mean (SD)	83.62 (21.39)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	3.49 (17.66)
Week 24 (MMRM)	
n	78
LS mean (SE)	83.62 (1.65)
95% CI of LS mean	(80.32, 86.91)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	3.49 (1.65)
95% CI of LS mean	(0.20, 6.78)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	4.63 (1.55)
95% CI of LS mean	(1.55, 7.71)
P-value	0.0038

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	82.19 (17.39)
Week 4 (MMRM)	
n	78
LS mean (SE)	82.91 (1.73)
95% CI of LS mean	(79.46, 86.35)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	0.71 (1.73)
95% CI of LS mean	(-2.73, 4.16)
Week 8 (MMRM)	
n	78
LS mean (SE)	82.62 (1.62)
95% CI of LS mean	(79.40, 85.85)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	0.43 (1.62)
95% CI of LS mean	(-2.80, 3.65)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	83.98 (1.52)
95% CI of LS mean	(80.94, 87.01)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	1.78 (1.52)
95% CI of LS mean	(-1.25, 4.82)
Week 16 (MMRM)	
n	78
LS mean (SE)	85.47 (1.29)
95% CI of LS mean	(82.91, 88.03)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	3.28 (1.29)
95% CI of LS mean	(0.71, 5.84)
Week 24	
n	78
Mean (SD)	81.48 (16.48)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	-0.71 (16.35)
Week 24 (MMRM)	
n	78
LS mean (SE)	81.48 (1.59)
95% CI of LS mean	(78.32, 84.64)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	-0.71 (1.59)
95% CI of LS mean	(-3.87, 2.45)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	1.28 (1.25)
95% CI of LS mean	(-1.21, 3.77)
P-value	0.3085

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	79.49 (25.61)
Week 4 (MMRM)	
n	78
LS mean (SE)	78.42 (1.87)
95% CI of LS mean	(74.70, 82.14)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	-1.07 (1.87)
95% CI of LS mean	(-4.79, 2.65)
Week 8 (MMRM)	
n	78
LS mean (SE)	79.27 (2.08)
95% CI of LS mean	(75.12, 83.42)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	-0.21 (2.08)
95% CI of LS mean	(-4.36, 3.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	78.19 (2.07)
95% CI of LS mean	(74.06, 82.31)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	-1.30 (2.07)
95% CI of LS mean	(-5.42, 2.82)
Week 16 (MMRM)	
n	78
LS mean (SE)	80.98 (1.65)
95% CI of LS mean	(77.70, 84.27)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	1.50 (1.65)
95% CI of LS mean	(-1.79, 4.78)
Week 24	
n	78
Mean (SD)	81.84 (24.05)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	2.35 (18.56)
Week 24 (MMRM)	
n	78
LS mean (SE)	81.84 (1.90)
95% CI of LS mean	(78.05, 85.62)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	2.35 (1.90)
95% CI of LS mean	(-1.43, 6.14)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	1.92 (1.57)
95% CI of LS mean	(-1.19, 5.04)
P-value	0.2230

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	86.52 (12.87)
Week 4 (MMRM)	
n	78
LS mean (SE)	87.01 (1.09)
95% CI of LS mean	(84.85, 89.17)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	0.49 (1.09)
95% CI of LS mean	(-1.67, 2.65)
Week 8 (MMRM)	
n	78
LS mean (SE)	86.71 (1.02)
95% CI of LS mean	(84.67, 88.75)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	0.19 (1.02)
95% CI of LS mean	(-1.84, 2.23)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	89.40 (1.02)
95% CI of LS mean	(87.36, 91.44)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	2.88 (1.02)
95% CI of LS mean	(0.84, 4.92)
Week 16 (MMRM)	
n	78
LS mean (SE)	89.49 (1.07)
95% CI of LS mean	(87.35, 91.62)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	2.97 (1.07)
95% CI of LS mean	(0.84, 5.10)
Week 24	
n	78
Mean (SD)	88.38 (11.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	1.86 (12.14)
Week 24 (MMRM)	
n	78
LS mean (SE)	88.38 (1.11)
95% CI of LS mean	(86.17, 90.59)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	1.86 (1.11)
95% CI of LS mean	(-0.35, 4.07)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	2.41 (0.84)
95% CI of LS mean	(0.74, 4.09)
P-value	0.0053

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	86.75 (13.76)
Week 4 (MMRM)	
n	78
LS mean (SE)	82.48 (1.60)
95% CI of LS mean	(79.30, 85.66)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	-4.27 (1.60)
95% CI of LS mean	(-7.46, -1.09)
Week 8 (MMRM)	
n	78
LS mean (SE)	85.90 (1.37)
95% CI of LS mean	(83.17, 88.62)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	-0.85 (1.37)
95% CI of LS mean	(-3.58, 1.87)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	86.87 (1.33)
95% CI of LS mean	(84.22, 89.53)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	0.12 (1.33)
95% CI of LS mean	(-2.53, 2.78)
Week 16 (MMRM)	
n	78
LS mean (SE)	88.46 (1.20)
95% CI of LS mean	(86.07, 90.85)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	1.71 (1.20)
95% CI of LS mean	(-0.68, 4.10)
Week 24	
n	78
Mean (SD)	87.46 (16.64)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	0.71 (16.45)
Week 24 (MMRM)	
n	78
LS mean (SE)	87.46 (1.73)
95% CI of LS mean	(84.02, 90.91)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	0.71 (1.73)
95% CI of LS mean	(-2.73, 4.16)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	1.21 (1.14)
95% CI of LS mean	(-1.07, 3.49)
P-value	0.2934

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	91.88 (13.34)
Week 4 (MMRM)	
n	78
LS mean (SE)	91.03 (1.27)
95% CI of LS mean	(88.49, 93.56)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	-0.85 (1.27)
95% CI of LS mean	(-3.39, 1.68)
Week 8 (MMRM)	
n	78
LS mean (SE)	90.13 (1.26)
95% CI of LS mean	(87.61, 92.64)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	-1.76 (1.26)
95% CI of LS mean	(-4.27, 0.76)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	94.43 (0.85)
95% CI of LS mean	(92.74, 96.12)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	2.55 (0.85)
95% CI of LS mean	(0.86, 4.24)
Week 16 (MMRM)	
n	78
LS mean (SE)	94.18 (1.22)
95% CI of LS mean	(91.74, 96.61)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	2.30 (1.22)
95% CI of LS mean	(-0.14, 4.73)
Week 24	
n	78
Mean (SD)	92.15 (14.76)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	0.27 (11.48)
Week 24 (MMRM)	
n	78
LS mean (SE)	92.15 (1.29)
95% CI of LS mean	(89.57, 94.72)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	0.27 (1.29)
95% CI of LS mean	(-2.31, 2.84)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	1.28 (0.95)
95% CI of LS mean	(-0.61, 3.17)
P-value	0.1805

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	80.45 (17.40)
Week 4 (MMRM)	
n	78
LS mean (SE)	82.48 (1.61)
95% CI of LS mean	(79.28, 85.68)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	2.03 (1.61)
95% CI of LS mean	(-1.17, 5.23)
Week 8 (MMRM)	
n	78
LS mean (SE)	81.41 (1.70)
95% CI of LS mean	(78.03, 84.79)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	0.96 (1.70)
95% CI of LS mean	(-2.42, 4.34)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	84.20 (1.43)
95% CI of LS mean	(81.35, 87.06)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	3.76 (1.43)
95% CI of LS mean	(0.90, 6.61)
Week 16 (MMRM)	
n	78
LS mean (SE)	85.04 (1.58)
95% CI of LS mean	(81.89, 88.20)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	4.59 (1.58)
95% CI of LS mean	(1.44, 7.75)
Week 24	
n	78
Mean (SD)	82.69 (17.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	2.24 (15.41)
Week 24 (MMRM)	
n	78
LS mean (SE)	82.69 (1.56)
95% CI of LS mean	(79.59, 85.80)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	2.24 (1.56)
95% CI of LS mean	(-0.86, 5.35)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	3.42 (1.33)
95% CI of LS mean	(0.77, 6.07)
P-value	0.0121

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	69.37 (21.20)
Week 4 (MMRM)	
n	78
LS mean (SE)	76.21 (1.53)
95% CI of LS mean	(73.17, 79.25)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	6.84 (1.53)
95% CI of LS mean	(3.79, 9.88)
Week 8 (MMRM)	
n	78
LS mean (SE)	78.06 (2.16)
95% CI of LS mean	(73.75, 82.38)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	8.69 (2.16)
95% CI of LS mean	(4.37, 13.00)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	75.69 (2.05)
95% CI of LS mean	(71.60, 79.78)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	6.32 (2.05)
95% CI of LS mean	(2.23, 10.41)
Week 16 (MMRM)	
n	78
LS mean (SE)	77.07 (1.63)
95% CI of LS mean	(73.82, 80.31)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	7.69 (1.63)
95% CI of LS mean	(4.45, 10.93)
Week 24	
n	78
Mean (SD)	78.21 (21.07)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	8.83 (19.07)
Week 24 (MMRM)	
n	78
LS mean (SE)	78.21 (1.95)
95% CI of LS mean	(74.32, 82.09)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	8.83 (1.95)
95% CI of LS mean	(4.95, 12.71)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	8.26 (1.58)
95% CI of LS mean	(5.11, 11.41)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	76.67 (12.47)
Week 4 (MMRM)	
n	78
LS mean (SE)	75.21 (1.40)
95% CI of LS mean	(72.43, 78.00)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	-1.45 (1.40)
95% CI of LS mean	(-4.24, 1.33)
Week 8 (MMRM)	
n	78
LS mean (SE)	75.30 (1.11)
95% CI of LS mean	(73.09, 77.51)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	-1.37 (1.11)
95% CI of LS mean	(-3.58, 0.85)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	77.57 (1.22)
95% CI of LS mean	(75.15, 80.00)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	0.91 (1.22)
95% CI of LS mean	(-1.51, 3.33)
Week 16 (MMRM)	
n	78
LS mean (SE)	78.63 (1.25)
95% CI of LS mean	(76.14, 81.12)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	1.97 (1.25)
95% CI of LS mean	(-0.52, 4.46)
Week 24	
n	78
Mean (SD)	75.81 (14.14)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	-0.85 (13.94)
Week 24 (MMRM)	
n	78
LS mean (SE)	75.81 (1.44)
95% CI of LS mean	(72.95, 78.67)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	-0.85 (1.44)
95% CI of LS mean	(-3.71, 2.00)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	0.56 (1.11)
95% CI of LS mean	(-1.65, 2.76)
P-value	0.6167

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Baseline	
n	78
Mean (SD)	69.23 (35.54)
Week 4 (MMRM)	
n	78
LS mean (SE)	70.51 (2.87)
95% CI of LS mean	(64.79, 76.24)
Absolute Change at Week 4 (MMRM)	
n	78
LS mean (SE)	1.28 (2.87)
95% CI of LS mean	(-4.44, 7.01)
Week 8 (MMRM)	
n	78
LS mean (SE)	75.21 (2.65)
95% CI of LS mean	(69.94, 80.48)
Absolute Change at Week 8 (MMRM)	
n	78
LS mean (SE)	5.98 (2.65)
95% CI of LS mean	(0.71, 11.25)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Week 12 (MMRM)	
n	77
LS mean (SE)	73.49 (2.70)
95% CI of LS mean	(68.11, 78.87)
Absolute Change at Week 12 (MMRM)	
n	77
LS mean (SE)	4.26 (2.70)
95% CI of LS mean	(-1.12, 9.64)
Week 16 (MMRM)	
n	78
LS mean (SE)	74.36 (2.68)
95% CI of LS mean	(69.03, 79.69)
Absolute Change at Week 16 (MMRM)	
n	78
LS mean (SE)	5.13 (2.68)
95% CI of LS mean	(-0.20, 10.46)
Week 24	
n	78
Mean (SD)	74.36 (33.94)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.1.10.4
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA N = 78
Absolute Change at Week 24	
n	78
Mean (SD)	5.13 (27.95)
Week 24 (MMRM)	
n	78
LS mean (SE)	74.36 (2.85)
95% CI of LS mean	(68.69, 80.03)
Absolute Change at Week 24 (MMRM)	
n	78
LS mean (SE)	5.13 (2.85)
95% CI of LS mean	(-0.54, 10.80)
Absolute Change through Week 24 (MMRM)	
n	78
LS mean (SE)	5.13 (2.39)
95% CI of LS mean	(0.37, 9.88)
P-value	0.0348

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

Table 3.2.1.13
Study VX21-121-105: Summary of Pulmonary Exacerbations through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78
Total number of days (years) of the PEx analysis period	13188 (39.3)
Pulmonary exacerbations	
Number of subjects with events, n (%)	6 (7.69)
Total number of events	6
Observed event rate per year	0.15
Pulmonary exacerbations requiring hospitalization	
Number of subjects with events, n (%)	1 (1.28)
Total number of events	1
Observed event rate per year	0.03
Pulmonary exacerbations requiring IV antibiotic therapy	
Number of subjects with events, n (%)	1 (1.28)
Total number of events	1
Observed event rate per year	0.03
Pulmonary exacerbations requiring hospitalization or IV antibiotic therapy	
Number of subjects with events, n (%)	1 (1.28)
Total number of events	1
Observed event rate per year	0.03

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Zusatzanalysen zur Studie VX21-121-105

Table 3.2.1.14.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Any Pulmonary Exacerbation	
Overall	
Subjects with Events	6 (7.69)
Subjects Censored	72 (92.31)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.1.15.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Any Pulmonary Exacerbation Requiring Hospitalization	
Overall	
Subjects with Events	1 (1.28)
Subjects Censored	77 (98.72)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring hospitalization during the PEx analysis period were censored at the PEx analysis period end date.

Zusatzanalysen zur Studie VX21-121-105

Table 3.2.1.16.1
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24
Full Analysis Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Any Pulmonary Exacerbation Requiring IV Antibiotics	
Overall	
Subjects with Events	1 (1.28)
Subjects Censored	77 (98.72)
Event-free time (weeks)	
75 percent subjects	-
50 percent subjects (Median)	-
25 percent subjects	-

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation requiring IV antibiotics during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.6683
Region (North America vs. Rest of the World)	0.8154
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.3831

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline $ppFEV_1$ as covariate.
- N/C: model does not converge.

Table 3.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	98.77 (13.79)
Week 24	
n	40
Mean (SD)	99.05 (14.86)
Absolute Change at Week 24	
n	40
Mean (SD)	-0.16 (9.40)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	0.03 (1.43)
95% CI of LS mean	(-2.86, 2.92)
P-value	0.9827

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	100.85 (16.77)
Week 24	
n	30
Mean (SD)	101.19 (11.73)
Absolute Change at Week 24	
n	29
Mean (SD)	-2.61 (6.81)
Absolute Change through Week 24 (MMRM)	
n	32
LS mean (SE)	-0.15 (1.37)
95% CI of LS mean	(-3.00, 2.70)
P-value	0.9123

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	101.64 (12.56)
Week 24	
n	44
Mean (SD)	100.40 (12.97)
Absolute Change at Week 24	
n	44
Mean (SD)	-1.61 (5.72)
Absolute Change through Week 24 (MMRM)	
n	46
LS mean (SE)	-0.65 (0.86)
95% CI of LS mean	(-2.39, 1.10)
P-value	0.4579

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	30
Mean (SD)	96.55 (18.13)
Week 24	
n	26
Mean (SD)	99.24 (14.74)
Absolute Change at Week 24	
n	25
Mean (SD)	-0.44 (11.94)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	0.81 (2.14)
95% CI of LS mean	(-3.61, 5.22)
P-value	0.7091

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	61
Mean (SD)	99.47 (13.81)
Week 24	
n	55
Mean (SD)	99.99 (11.40)
Absolute Change at Week 24	
n	54
Mean (SD)	-1.56 (7.10)
Absolute Change through Week 24 (MMRM)	
n	58
LS mean (SE)	-0.19 (1.00)
95% CI of LS mean	(-2.20, 1.82)
P-value	0.8481

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	96.30 (23.75)
Week 24	
n	10
Mean (SD)	97.99 (24.49)
Absolute Change at Week 24	
n	10
Mean (SD)	1.68 (14.47)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	1.56 (4.64)
95% CI of LS mean	(-9.05, 12.16)
P-value	0.7451

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $ppFEV_1$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.2.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0273
Region (North America vs. Rest of the World)	0.5376
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.3926

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline BMI as covariate.
- N/C: model does not converge.

Table 3.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	17.30 (2.33)
Week 24	
n	44
Mean (SD)	17.41 (2.64)
Absolute Change at Week 24	
n	44
Mean (SD)	0.11 (0.67)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	0.11 (0.10)
95% CI of LS mean	(-0.08, 0.31)
P-value	0.2538

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	16.23 (1.70)
Week 24	
n	34
Mean (SD)	16.58 (2.07)
Absolute Change at Week 24	
n	34
Mean (SD)	0.35 (0.79)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	0.35 (0.13)
95% CI of LS mean	(0.08, 0.62)
P-value	0.0137

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	17.39 (2.14)
Week 24	
n	47
Mean (SD)	17.76 (2.41)
Absolute Change at Week 24	
n	47
Mean (SD)	0.37 (0.79)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	0.37 (0.11)
95% CI of LS mean	(0.14, 0.59)
P-value	0.0025

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	15.98 (1.85)
Week 24	
n	31
Mean (SD)	15.97 (2.05)
Absolute Change at Week 24	
n	31
Mean (SD)	-0.01 (0.57)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-0.01 (0.10)
95% CI of LS mean	(-0.22, 0.19)
P-value	0.9090

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	16.69 (2.10)
Week 24	
n	62
Mean (SD)	16.88 (2.37)
Absolute Change at Week 24	
n	62
Mean (SD)	0.19 (0.71)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	0.19 (0.09)
95% CI of LS mean	(0.01, 0.37)
P-value	0.0368

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	17.60 (2.64)
Week 24	
n	10
Mean (SD)	17.94 (2.92)
Absolute Change at Week 24	
n	10
Mean (SD)	0.34 (0.85)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	0.34 (0.23)
95% CI of LS mean	(-0.19, 0.87)
P-value	0.1833

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0135
Region (North America vs. Rest of the World)	0.0510
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9218

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline BMI z-score as covariate.
- N/C: model does not converge.

Table 3.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	0.30 (0.86)
Week 24	
n	44
Mean (SD)	0.20 (0.97)
Absolute Change at Week 24	
n	44
Mean (SD)	-0.10 (0.26)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	-0.10 (0.04)
95% CI of LS mean	(-0.18, -0.02)
P-value	0.0138

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	-0.22 (0.81)
Week 24	
n	34
Mean (SD)	-0.21 (0.91)
Absolute Change at Week 24	
n	34
Mean (SD)	0.01 (0.36)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	0.01 (0.06)
95% CI of LS mean	(-0.11, 0.14)
P-value	0.8290

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	0.28 (0.77)
Week 24	
n	47
Mean (SD)	0.30 (0.81)
Absolute Change at Week 24	
n	47
Mean (SD)	0.02 (0.30)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	0.02 (0.04)
95% CI of LS mean	(-0.07, 0.10)
P-value	0.7044

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	-0.24 (0.94)
Week 24	
n	31
Mean (SD)	-0.39 (1.03)
Absolute Change at Week 24	
n	31
Mean (SD)	-0.15 (0.30)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-0.15 (0.05)
95% CI of LS mean	(-0.26, -0.04)
P-value	0.0087

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	-0.01 (0.85)
Week 24	
n	62
Mean (SD)	-0.07 (0.92)
Absolute Change at Week 24	
n	62
Mean (SD)	-0.05 (0.30)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	-0.05 (0.04)
95% CI of LS mean	(-0.13, 0.02)
P-value	0.1748

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in BMI Z-score at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	0.26 (1.01)
Week 24	
n	10
Mean (SD)	0.24 (1.09)
Absolute Change at Week 24	
n	10
Mean (SD)	-0.02 (0.37)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	-0.02 (0.11)
95% CI of LS mean	(-0.26, 0.23)
P-value	0.8646

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline BMI z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.2365
Region (North America vs. Rest of the World)	0.2724
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.5693

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline sweat chloride as covariate.
- N/C: model does not converge.

Table 3.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	43
Mean (SD)	43.05 (22.47)
Week 24	
n	41
Mean (SD)	35.39 (17.60)
Absolute Change at Week 24	
n	41
Mean (SD)	-8.44 (14.34)
Absolute Change through Week 24 (MMRM)	
n	43
LS mean (SE)	-8.86 (1.87)
95% CI of LS mean	(-12.64, -5.08)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for genotype group (F/MF vs rest) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	37.07 (18.62)
Week 24	
n	33
Mean (SD)	28.09 (11.40)
Absolute Change at Week 24	
n	33
Mean (SD)	-9.08 (13.67)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	-8.40 (1.26)
95% CI of LS mean	(-10.96, -5.84)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for genotype group (F/MF vs rest) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	39.91 (22.21)
Week 24	
n	45
Mean (SD)	32.22 (15.97)
Absolute Change at Week 24	
n	45
Mean (SD)	-8.11 (15.53)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	-8.06 (1.66)
95% CI of LS mean	(-11.41, -4.70)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for genotype group (F/MF vs rest) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	30
Mean (SD)	41.18 (19.12)
Week 24	
n	29
Mean (SD)	32.00 (14.99)
Absolute Change at Week 24	
n	29
Mean (SD)	-9.67 (11.27)
Absolute Change through Week 24 (MMRM)	
n	30
LS mean (SE)	-9.59 (1.56)
95% CI of LS mean	(-12.79, -6.39)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for genotype group (F/MF vs rest) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	39.27 (21.31)
Week 24	
n	59
Mean (SD)	32.32 (16.01)
Absolute Change at Week 24	
n	59
Mean (SD)	-7.45 (14.58)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	-7.77 (1.37)
95% CI of LS mean	(-10.51, -5.02)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for genotype group (F/MF vs rest) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	9
Mean (SD)	46.39 (18.60)
Week 24	
n	9
Mean (SD)	32.61 (15.93)
Absolute Change at Week 24	
n	9
Mean (SD)	-13.78 (8.91)
Absolute Change through Week 24 (MMRM)	
n	9
LS mean (SE)	-12.00 (3.19)
95% CI of LS mean	(-25.82, 1.82)
P-value	0.0647

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for genotype group (F/MF vs rest) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.4.2.1
Study VX21-121-105: Subgroup Factor Test for
Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0367
Region (North America vs. Rest of the World)	0.7593
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.4396

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Chi-square test.

Table 3.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Non-missing value at Week 24, N1	41
Number of subjects with missing value at Week 24	3
SwCl <60 mmol/L at Week 24, n (%)	36 (81.82)
95% CI for the proportion	(67.29, 91.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 3.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Non-missing value at Week 24, N1	33
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	33 (97.06)
95% CI for the proportion	(84.67, 99.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 3.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Non-missing value at Week 24, N1	45
Number of subjects with missing value at Week 24	2
SwCl <60 mmol/L at Week 24, n (%)	42 (89.36)
95% CI for the proportion	(76.90, 96.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 3.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Non-missing value at Week 24, N1	29
Number of subjects with missing value at Week 24	2
SwCl <60 mmol/L at Week 24, n (%)	27 (87.10)
95% CI for the proportion	(70.17, 96.37)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 3.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Non-missing value at Week 24, N1	59
Number of subjects with missing value at Week 24	3
SwCl <60 mmol/L at Week 24, n (%)	55 (88.71)
95% CI for the proportion	(78.11, 95.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 3.2.2.4.2.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <60 mmol/L at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Non-missing value at Week 24, N1	9
Number of subjects with missing value at Week 24	1
SwCl <60 mmol/L at Week 24, n (%)	8 (80.00)
95% CI for the proportion	(44.39, 97.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method.

Table 3.2.2.4.3.1
Study VX21-121-105: Subgroup Factor Test for
Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1165
Region (North America vs. Rest of the World)	0.6778
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.5571

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Chi-square test.

Table 3.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Non-missing value at Week 24, N1	41
Number of subjects with missing value at Week 24	3
SwCl <30 mmol/L at Week 24, n (%)	18 (40.91)
95% CI for the proportion	(26.34, 56.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 3.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Non-missing value at Week 24, N1	33
Number of subjects with missing value at Week 24	1
SwCl <30 mmol/L at Week 24, n (%)	20 (58.82)
95% CI for the proportion	(40.70, 75.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 3.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Non-missing value at Week 24, N1	45
Number of subjects with missing value at Week 24	2
SwCl <30 mmol/L at Week 24, n (%)	22 (46.81)
95% CI for the proportion	(32.11, 61.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 3.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Non-missing value at Week 24, N1	29
Number of subjects with missing value at Week 24	2
SwCl <30 mmol/L at Week 24, n (%)	16 (51.61)
95% CI for the proportion	(33.06, 69.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 3.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Non-missing value at Week 24, N1	59
Number of subjects with missing value at Week 24	3
SwCl <30 mmol/L at Week 24, n (%)	31 (50.00)
95% CI for the proportion	(37.02, 62.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 3.2.2.4.3.2
Study VX21-121-105: Proportion of Subjects with Sweat Chloride <30 mmol/L at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Non-missing value at Week 24, N1	9
Number of subjects with missing value at Week 24	1
SwCl <30 mmol/L at Week 24, n (%)	4 (40.00)
95% CI for the proportion	(12.16, 73.76)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- N1: number of subjects with non-missing SwCl at Week 24
- 95% CI is based on the Clopper-Pearson method

Table 3.2.2.5.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1330
Region (North America vs. Rest of the World)	0.5313
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.7054

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline weight as covariate.
- N/C: model does not converge.

Table 3.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	30.79 (7.89)
Week 24	
n	44
Mean (SD)	32.26 (8.68)
Absolute Change at Week 24	
n	44
Mean (SD)	1.47 (1.50)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	1.47 (0.21)
95% CI of LS mean	(1.04, 1.89)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	29.46 (6.96)
Week 24	
n	34
Mean (SD)	31.40 (7.66)
Absolute Change at Week 24	
n	34
Mean (SD)	1.94 (1.52)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	1.94 (0.26)
95% CI of LS mean	(1.41, 2.47)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	31.70 (7.73)
Week 24	
n	47
Mean (SD)	33.59 (8.43)
Absolute Change at Week 24	
n	47
Mean (SD)	1.89 (1.64)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	1.89 (0.23)
95% CI of LS mean	(1.42, 2.35)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	27.95 (6.57)
Week 24	
n	31
Mean (SD)	29.30 (7.26)
Absolute Change at Week 24	
n	31
Mean (SD)	1.35 (1.26)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	1.35 (0.22)
95% CI of LS mean	(0.90, 1.80)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	30.01 (7.76)
Week 24	
n	62
Mean (SD)	31.59 (8.48)
Absolute Change at Week 24	
n	62
Mean (SD)	1.58 (1.49)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	1.58 (0.18)
95% CI of LS mean	(1.22, 1.95)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.5.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	33.05 (6.73)
Week 24	
n	10
Mean (SD)	35.22 (7.55)
Absolute Change at Week 24	
n	10
Mean (SD)	2.17 (1.82)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	2.17 (0.62)
95% CI of LS mean	(0.73, 3.62)
P-value	0.0088

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.6.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0153
Region (North America vs. Rest of the World)	0.4962
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.8992

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline weight z-score as covariate.
- N/C: model does not converge.

Table 3.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	0.15 (0.92)
Week 24	
n	44
Mean (SD)	0.09 (1.02)
Absolute Change at Week 24	
n	44
Mean (SD)	-0.06 (0.20)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	-0.06 (0.03)
95% CI of LS mean	(-0.12, 0.00)
P-value	0.0455

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	-0.18 (0.84)
Week 24	
n	34
Mean (SD)	-0.15 (0.86)
Absolute Change at Week 24	
n	34
Mean (SD)	0.04 (0.24)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	0.04 (0.04)
95% CI of LS mean	(-0.05, 0.12)
P-value	0.4040

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	0.08 (0.85)
Week 24	
n	47
Mean (SD)	0.10 (0.90)
Absolute Change at Week 24	
n	47
Mean (SD)	0.01 (0.23)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	0.01 (0.03)
95% CI of LS mean	(-0.06, 0.08)
P-value	0.7332

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	-0.12 (0.96)
Week 24	
n	31
Mean (SD)	-0.18 (1.02)
Absolute Change at Week 24	
n	31
Mean (SD)	-0.06 (0.21)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-0.06 (0.04)
95% CI of LS mean	(-0.14, 0.01)
P-value	0.1001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	-0.10 (0.90)
Week 24	
n	62
Mean (SD)	-0.13 (0.95)
Absolute Change at Week 24	
n	62
Mean (SD)	-0.03 (0.22)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	-0.03 (0.03)
95% CI of LS mean	(-0.08, 0.03)
P-value	0.3315

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.6.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Weight Z-score at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	0.22 (0.83)
Week 24	
n	10
Mean (SD)	0.24 (0.90)
Absolute Change at Week 24	
n	10
Mean (SD)	0.02 (0.28)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	0.02 (0.08)
95% CI of LS mean	(-0.16, 0.20)
P-value	0.8083

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline weight z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.7.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0986
Region (North America vs. Rest of the World)	0.4089
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.1315

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline height as covariate.
- N/C: model does not converge.

Table 3.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	132.38 (9.87)
Week 24	
n	44
Mean (SD)	135.00 (9.94)
Absolute Change at Week 24	
n	44
Mean (SD)	2.63 (0.91)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	2.63 (0.14)
95% CI of LS mean	(2.35, 2.91)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	133.72 (11.39)
Week 24	
n	34
Mean (SD)	136.59 (11.72)
Absolute Change at Week 24	
n	34
Mean (SD)	2.87 (1.20)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	2.87 (0.20)
95% CI of LS mean	(2.45, 3.28)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	133.98 (10.67)
Week 24	
n	47
Mean (SD)	136.47 (10.82)
Absolute Change at Week 24	
n	47
Mean (SD)	2.49 (0.99)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	2.49 (0.14)
95% CI of LS mean	(2.20, 2.78)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	131.42 (10.23)
Week 24	
n	31
Mean (SD)	134.52 (10.60)
Absolute Change at Week 24	
n	31
Mean (SD)	3.10 (1.03)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	3.10 (0.19)
95% CI of LS mean	(2.71, 3.49)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	132.93 (10.44)
Week 24	
n	62
Mean (SD)	135.58 (10.56)
Absolute Change at Week 24	
n	62
Mean (SD)	2.65 (1.08)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	2.65 (0.14)
95% CI of LS mean	(2.37, 2.92)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.7.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height (cm) at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	136.69 (11.47)
Week 24	
n	10
Mean (SD)	139.76 (11.86)
Absolute Change at Week 24	
n	10
Mean (SD)	3.07 (0.70)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	3.07 (0.47)
95% CI of LS mean	(1.89, 4.25)
P-value	0.0009

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.8.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1914
Region (North America vs. Rest of the World)	0.5643
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.2901

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) and subgroup as fixed effect and baseline height z-score as covariate.
- N/C: model does not converge.

Table 3.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	-0.09 (0.97)
Week 24	
n	44
Mean (SD)	-0.08 (0.97)
Absolute Change at Week 24	
n	44
Mean (SD)	0.02 (0.16)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	0.02 (0.02)
95% CI of LS mean	(-0.03, 0.07)
P-value	0.5165

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	0.06 (0.91)
Week 24	
n	34
Mean (SD)	0.06 (0.97)
Absolute Change at Week 24	
n	34
Mean (SD)	0.01 (0.19)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	0.01 (0.03)
95% CI of LS mean	(-0.06, 0.07)
P-value	0.8353

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	-0.12 (0.98)
Week 24	
n	47
Mean (SD)	-0.14 (1.00)
Absolute Change at Week 24	
n	47
Mean (SD)	-0.01 (0.18)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	-0.01 (0.03)
95% CI of LS mean	(-0.06, 0.04)
P-value	0.6255

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	0.12 (0.88)
Week 24	
n	31
Mean (SD)	0.17 (0.89)
Absolute Change at Week 24	
n	31
Mean (SD)	0.05 (0.16)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	0.05 (0.03)
95% CI of LS mean	(-0.01, 0.11)
P-value	0.0984

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	-0.10 (0.97)
Week 24	
n	62
Mean (SD)	-0.10 (0.97)
Absolute Change at Week 24	
n	62
Mean (SD)	0.00 (0.18)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	0.00 (0.02)
95% CI of LS mean	(-0.04, 0.05)
P-value	0.9010

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.8.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in Height Z-score at Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	0.10 (0.82)
Week 24	
n	10
Mean (SD)	0.15 (0.86)
Absolute Change at Week 24	
n	10
Mean (SD)	0.06 (0.13)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	0.06 (0.05)
95% CI of LS mean	(-0.06, 0.17)
P-value	0.2747

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline height z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- N/C: model does not converge.

Table 3.2.2.9.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.0004
Region (North America vs. Rest of the World)	0.5202
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.8616

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline $LCI_{2.5}$ as covariate.
- N/C: model does not converge.

Table 3.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	40
Mean (SD)	6.60 (0.78)
Week 24	
n	34
Mean (SD)	6.35 (0.43)
Absolute Change at Week 24	
n	32
Mean (SD)	-0.28 (0.53)
Absolute Change through Week 24 (MMRM)	
n	32
LS mean (SE)	-0.20 (0.05)
95% CI of LS mean	(-0.31, -0.09)
P-value	0.0013

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	32
Mean (SD)	6.67 (0.71)
Week 24	
n	27
Mean (SD)	6.60 (0.64)
Absolute Change at Week 24	
n	26
Mean (SD)	-0.03 (0.53)
Absolute Change through Week 24 (MMRM)	
n	26
LS mean (SE)	0.05 (0.07)
95% CI of LS mean	(-0.10, 0.20)
P-value	0.5087

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	43
Mean (SD)	6.60 (0.68)
Week 24	
n	37
Mean (SD)	6.47 (0.56)
Absolute Change at Week 24	
n	35
Mean (SD)	-0.15 (0.54)
Absolute Change through Week 24 (MMRM)	
n	35
LS mean (SE)	-0.10 (0.06)
95% CI of LS mean	(-0.22, 0.03)
P-value	0.1210

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	29
Mean (SD)	6.67 (0.84)
Week 24	
n	24
Mean (SD)	6.45 (0.53)
Absolute Change at Week 24	
n	23
Mean (SD)	-0.19 (0.56)
Absolute Change through Week 24 (MMRM)	
n	23
LS mean (SE)	-0.07 (0.09)
95% CI of LS mean	(-0.24, 0.11)
P-value	0.4571

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	6.40 (0.46)
Week 24	
n	50
Mean (SD)	6.34 (0.47)
Absolute Change at Week 24	
n	50
Mean (SD)	-0.06 (0.48)
Absolute Change through Week 24 (MMRM)	
n	50
LS mean (SE)	-0.01 (0.05)
95% CI of LS mean	(-0.11, 0.08)
P-value	0.7508

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.2.9.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	8.04 (0.60)
Week 24	
n	8
Mean (SD)	6.97 (0.52)
Absolute Change at Week 24	
n	8
Mean (SD)	-0.82 (0.47)
Absolute Change through Week 24 (MMRM)	
n	8
LS mean (SE)	-0.47 (0.18)
95% CI of LS mean	(-0.91, -0.02)
P-value	0.0421

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the average of pre-dose Day 1 values. For subjects who are on stable ELX/TEZ/IVA, if the pre-dose Day 1 value is missing, the most recent available pre-dose value, including the screening assessment, is used as baseline.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline $LCI_{2.5}$ as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 12 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3066
Region (North America vs. Rest of the World)	0.2465
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.8058

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Respiratory domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	84.33 (14.04)
Week 4 (MMRM)	
n	42
LS mean (SE)	85.12 (1.62)
95% CI of LS mean	(81.84, 88.40)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	0.79 (1.62)
95% CI of LS mean	(-2.49, 4.08)
Week 8 (MMRM)	
n	42
LS mean (SE)	85.12 (2.14)
95% CI of LS mean	(80.80, 89.44)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	0.79 (2.14)
95% CI of LS mean	(-3.53, 5.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	88.33 (1.69)
95% CI of LS mean	(84.91, 91.76)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	4.01 (1.69)
95% CI of LS mean	(0.59, 7.43)
Week 16 (MMRM)	
n	42
LS mean (SE)	90.28 (1.70)
95% CI of LS mean	(86.84, 93.72)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	5.95 (1.70)
95% CI of LS mean	(2.51, 9.39)
Week 24	
n	44
Mean (SD)	86.55 (15.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	2.58 (16.72)
Week 24 (MMRM)	
n	44
LS mean (SE)	86.90 (2.24)
95% CI of LS mean	(82.38, 91.43)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	2.58 (2.24)
95% CI of LS mean	(-1.95, 7.11)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	4.27 (1.53)
95% CI of LS mean	(1.17, 7.37)
P-value	0.0082

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	85.35 (18.64)
Week 4 (MMRM)	
n	33
LS mean (SE)	85.86 (3.00)
95% CI of LS mean	(79.74, 91.97)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	0.51 (3.00)
95% CI of LS mean	(-5.61, 6.62)
Week 8 (MMRM)	
n	33
LS mean (SE)	88.13 (2.92)
95% CI of LS mean	(82.17, 94.09)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	2.78 (2.92)
95% CI of LS mean	(-3.18, 8.74)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	92.93 (1.75)
95% CI of LS mean	(89.36, 96.50)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	7.58 (1.75)
95% CI of LS mean	(4.01, 11.14)
Week 16 (MMRM)	
n	33
LS mean (SE)	91.67 (1.96)
95% CI of LS mean	(87.67, 95.66)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	6.31 (1.96)
95% CI of LS mean	(2.32, 10.31)
Week 24	
n	34
Mean (SD)	84.80 (16.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	0.76 (21.18)
Week 24 (MMRM)	
n	34
LS mean (SE)	86.11 (2.56)
95% CI of LS mean	(80.90, 91.33)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	0.76 (2.56)
95% CI of LS mean	(-4.46, 5.97)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	3.54 (1.91)
95% CI of LS mean	(-0.36, 7.44)
P-value	0.0740

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	82.80 (17.32)
Week 4 (MMRM)	
n	47
LS mean (SE)	82.09 (2.36)
95% CI of LS mean	(77.34, 86.85)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-0.71 (2.36)
95% CI of LS mean	(-5.46, 4.05)
Week 8 (MMRM)	
n	47
LS mean (SE)	85.11 (2.28)
95% CI of LS mean	(80.51, 89.70)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	2.30 (2.28)
95% CI of LS mean	(-2.29, 6.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	89.54 (1.66)
95% CI of LS mean	(86.20, 92.88)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	6.74 (1.66)
95% CI of LS mean	(3.40, 10.07)
Week 16 (MMRM)	
n	47
LS mean (SE)	89.89 (1.73)
95% CI of LS mean	(86.41, 93.37)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	7.09 (1.73)
95% CI of LS mean	(3.61, 10.57)
Week 24	
n	47
Mean (SD)	85.11 (15.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	2.30 (19.48)
Week 24 (MMRM)	
n	47
LS mean (SE)	85.11 (2.14)
95% CI of LS mean	(80.80, 89.41)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	2.30 (2.14)
95% CI of LS mean	(-2.00, 6.61)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	4.70 (1.59)
95% CI of LS mean	(1.51, 7.89)
P-value	0.0048

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	88.10 (13.50)
Week 4 (MMRM)	
n	28
LS mean (SE)	91.07 (1.94)
95% CI of LS mean	(87.08, 95.07)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	2.98 (1.94)
95% CI of LS mean	(-1.02, 6.97)
Week 8 (MMRM)	
n	28
LS mean (SE)	88.69 (2.45)
95% CI of LS mean	(83.64, 93.74)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	0.60 (2.45)
95% CI of LS mean	(-4.45, 5.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	92.06 (2.26)
95% CI of LS mean	(87.41, 96.72)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	3.97 (2.26)
95% CI of LS mean	(-0.69, 8.63)
Week 16 (MMRM)	
n	28
LS mean (SE)	92.56 (2.35)
95% CI of LS mean	(87.70, 97.42)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	4.46 (2.35)
95% CI of LS mean	(-0.39, 9.32)
Week 24	
n	31
Mean (SD)	86.83 (16.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	0.89 (17.62)
Week 24 (MMRM)	
n	31
LS mean (SE)	88.99 (2.64)
95% CI of LS mean	(83.55, 94.43)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	0.89 (2.64)
95% CI of LS mean	(-4.54, 6.33)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	2.68 (2.01)
95% CI of LS mean	(-1.48, 6.84)
P-value	0.1957

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	84.18 (16.50)
Week 4 (MMRM)	
n	59
LS mean (SE)	85.88 (1.74)
95% CI of LS mean	(82.40, 89.35)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	1.69 (1.74)
95% CI of LS mean	(-1.78, 5.17)
Week 8 (MMRM)	
n	59
LS mean (SE)	87.43 (2.01)
95% CI of LS mean	(83.40, 91.45)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	3.25 (2.01)
95% CI of LS mean	(-0.78, 7.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	90.77 (1.57)
95% CI of LS mean	(87.62, 93.91)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	6.59 (1.57)
95% CI of LS mean	(3.44, 9.73)
Week 16 (MMRM)	
n	59
LS mean (SE)	91.38 (1.50)
95% CI of LS mean	(88.39, 94.38)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	7.20 (1.50)
95% CI of LS mean	(4.21, 10.20)
Week 24	
n	62
Mean (SD)	84.54 (16.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	1.27 (19.50)
Week 24 (MMRM)	
n	62
LS mean (SE)	85.45 (1.98)
95% CI of LS mean	(81.49, 89.41)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	1.27 (1.98)
95% CI of LS mean	(-2.69, 5.23)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	4.24 (1.39)
95% CI of LS mean	(1.45, 7.02)
P-value	0.0035

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	90.00 (15.61)
Week 4 (MMRM)	
n	10
LS mean (SE)	85.00 (6.12)
95% CI of LS mean	(70.88, 99.12)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-5.00 (6.12)
95% CI of LS mean	(-19.12, 9.12)
Week 8 (MMRM)	
n	10
LS mean (SE)	85.83 (2.87)
95% CI of LS mean	(49.32, 122.34)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-4.17 (2.87)
95% CI of LS mean	(-40.68, 32.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	89.17 (4.73)
95% CI of LS mean	(66.22, 112.12)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-0.83 (4.73)
95% CI of LS mean	(-23.78, 22.12)
Week 16 (MMRM)	
n	10
LS mean (SE)	92.50 (5.24)
95% CI of LS mean	(76.27, 108.73)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	2.50 (5.24)
95% CI of LS mean	(-13.73, 18.73)
Week 24	
n	10
Mean (SD)	95.00 (8.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.1.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	5.00 (20.11)
Week 24 (MMRM)	
n	10
LS mean (SE)	95.00 (6.52)
95% CI of LS mean	(75.72, 114.28)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	5.00 (6.52)
95% CI of LS mean	(-14.28, 24.28)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	3.75 (5.61)
95% CI of LS mean	(-14.40, 21.90)
P-value	0.5529

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3142
Region (North America vs. Rest of the World)	0.2057
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.6296

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Respiratory domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	86.84 (14.27)
Week 4 (MMRM)	
n	44
LS mean (SE)	82.95 (2.47)
95% CI of LS mean	(77.98, 87.93)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	-3.89 (2.47)
95% CI of LS mean	(-8.87, 1.09)
Week 8 (MMRM)	
n	44
LS mean (SE)	84.22 (2.53)
95% CI of LS mean	(79.10, 89.33)
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	-2.63 (2.53)
95% CI of LS mean	(-7.74, 2.49)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	43
LS mean (SE)	91.91 (1.29)
95% CI of LS mean	(89.31, 94.50)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	5.06 (1.29)
95% CI of LS mean	(2.46, 7.66)
Week 16 (MMRM)	
n	44
LS mean (SE)	88.96 (2.27)
95% CI of LS mean	(84.39, 93.54)
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	2.12 (2.27)
95% CI of LS mean	(-2.46, 6.70)
Week 24	
n	44
Mean (SD)	88.38 (15.24)
Absolute Change at Week 24	
n	44
Mean (SD)	1.54 (17.88)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 24 (MMRM)	
n	44
LS mean (SE)	88.38 (2.23)
95% CI of LS mean	(83.88, 92.88)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	1.54 (2.23)
95% CI of LS mean	(-2.96, 6.04)
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	1.83 (1.73)
95% CI of LS mean	(-1.66, 5.32)
P-value	0.2957

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	88.10 (17.81)
Week 4 (MMRM)	
n	34
LS mean (SE)	86.76 (3.20)
95% CI of LS mean	(80.26, 93.27)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-1.34 (3.20)
95% CI of LS mean	(-7.84, 5.16)
Week 8 (MMRM)	
n	34
LS mean (SE)	90.03 (2.44)
95% CI of LS mean	(85.07, 95.00)
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	1.93 (2.44)
95% CI of LS mean	(-3.04, 6.89)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	34
LS mean (SE)	92.48 (2.32)
95% CI of LS mean	(87.75, 97.21)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	4.38 (2.32)
95% CI of LS mean	(-0.35, 9.11)
Week 16 (MMRM)	
n	34
LS mean (SE)	94.44 (1.80)
95% CI of LS mean	(90.78, 98.11)
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	6.34 (1.80)
95% CI of LS mean	(2.68, 10.00)
Week 24	
n	34
Mean (SD)	85.29 (17.19)
Absolute Change at Week 24	
n	34
Mean (SD)	-2.81 (24.53)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 24 (MMRM)	
n	34
LS mean (SE)	85.29 (2.99)
95% CI of LS mean	(79.20, 91.39)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	-2.81 (2.99)
95% CI of LS mean	(-8.91, 3.29)
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	1.76 (2.01)
95% CI of LS mean	(-2.34, 5.87)
P-value	0.3872

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	85.84 (17.50)
Week 4 (MMRM)	
n	47
LS mean (SE)	84.04 (2.31)
95% CI of LS mean	(79.40, 88.68)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-1.80 (2.31)
95% CI of LS mean	(-6.44, 2.84)
Week 8 (MMRM)	
n	47
LS mean (SE)	86.88 (2.30)
95% CI of LS mean	(82.26, 91.50)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	1.04 (2.30)
95% CI of LS mean	(-3.58, 5.66)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Region = North America

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	93.03 (1.68)
95% CI of LS mean	(89.65, 96.40)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	7.19 (1.68)
95% CI of LS mean	(3.81, 10.56)
Week 16 (MMRM)	
n	47
LS mean (SE)	92.55 (1.38)
95% CI of LS mean	(89.77, 95.34)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	6.71 (1.38)
95% CI of LS mean	(3.93, 9.50)
Week 24	
n	47
Mean (SD)	87.59 (15.59)
Absolute Change at Week 24	
n	47
Mean (SD)	1.75 (19.92)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 24 (MMRM)	
n	47
LS mean (SE)	87.59 (2.23)
95% CI of LS mean	(83.10, 92.08)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	1.75 (2.23)
95% CI of LS mean	(-2.74, 6.24)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	4.23 (1.38)
95% CI of LS mean	(1.45, 7.01)
P-value	0.0037

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	89.75 (12.75)
Week 4 (MMRM)	
n	31
LS mean (SE)	85.48 (3.61)
95% CI of LS mean	(78.10, 92.86)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	-4.27 (3.61)
95% CI of LS mean	(-11.65, 3.12)
Week 8 (MMRM)	
n	31
LS mean (SE)	86.56 (3.01)
95% CI of LS mean	(80.35, 92.77)
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	-3.19 (3.01)
95% CI of LS mean	(-9.40, 3.02)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	30
LS mean (SE)	90.87 (1.90)
95% CI of LS mean	(86.98, 94.76)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	1.12 (1.90)
95% CI of LS mean	(-2.77, 5.01)
Week 16 (MMRM)	
n	31
LS mean (SE)	89.53 (3.06)
95% CI of LS mean	(83.28, 95.79)
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	-0.22 (3.06)
95% CI of LS mean	(-6.47, 6.04)
Week 24	
n	31
Mean (SD)	86.20 (17.03)
Absolute Change at Week 24	
n	31
Mean (SD)	-3.55 (22.50)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 24 (MMRM)	
n	31
LS mean (SE)	86.20 (3.25)
95% CI of LS mean	(79.53, 92.87)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	-3.55 (3.25)
95% CI of LS mean	(-10.22, 3.12)
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-1.88 (2.54)
95% CI of LS mean	(-7.09, 3.32)
P-value	0.4655

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	86.83 (16.08)
Week 4 (MMRM)	
n	62
LS mean (SE)	83.33 (2.40)
95% CI of LS mean	(78.53, 88.14)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	-3.49 (2.40)
95% CI of LS mean	(-8.30, 1.31)
Week 8 (MMRM)	
n	62
LS mean (SE)	86.83 (2.14)
95% CI of LS mean	(82.54, 91.12)
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	0.00 (2.14)
95% CI of LS mean	(-4.29, 4.29)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	61
LS mean (SE)	92.42 (1.45)
95% CI of LS mean	(89.51, 95.32)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	5.59 (1.45)
95% CI of LS mean	(2.69, 8.50)
Week 16 (MMRM)	
n	62
LS mean (SE)	90.82 (1.83)
95% CI of LS mean	(87.17, 94.48)
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	4.00 (1.83)
95% CI of LS mean	(0.34, 7.65)
Week 24	
n	62
Mean (SD)	85.13 (17.27)
Absolute Change at Week 24	
n	62
Mean (SD)	-1.70 (21.82)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 24 (MMRM)	
n	62
LS mean (SE)	85.13 (2.18)
95% CI of LS mean	(80.76, 89.49)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	-1.70 (2.18)
95% CI of LS mean	(-6.07, 2.66)
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	1.15 (1.58)
95% CI of LS mean	(-2.02, 4.31)
P-value	0.4718

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	87.22 (17.18)
Week 4 (MMRM)	
n	10
LS mean (SE)	91.67 (2.90)
95% CI of LS mean	(84.49, 98.84)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	4.44 (2.90)
95% CI of LS mean	(-2.73, 11.62)
Week 8 (MMRM)	
n	10
LS mean (SE)	86.11 (2.60)
95% CI of LS mean	(79.74, 92.49)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-1.11 (2.60)
95% CI of LS mean	(-7.49, 5.26)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	89.44 (3.22)
95% CI of LS mean	(82.09, 96.79)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	2.22 (3.22)
95% CI of LS mean	(-5.13, 9.57)
Week 16 (MMRM)	
n	10
LS mean (SE)	93.89 (2.11)
95% CI of LS mean	(87.92, 99.86)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	6.67 (2.11)
95% CI of LS mean	(0.70, 12.64)
Week 24	
n	10
Mean (SD)	96.11 (5.27)
Absolute Change at Week 24	
n	10
Mean (SD)	8.89 (17.99)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.2.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 24 (MMRM)	
n	10
LS mean (SE)	96.11 (4.40)
95% CI of LS mean	(84.88, 107.35)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	8.89 (4.40)
95% CI of LS mean	(-2.35, 20.12)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	7.78 (3.02)
95% CI of LS mean	(-0.93, 16.49)
P-value	0.0674

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiratory Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Body

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.8997
Region (North America vs. Rest of the World)	0.3891
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.8784

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Body domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Digestion

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.5173
Region (North America vs. Rest of the World)	0.1967
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.4427

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Digestion domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Eat

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.2115
Region (North America vs. Rest of the World)	0.2904
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9535

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Eat domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Emotion

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.2229
Region (North America vs. Rest of the World)	0.5092
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.3430

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Emotion domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Physical

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3477
Region (North America vs. Rest of the World)	0.6533
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9955

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Physical domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Social

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.6920
Region (North America vs. Rest of the World)	0.3202
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9277

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Social domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
Full Analysis Set
Domain: Treatment Burden

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9678
Region (North America vs. Rest of the World)	0.0379
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.4272

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Treatment Burden domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	85.71 (21.43)
Week 4 (MMRM)	
n	42
LS mean (SE)	86.77 (3.19)
95% CI of LS mean	(80.33, 93.22)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	1.06 (3.19)
95% CI of LS mean	(-5.38, 7.50)
Week 8 (MMRM)	
n	42
LS mean (SE)	89.95 (2.59)
95% CI of LS mean	(84.71, 95.19)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	4.23 (2.59)
95% CI of LS mean	(-1.01, 9.47)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	88.78 (2.23)
95% CI of LS mean	(84.28, 93.29)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	3.07 (2.23)
95% CI of LS mean	(-1.43, 7.57)
Week 16 (MMRM)	
n	42
LS mean (SE)	92.06 (1.86)
95% CI of LS mean	(88.30, 95.83)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	6.35 (1.86)
95% CI of LS mean	(2.58, 10.11)
Week 24	
n	44
Mean (SD)	89.39 (19.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	4.23 (25.14)
Week 24 (MMRM)	
n	44
LS mean (SE)	89.95 (2.94)
95% CI of LS mean	(84.00, 95.90)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	4.23 (2.94)
95% CI of LS mean	(-1.72, 10.18)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	5.29 (2.08)
95% CI of LS mean	(1.08, 9.50)
P-value	0.0151

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	78.79 (25.66)
Week 4 (MMRM)	
n	33
LS mean (SE)	82.49 (2.64)
95% CI of LS mean	(77.08, 87.90)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	3.70 (2.64)
95% CI of LS mean	(-1.71, 9.11)
Week 8 (MMRM)	
n	33
LS mean (SE)	84.51 (3.41)
95% CI of LS mean	(77.56, 91.46)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	5.72 (3.41)
95% CI of LS mean	(-1.23, 12.68)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	88.22 (2.89)
95% CI of LS mean	(82.31, 94.12)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	9.43 (2.89)
95% CI of LS mean	(3.53, 15.33)
Week 16 (MMRM)	
n	33
LS mean (SE)	90.24 (2.41)
95% CI of LS mean	(85.32, 95.15)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	11.45 (2.41)
95% CI of LS mean	(6.53, 16.36)
Week 24	
n	34
Mean (SD)	86.27 (22.23)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	7.41 (23.19)
Week 24 (MMRM)	
n	34
LS mean (SE)	86.20 (3.29)
95% CI of LS mean	(79.49, 92.90)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	7.41 (3.29)
95% CI of LS mean	(0.70, 14.11)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	9.43 (2.58)
95% CI of LS mean	(4.16, 14.70)
P-value	0.0010

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	78.49 (25.10)
Week 4 (MMRM)	
n	47
LS mean (SE)	83.22 (3.15)
95% CI of LS mean	(76.87, 89.56)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	4.73 (3.15)
95% CI of LS mean	(-1.62, 11.08)
Week 8 (MMRM)	
n	47
LS mean (SE)	85.34 (2.84)
95% CI of LS mean	(79.61, 91.07)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	6.86 (2.84)
95% CI of LS mean	(1.12, 12.59)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	89.13 (1.99)
95% CI of LS mean	(85.12, 93.13)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	10.64 (1.99)
95% CI of LS mean	(6.63, 14.65)
Week 16 (MMRM)	
n	47
LS mean (SE)	90.07 (2.18)
95% CI of LS mean	(85.67, 94.47)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	11.58 (2.18)
95% CI of LS mean	(7.19, 15.98)
Week 24	
n	47
Mean (SD)	85.11 (24.33)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	6.62 (28.34)
Week 24 (MMRM)	
n	47
LS mean (SE)	85.11 (3.37)
95% CI of LS mean	(78.32, 91.89)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	6.62 (3.37)
95% CI of LS mean	(-0.17, 13.41)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	9.10 (2.51)
95% CI of LS mean	(4.05, 14.16)
P-value	0.0007

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	89.68 (18.87)
Week 4 (MMRM)	
n	28
LS mean (SE)	87.70 (2.54)
95% CI of LS mean	(82.47, 92.93)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	-1.98 (2.54)
95% CI of LS mean	(-7.22, 3.25)
Week 8 (MMRM)	
n	28
LS mean (SE)	91.27 (2.62)
95% CI of LS mean	(85.88, 96.66)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	1.59 (2.62)
95% CI of LS mean	(-3.80, 6.98)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	87.62 (3.23)
95% CI of LS mean	(80.98, 94.25)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	-2.07 (3.23)
95% CI of LS mean	(-8.70, 4.57)
Week 16 (MMRM)	
n	28
LS mean (SE)	93.25 (1.85)
95% CI of LS mean	(89.43, 97.08)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	3.57 (1.85)
95% CI of LS mean	(-0.26, 7.40)
Week 24	
n	31
Mean (SD)	92.47 (13.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	3.97 (15.18)
Week 24 (MMRM)	
n	31
LS mean (SE)	93.65 (1.86)
95% CI of LS mean	(89.82, 97.48)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	3.97 (1.86)
95% CI of LS mean	(0.14, 7.80)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	3.77 (1.56)
95% CI of LS mean	(0.55, 6.99)
P-value	0.0238

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	83.80 (23.64)
Week 4 (MMRM)	
n	59
LS mean (SE)	84.56 (2.49)
95% CI of LS mean	(79.56, 89.55)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	0.75 (2.49)
95% CI of LS mean	(-4.24, 5.75)
Week 8 (MMRM)	
n	59
LS mean (SE)	90.02 (1.95)
95% CI of LS mean	(86.12, 93.92)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	6.21 (1.95)
95% CI of LS mean	(2.31, 10.12)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	88.83 (1.98)
95% CI of LS mean	(84.87, 92.80)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	5.03 (1.98)
95% CI of LS mean	(1.06, 9.00)
Week 16 (MMRM)	
n	59
LS mean (SE)	91.71 (1.64)
95% CI of LS mean	(88.43, 95.00)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	7.91 (1.64)
95% CI of LS mean	(4.63, 11.19)
Week 24	
n	62
Mean (SD)	88.71 (19.03)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	5.27 (25.05)
Week 24 (MMRM)	
n	62
LS mean (SE)	89.08 (2.38)
95% CI of LS mean	(84.31, 93.84)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	5.27 (2.38)
95% CI of LS mean	(0.51, 10.04)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	6.59 (1.74)
95% CI of LS mean	(3.10, 10.08)
P-value	0.0004

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	77.78 (27.22)
Week 4 (MMRM)	
n	10
LS mean (SE)	88.89 (5.50)
95% CI of LS mean	(77.16, 100.61)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	11.11 (5.50)
95% CI of LS mean	(-0.61, 22.84)
Week 8 (MMRM)	
n	10
LS mean (SE)	81.11 (5.50)
95% CI of LS mean	(69.39, 92.84)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	3.33 (5.50)
95% CI of LS mean	(-8.39, 15.06)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	86.67 (5.50)
95% CI of LS mean	(74.94, 98.39)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	8.89 (5.50)
95% CI of LS mean	(-2.84, 20.61)
Week 16 (MMRM)	
n	10
LS mean (SE)	87.78 (5.50)
95% CI of LS mean	(76.05, 99.50)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	10.00 (5.50)
95% CI of LS mean	(-1.73, 21.73)
Week 24	
n	10
Mean (SD)	83.33 (32.81)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	5.56 (19.77)
Week 24 (MMRM)	
n	10
LS mean (SE)	83.33 (5.50)
95% CI of LS mean	(71.61, 95.06)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	5.56 (5.50)
95% CI of LS mean	(-6.17, 17.28)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	7.78 (4.90)
95% CI of LS mean	(-3.18, 18.73)
P-value	0.1442

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	41
Mean (SD)	79.67 (22.21)
Week 4 (MMRM)	
n	42
LS mean (SE)	78.86 (3.64)
95% CI of LS mean	(71.49, 86.24)
Absolute Change at Week 4 (MMRM)	
n	41
LS mean (SE)	-0.81 (3.64)
95% CI of LS mean	(-8.19, 6.56)
Week 8 (MMRM)	
n	42
LS mean (SE)	78.05 (3.54)
95% CI of LS mean	(70.90, 85.20)
Absolute Change at Week 8 (MMRM)	
n	41
LS mean (SE)	-1.63 (3.54)
95% CI of LS mean	(-8.78, 5.53)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	82.00 (3.00)
95% CI of LS mean	(75.92, 88.09)
Absolute Change at Week 12 (MMRM)	
n	40
LS mean (SE)	2.33 (3.00)
95% CI of LS mean	(-3.76, 8.41)
Week 16 (MMRM)	
n	42
LS mean (SE)	84.55 (3.22)
95% CI of LS mean	(78.03, 91.08)
Absolute Change at Week 16 (MMRM)	
n	41
LS mean (SE)	4.88 (3.22)
95% CI of LS mean	(-1.64, 11.40)
Week 24	
n	44
Mean (SD)	87.12 (20.61)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	41
Mean (SD)	8.13 (26.65)
Week 24 (MMRM)	
n	44
LS mean (SE)	87.80 (3.29)
95% CI of LS mean	(81.13, 94.48)
Absolute Change at Week 24 (MMRM)	
n	41
LS mean (SE)	8.13 (3.29)
95% CI of LS mean	(1.45, 14.81)
Absolute Change through Week 24 (MMRM)	
n	41
LS mean (SE)	6.50 (2.76)
95% CI of LS mean	(0.91, 12.09)
P-value	0.0238

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	79.80 (20.31)
Week 4 (MMRM)	
n	33
LS mean (SE)	75.76 (4.88)
95% CI of LS mean	(65.81, 85.70)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	-4.04 (4.88)
95% CI of LS mean	(-13.99, 5.90)
Week 8 (MMRM)	
n	33
LS mean (SE)	81.82 (4.05)
95% CI of LS mean	(73.57, 90.07)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	2.02 (4.05)
95% CI of LS mean	(-6.23, 10.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	77.78 (3.33)
95% CI of LS mean	(70.98, 84.57)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	-2.02 (3.33)
95% CI of LS mean	(-8.81, 4.77)
Week 16 (MMRM)	
n	33
LS mean (SE)	82.83 (3.67)
95% CI of LS mean	(75.33, 90.33)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	3.03 (3.67)
95% CI of LS mean	(-4.47, 10.53)
Week 24	
n	34
Mean (SD)	81.37 (23.49)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	1.01 (25.66)
Week 24 (MMRM)	
n	34
LS mean (SE)	80.81 (4.04)
95% CI of LS mean	(72.56, 89.05)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	1.01 (4.04)
95% CI of LS mean	(-7.24, 9.26)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	2.02 (3.11)
95% CI of LS mean	(-4.32, 8.36)
P-value	0.5206

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	80.85 (22.78)
Week 4 (MMRM)	
n	47
LS mean (SE)	76.60 (4.08)
95% CI of LS mean	(68.38, 84.81)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-4.26 (4.08)
95% CI of LS mean	(-12.47, 3.96)
Week 8 (MMRM)	
n	47
LS mean (SE)	77.30 (3.55)
95% CI of LS mean	(70.16, 84.45)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	-3.55 (3.55)
95% CI of LS mean	(-10.69, 3.60)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	79.43 (2.91)
95% CI of LS mean	(73.56, 85.30)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	-1.42 (2.91)
95% CI of LS mean	(-7.29, 4.45)
Week 16 (MMRM)	
n	47
LS mean (SE)	79.43 (3.32)
95% CI of LS mean	(72.74, 86.13)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	-1.42 (3.32)
95% CI of LS mean	(-8.11, 5.28)
Week 24	
n	47
Mean (SD)	82.98 (22.92)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	2.13 (26.38)
Week 24 (MMRM)	
n	47
LS mean (SE)	82.98 (3.17)
95% CI of LS mean	(76.60, 89.36)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	2.13 (3.17)
95% CI of LS mean	(-4.25, 8.50)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	0.35 (2.77)
95% CI of LS mean	(-5.22, 5.93)
P-value	0.8986

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	27
Mean (SD)	77.78 (18.49)
Week 4 (MMRM)	
n	28
LS mean (SE)	79.01 (4.72)
95% CI of LS mean	(69.17, 88.86)
Absolute Change at Week 4 (MMRM)	
n	27
LS mean (SE)	1.23 (4.72)
95% CI of LS mean	(-8.61, 11.08)
Week 8 (MMRM)	
n	28
LS mean (SE)	83.95 (4.20)
95% CI of LS mean	(75.20, 92.70)
Absolute Change at Week 8 (MMRM)	
n	27
LS mean (SE)	6.17 (4.20)
95% CI of LS mean	(-2.58, 14.93)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	80.90 (3.45)
95% CI of LS mean	(73.74, 88.06)
Absolute Change at Week 12 (MMRM)	
n	26
LS mean (SE)	3.12 (3.45)
95% CI of LS mean	(-4.04, 10.28)
Week 16 (MMRM)	
n	28
LS mean (SE)	91.36 (2.89)
95% CI of LS mean	(85.41, 97.31)
Absolute Change at Week 16 (MMRM)	
n	27
LS mean (SE)	13.58 (2.89)
95% CI of LS mean	(7.63, 19.53)
Week 24	
n	31
Mean (SD)	87.10 (20.51)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	27
Mean (SD)	9.88 (25.84)
Week 24 (MMRM)	
n	31
LS mean (SE)	87.65 (4.05)
95% CI of LS mean	(79.33, 95.97)
Absolute Change at Week 24 (MMRM)	
n	27
LS mean (SE)	9.88 (4.05)
95% CI of LS mean	(1.56, 18.20)
Absolute Change through Week 24 (MMRM)	
n	27
LS mean (SE)	11.73 (2.56)
95% CI of LS mean	(6.45, 17.01)
P-value	0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	58
Mean (SD)	79.31 (22.36)
Week 4 (MMRM)	
n	59
LS mean (SE)	75.29 (3.49)
95% CI of LS mean	(68.30, 82.27)
Absolute Change at Week 4 (MMRM)	
n	58
LS mean (SE)	-4.02 (3.49)
95% CI of LS mean	(-11.01, 2.96)
Week 8 (MMRM)	
n	59
LS mean (SE)	78.74 (3.07)
95% CI of LS mean	(72.58, 84.89)
Absolute Change at Week 8 (MMRM)	
n	58
LS mean (SE)	-0.57 (3.07)
95% CI of LS mean	(-6.73, 5.58)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	80.91 (2.31)
95% CI of LS mean	(76.28, 85.54)
Absolute Change at Week 12 (MMRM)	
n	57
LS mean (SE)	1.60 (2.31)
95% CI of LS mean	(-3.03, 6.23)
Week 16 (MMRM)	
n	59
LS mean (SE)	83.33 (2.71)
95% CI of LS mean	(77.90, 88.76)
Absolute Change at Week 16 (MMRM)	
n	58
LS mean (SE)	4.02 (2.71)
95% CI of LS mean	(-1.41, 9.45)
Week 24	
n	62
Mean (SD)	86.02 (21.38)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	58
Mean (SD)	6.90 (26.31)
Week 24 (MMRM)	
n	62
LS mean (SE)	86.21 (2.76)
95% CI of LS mean	(80.67, 91.74)
Absolute Change at Week 24 (MMRM)	
n	58
LS mean (SE)	6.90 (2.76)
95% CI of LS mean	(1.36, 12.43)
Absolute Change through Week 24 (MMRM)	
n	58
LS mean (SE)	5.46 (2.18)
95% CI of LS mean	(1.09, 9.83)
P-value	0.0152

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	83.33 (17.57)
Week 4 (MMRM)	
n	10
LS mean (SE)	90.00 (6.99)
95% CI of LS mean	(73.39, 106.61)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	6.67 (6.99)
95% CI of LS mean	(-9.94, 23.28)
Week 8 (MMRM)	
n	10
LS mean (SE)	86.67 (7.51)
95% CI of LS mean	(69.08, 104.26)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	3.33 (7.51)
95% CI of LS mean	(-14.26, 20.92)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	83.33 (7.28)
95% CI of LS mean	(66.01, 100.66)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	0.00 (7.28)
95% CI of LS mean	(-17.33, 17.33)
Week 16 (MMRM)	
n	10
LS mean (SE)	96.67 (3.02)
95% CI of LS mean	(89.66, 103.67)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	13.33 (3.02)
95% CI of LS mean	(6.33, 20.34)
Week 24	
n	10
Mean (SD)	90.00 (16.10)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	6.67 (21.08)
Week 24 (MMRM)	
n	10
LS mean (SE)	90.00 (5.28)
95% CI of LS mean	(77.52, 102.48)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	6.67 (5.28)
95% CI of LS mean	(-5.81, 19.15)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	10.00 (2.72)
95% CI of LS mean	(2.21, 17.79)
P-value	0.0242

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	80.95 (23.06)
Week 4 (MMRM)	
n	42
LS mean (SE)	84.66 (2.21)
95% CI of LS mean	(80.19, 89.12)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	3.70 (2.21)
95% CI of LS mean	(-0.76, 8.17)
Week 8 (MMRM)	
n	42
LS mean (SE)	82.01 (2.67)
95% CI of LS mean	(76.60, 87.42)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	1.06 (2.67)
95% CI of LS mean	(-4.35, 6.47)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	84.08 (3.10)
95% CI of LS mean	(77.83, 90.34)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	3.13 (3.10)
95% CI of LS mean	(-3.13, 9.39)
Week 16 (MMRM)	
n	42
LS mean (SE)	83.07 (3.31)
95% CI of LS mean	(76.38, 89.76)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	2.12 (3.31)
95% CI of LS mean	(-4.57, 8.80)
Week 24	
n	44
Mean (SD)	88.89 (19.76)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	7.41 (16.40)
Week 24 (MMRM)	
n	44
LS mean (SE)	88.36 (2.22)
95% CI of LS mean	(83.87, 92.85)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	7.41 (2.22)
95% CI of LS mean	(2.92, 11.90)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	4.76 (2.32)
95% CI of LS mean	(0.07, 9.46)
P-value	0.0469

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	82.15 (19.43)
Week 4 (MMRM)	
n	33
LS mean (SE)	78.11 (3.63)
95% CI of LS mean	(70.71, 85.52)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	-4.04 (3.63)
95% CI of LS mean	(-11.45, 3.37)
Week 8 (MMRM)	
n	33
LS mean (SE)	77.10 (3.65)
95% CI of LS mean	(69.67, 84.54)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	-5.05 (3.65)
95% CI of LS mean	(-12.49, 2.39)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	82.49 (3.23)
95% CI of LS mean	(75.91, 89.08)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	0.34 (3.23)
95% CI of LS mean	(-6.25, 6.92)
Week 16 (MMRM)	
n	33
LS mean (SE)	86.20 (2.54)
95% CI of LS mean	(81.01, 91.38)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	4.04 (2.54)
95% CI of LS mean	(-1.14, 9.22)
Week 24	
n	34
Mean (SD)	88.89 (16.18)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	7.07 (18.39)
Week 24 (MMRM)	
n	34
LS mean (SE)	89.23 (2.55)
95% CI of LS mean	(84.01, 94.44)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	7.07 (2.55)
95% CI of LS mean	(1.86, 12.28)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	5.56 (2.21)
95% CI of LS mean	(1.04, 10.07)
P-value	0.0176

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	78.01 (23.57)
Week 4 (MMRM)	
n	47
LS mean (SE)	79.20 (2.61)
95% CI of LS mean	(73.93, 84.46)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	1.18 (2.61)
95% CI of LS mean	(-4.08, 6.44)
Week 8 (MMRM)	
n	47
LS mean (SE)	79.67 (2.64)
95% CI of LS mean	(74.35, 84.99)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	1.65 (2.64)
95% CI of LS mean	(-3.66, 6.97)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	82.51 (2.96)
95% CI of LS mean	(76.54, 88.47)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	4.49 (2.96)
95% CI of LS mean	(-1.47, 10.45)
Week 16 (MMRM)	
n	47
LS mean (SE)	81.56 (3.21)
95% CI of LS mean	(75.09, 88.03)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	3.55 (3.21)
95% CI of LS mean	(-2.92, 10.02)
Week 24	
n	47
Mean (SD)	88.42 (19.10)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	10.40 (18.01)
Week 24 (MMRM)	
n	47
LS mean (SE)	88.42 (2.15)
95% CI of LS mean	(84.08, 92.75)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	10.40 (2.15)
95% CI of LS mean	(6.06, 14.74)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	6.97 (2.31)
95% CI of LS mean	(2.33, 11.62)
P-value	0.0042

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	87.30 (15.92)
Week 4 (MMRM)	
n	28
LS mean (SE)	86.11 (3.39)
95% CI of LS mean	(79.16, 93.06)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	-1.19 (3.39)
95% CI of LS mean	(-8.14, 5.76)
Week 8 (MMRM)	
n	28
LS mean (SE)	80.16 (4.08)
95% CI of LS mean	(71.75, 88.57)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	-7.14 (4.08)
95% CI of LS mean	(-15.55, 1.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	84.88 (3.44)
95% CI of LS mean	(77.79, 91.96)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	-2.43 (3.44)
95% CI of LS mean	(-9.51, 4.66)
Week 16 (MMRM)	
n	28
LS mean (SE)	89.29 (2.28)
95% CI of LS mean	(84.59, 93.98)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	1.98 (2.28)
95% CI of LS mean	(-2.71, 6.68)
Week 24	
n	31
Mean (SD)	89.61 (16.96)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	1.98 (14.52)
Week 24 (MMRM)	
n	31
LS mean (SE)	89.29 (2.65)
95% CI of LS mean	(83.84, 94.73)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	1.98 (2.65)
95% CI of LS mean	(-3.46, 7.43)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	1.98 (2.11)
95% CI of LS mean	(-2.37, 6.33)
P-value	0.3569

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	82.11 (20.63)
Week 4 (MMRM)	
n	59
LS mean (SE)	81.92 (2.28)
95% CI of LS mean	(77.35, 86.49)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	-0.19 (2.28)
95% CI of LS mean	(-4.76, 4.39)
Week 8 (MMRM)	
n	59
LS mean (SE)	82.49 (1.61)
95% CI of LS mean	(79.26, 85.71)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	0.38 (1.61)
95% CI of LS mean	(-2.85, 3.60)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	87.16 (2.01)
95% CI of LS mean	(83.13, 91.19)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	5.05 (2.01)
95% CI of LS mean	(1.02, 9.08)
Week 16 (MMRM)	
n	59
LS mean (SE)	87.38 (2.21)
95% CI of LS mean	(82.96, 91.81)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	5.27 (2.21)
95% CI of LS mean	(0.85, 9.70)
Week 24	
n	62
Mean (SD)	89.07 (18.71)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	6.78 (15.72)
Week 24 (MMRM)	
n	62
LS mean (SE)	88.89 (1.82)
95% CI of LS mean	(85.25, 92.52)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	6.78 (1.82)
95% CI of LS mean	(3.14, 10.41)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	6.03 (1.75)
95% CI of LS mean	(2.53, 9.53)
P-value	0.0011

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	87.78 (17.72)
Week 4 (MMRM)	
n	10
LS mean (SE)	85.56 (4.62)
95% CI of LS mean	(76.09, 95.03)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-2.22 (4.62)
95% CI of LS mean	(-11.69, 7.25)
Week 8 (MMRM)	
n	10
LS mean (SE)	85.56 (4.62)
95% CI of LS mean	(76.09, 95.03)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-2.22 (4.62)
95% CI of LS mean	(-11.69, 7.25)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	86.67 (4.62)
95% CI of LS mean	(77.20, 96.14)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-1.11 (4.62)
95% CI of LS mean	(-10.58, 8.36)
Week 16 (MMRM)	
n	10
LS mean (SE)	85.56 (4.62)
95% CI of LS mean	(76.09, 95.03)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	-2.22 (4.62)
95% CI of LS mean	(-11.69, 7.25)
Week 24	
n	10
Mean (SD)	94.44 (10.80)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	6.67 (21.72)
Week 24 (MMRM)	
n	10
LS mean (SE)	94.44 (4.62)
95% CI of LS mean	(84.97, 103.91)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	6.67 (4.62)
95% CI of LS mean	(-2.80, 16.14)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	2.22 (3.72)
95% CI of LS mean	(-5.74, 10.18)
P-value	0.5599

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	78.77 (12.84)
Week 4 (MMRM)	
n	42
LS mean (SE)	79.96 (1.87)
95% CI of LS mean	(76.17, 83.75)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	1.19 (1.87)
95% CI of LS mean	(-2.60, 4.98)
Week 8 (MMRM)	
n	42
LS mean (SE)	81.85 (1.67)
95% CI of LS mean	(78.46, 85.23)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	3.08 (1.67)
95% CI of LS mean	(-0.31, 6.46)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	83.48 (2.05)
95% CI of LS mean	(79.34, 87.62)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	4.71 (2.05)
95% CI of LS mean	(0.57, 8.85)
Week 16 (MMRM)	
n	42
LS mean (SE)	84.13 (2.25)
95% CI of LS mean	(79.57, 88.68)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	5.36 (2.25)
95% CI of LS mean	(0.80, 9.91)
Week 24	
n	44
Mean (SD)	81.34 (14.83)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	3.27 (10.95)
Week 24 (MMRM)	
n	44
LS mean (SE)	82.04 (1.70)
95% CI of LS mean	(78.61, 85.48)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	3.27 (1.70)
95% CI of LS mean	(-0.16, 6.71)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	4.32 (1.80)
95% CI of LS mean	(0.67, 7.96)
P-value	0.0216

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	73.61 (16.46)
Week 4 (MMRM)	
n	33
LS mean (SE)	72.13 (2.10)
95% CI of LS mean	(67.85, 76.41)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	-1.48 (2.10)
95% CI of LS mean	(-5.76, 2.80)
Week 8 (MMRM)	
n	33
LS mean (SE)	72.98 (2.40)
95% CI of LS mean	(68.09, 77.87)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	-0.63 (2.40)
95% CI of LS mean	(-5.53, 4.26)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	74.62 (2.48)
95% CI of LS mean	(69.56, 79.68)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	1.01 (2.48)
95% CI of LS mean	(-4.05, 6.07)
Week 16 (MMRM)	
n	33
LS mean (SE)	75.25 (2.42)
95% CI of LS mean	(70.32, 80.18)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	1.64 (2.42)
95% CI of LS mean	(-3.29, 6.57)
Week 24	
n	34
Mean (SD)	77.82 (15.24)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	4.42 (14.13)
Week 24 (MMRM)	
n	34
LS mean (SE)	78.03 (2.10)
95% CI of LS mean	(73.75, 82.31)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	4.42 (2.10)
95% CI of LS mean	(0.14, 8.70)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	3.03 (2.00)
95% CI of LS mean	(-1.06, 7.12)
P-value	0.1406

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	72.96 (14.48)
Week 4 (MMRM)	
n	47
LS mean (SE)	72.54 (1.98)
95% CI of LS mean	(68.56, 76.53)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-0.42 (1.98)
95% CI of LS mean	(-4.41, 3.57)
Week 8 (MMRM)	
n	47
LS mean (SE)	75.71 (1.92)
95% CI of LS mean	(71.84, 79.58)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	2.75 (1.92)
95% CI of LS mean	(-1.13, 6.62)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	77.84 (2.02)
95% CI of LS mean	(73.77, 81.90)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	4.88 (2.02)
95% CI of LS mean	(0.81, 8.94)
Week 16 (MMRM)	
n	47
LS mean (SE)	78.28 (2.28)
95% CI of LS mean	(73.68, 82.88)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	5.32 (2.28)
95% CI of LS mean	(0.72, 9.92)
Week 24	
n	47
Mean (SD)	77.75 (15.40)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	4.79 (12.04)
Week 24 (MMRM)	
n	47
LS mean (SE)	77.75 (1.69)
95% CI of LS mean	(74.33, 81.16)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	4.79 (1.69)
95% CI of LS mean	(1.37, 8.20)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	5.05 (1.79)
95% CI of LS mean	(1.44, 8.66)
P-value	0.0072

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	82.44 (13.19)
Week 4 (MMRM)	
n	28
LS mean (SE)	83.18 (2.14)
95% CI of LS mean	(78.79, 87.58)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	0.74 (2.14)
95% CI of LS mean	(-3.65, 5.14)
Week 8 (MMRM)	
n	28
LS mean (SE)	81.70 (2.38)
95% CI of LS mean	(76.81, 86.58)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	-0.74 (2.38)
95% CI of LS mean	(-5.63, 4.14)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	82.49 (2.76)
95% CI of LS mean	(76.82, 88.17)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	0.05 (2.76)
95% CI of LS mean	(-5.62, 5.73)
Week 16 (MMRM)	
n	28
LS mean (SE)	83.48 (2.39)
95% CI of LS mean	(78.54, 88.43)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	1.04 (2.39)
95% CI of LS mean	(-3.90, 5.99)
Week 24	
n	31
Mean (SD)	82.93 (14.08)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	2.08 (12.95)
Week 24 (MMRM)	
n	31
LS mean (SE)	84.52 (2.21)
95% CI of LS mean	(79.97, 89.08)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	2.08 (2.21)
95% CI of LS mean	(-2.47, 6.64)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	1.56 (2.08)
95% CI of LS mean	(-2.74, 5.86)
P-value	0.4602

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	75.99 (14.27)
Week 4 (MMRM)	
n	59
LS mean (SE)	76.41 (1.61)
95% CI of LS mean	(73.18, 79.64)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	0.42 (1.61)
95% CI of LS mean	(-2.81, 3.65)
Week 8 (MMRM)	
n	59
LS mean (SE)	78.39 (1.70)
95% CI of LS mean	(74.98, 81.80)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	2.40 (1.70)
95% CI of LS mean	(-1.00, 5.81)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	79.62 (1.85)
95% CI of LS mean	(75.91, 83.32)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	3.63 (1.85)
95% CI of LS mean	(-0.07, 7.33)
Week 16 (MMRM)	
n	59
LS mean (SE)	81.57 (1.64)
95% CI of LS mean	(78.27, 84.86)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	5.58 (1.64)
95% CI of LS mean	(2.28, 8.87)
Week 24	
n	62
Mean (SD)	79.64 (14.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	4.24 (12.46)
Week 24 (MMRM)	
n	62
LS mean (SE)	80.23 (1.43)
95% CI of LS mean	(77.36, 83.09)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	4.24 (1.43)
95% CI of LS mean	(1.38, 7.10)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	4.91 (1.35)
95% CI of LS mean	(2.21, 7.60)
P-value	0.0006

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	77.92 (19.15)
Week 4 (MMRM)	
n	10
LS mean (SE)	80.54 (3.02)
95% CI of LS mean	(73.67, 87.40)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	2.62 (3.02)
95% CI of LS mean	(-4.25, 9.48)
Week 8 (MMRM)	
n	10
LS mean (SE)	79.58 (2.84)
95% CI of LS mean	(73.15, 86.01)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	1.67 (2.84)
95% CI of LS mean	(-4.76, 8.10)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	82.50 (2.02)
95% CI of LS mean	(77.82, 87.18)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	4.58 (2.02)
95% CI of LS mean	(-0.09, 9.26)
Week 16 (MMRM)	
n	10
LS mean (SE)	80.42 (3.32)
95% CI of LS mean	(72.89, 87.94)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	2.50 (3.32)
95% CI of LS mean	(-5.03, 10.03)
Week 24	
n	10
Mean (SD)	84.58 (19.74)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	6.67 (11.49)
Week 24 (MMRM)	
n	10
LS mean (SE)	84.58 (4.11)
95% CI of LS mean	(75.23, 93.94)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	6.67 (4.11)
95% CI of LS mean	(-2.69, 16.02)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	4.58 (3.45)
95% CI of LS mean	(-3.27, 12.44)
P-value	0.2184

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	88.36 (11.88)
Week 4 (MMRM)	
n	42
LS mean (SE)	86.90 (1.85)
95% CI of LS mean	(83.17, 90.64)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	-1.46 (1.85)
95% CI of LS mean	(-5.19, 2.28)
Week 8 (MMRM)	
n	42
LS mean (SE)	84.79 (2.57)
95% CI of LS mean	(79.59, 89.99)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	-3.57 (2.57)
95% CI of LS mean	(-8.77, 1.63)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	86.65 (1.98)
95% CI of LS mean	(82.65, 90.64)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	-1.71 (1.98)
95% CI of LS mean	(-5.71, 2.28)
Week 16 (MMRM)	
n	42
LS mean (SE)	87.57 (2.49)
95% CI of LS mean	(82.54, 92.59)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	-0.79 (2.49)
95% CI of LS mean	(-5.82, 4.23)
Week 24	
n	44
Mean (SD)	90.40 (15.91)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	1.72 (15.15)
Week 24 (MMRM)	
n	44
LS mean (SE)	90.08 (2.25)
95% CI of LS mean	(85.53, 94.63)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	1.72 (2.25)
95% CI of LS mean	(-2.83, 6.27)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	0.46 (1.92)
95% CI of LS mean	(-3.42, 4.34)
P-value	0.8106

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	85.86 (14.37)
Week 4 (MMRM)	
n	33
LS mean (SE)	87.04 (2.22)
95% CI of LS mean	(82.49, 91.58)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	1.18 (2.22)
95% CI of LS mean	(-3.37, 5.72)
Week 8 (MMRM)	
n	33
LS mean (SE)	86.43 (2.52)
95% CI of LS mean	(81.29, 91.57)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	0.57 (2.52)
95% CI of LS mean	(-4.57, 5.72)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	85.86 (3.33)
95% CI of LS mean	(79.08, 92.64)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	0.00 (3.33)
95% CI of LS mean	(-6.78, 6.78)
Week 16 (MMRM)	
n	33
LS mean (SE)	89.73 (2.13)
95% CI of LS mean	(85.39, 94.07)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	3.87 (2.13)
95% CI of LS mean	(-0.47, 8.22)
Week 24	
n	34
Mean (SD)	90.36 (12.48)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	5.39 (12.99)
Week 24 (MMRM)	
n	34
LS mean (SE)	91.25 (1.76)
95% CI of LS mean	(87.64, 94.85)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	5.39 (1.76)
95% CI of LS mean	(1.79, 8.99)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	4.63 (1.75)
95% CI of LS mean	(1.05, 8.21)
P-value	0.0129

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	86.05 (12.79)
Week 4 (MMRM)	
n	47
LS mean (SE)	85.22 (1.90)
95% CI of LS mean	(81.40, 89.05)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-0.83 (1.90)
95% CI of LS mean	(-4.65, 3.00)
Week 8 (MMRM)	
n	47
LS mean (SE)	84.80 (2.22)
95% CI of LS mean	(80.32, 89.28)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	-1.25 (2.22)
95% CI of LS mean	(-5.74, 3.23)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	86.88 (2.19)
95% CI of LS mean	(82.46, 91.29)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	0.83 (2.19)
95% CI of LS mean	(-3.59, 5.24)
Week 16 (MMRM)	
n	47
LS mean (SE)	89.95 (2.03)
95% CI of LS mean	(85.86, 94.05)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	3.90 (2.03)
95% CI of LS mean	(-0.19, 7.99)
Week 24	
n	47
Mean (SD)	89.48 (16.27)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	3.43 (16.49)
Week 24 (MMRM)	
n	47
LS mean (SE)	89.48 (2.24)
95% CI of LS mean	(84.96, 94.00)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	3.43 (2.24)
95% CI of LS mean	(-1.09, 7.95)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	3.66 (1.81)
95% CI of LS mean	(0.02, 7.31)
P-value	0.0490

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	89.29 (13.35)
Week 4 (MMRM)	
n	28
LS mean (SE)	89.88 (1.67)
95% CI of LS mean	(86.45, 93.31)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	0.60 (1.67)
95% CI of LS mean	(-2.84, 4.03)
Week 8 (MMRM)	
n	28
LS mean (SE)	86.71 (3.12)
95% CI of LS mean	(80.30, 93.11)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	-2.58 (3.12)
95% CI of LS mean	(-8.98, 3.82)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	85.76 (3.34)
95% CI of LS mean	(78.89, 92.63)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	-3.53 (3.34)
95% CI of LS mean	(-10.40, 3.34)
Week 16 (MMRM)	
n	28
LS mean (SE)	86.11 (2.89)
95% CI of LS mean	(80.17, 92.05)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	-3.17 (2.89)
95% CI of LS mean	(-9.12, 2.77)
Week 24	
n	31
Mean (SD)	91.76 (11.19)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	3.17 (9.73)
Week 24 (MMRM)	
n	31
LS mean (SE)	92.46 (1.32)
95% CI of LS mean	(89.74, 95.18)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	3.17 (1.32)
95% CI of LS mean	(0.45, 5.89)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	0.00 (1.89)
95% CI of LS mean	(-3.89, 3.89)
P-value	>0.9999

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	85.12 (13.59)
Week 4 (MMRM)	
n	59
LS mean (SE)	85.97 (1.56)
95% CI of LS mean	(82.84, 89.10)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	0.85 (1.56)
95% CI of LS mean	(-2.28, 3.98)
Week 8 (MMRM)	
n	59
LS mean (SE)	84.78 (1.92)
95% CI of LS mean	(80.93, 88.63)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	-0.34 (1.92)
95% CI of LS mean	(-4.19, 3.51)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	87.29 (1.63)
95% CI of LS mean	(84.04, 90.55)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	2.17 (1.63)
95% CI of LS mean	(-1.08, 5.43)
Week 16 (MMRM)	
n	59
LS mean (SE)	88.32 (1.82)
95% CI of LS mean	(84.68, 91.96)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	3.20 (1.82)
95% CI of LS mean	(-0.44, 6.84)
Week 24	
n	62
Mean (SD)	89.52 (15.23)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	4.61 (14.63)
Week 24 (MMRM)	
n	62
LS mean (SE)	89.74 (1.74)
95% CI of LS mean	(86.26, 93.22)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	4.61 (1.74)
95% CI of LS mean	(1.14, 8.09)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	3.91 (1.44)
95% CI of LS mean	(1.03, 6.79)
P-value	0.0088

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	94.44 (7.41)
Week 4 (MMRM)	
n	10
LS mean (SE)	94.44 (4.54)
95% CI of LS mean	(84.36, 104.53)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	0.00 (4.54)
95% CI of LS mean	(-10.08, 10.08)
Week 8 (MMRM)	
n	10
LS mean (SE)	92.78 (4.54)
95% CI of LS mean	(82.69, 102.86)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-1.67 (4.54)
95% CI of LS mean	(-11.75, 8.42)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	89.44 (4.54)
95% CI of LS mean	(79.36, 99.53)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-5.00 (4.54)
95% CI of LS mean	(-15.08, 5.08)
Week 16 (MMRM)	
n	10
LS mean (SE)	92.78 (4.54)
95% CI of LS mean	(82.69, 102.86)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	-1.67 (4.54)
95% CI of LS mean	(-11.75, 8.42)
Week 24	
n	10
Mean (SD)	94.44 (12.83)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	0.00 (14.10)
Week 24 (MMRM)	
n	10
LS mean (SE)	94.44 (4.54)
95% CI of LS mean	(84.36, 104.53)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	0.00 (4.54)
95% CI of LS mean	(-10.08, 10.08)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	-0.83 (4.28)
95% CI of LS mean	(-10.68, 9.01)
P-value	0.8505

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	66.33 (16.44)
Week 4 (MMRM)	
n	42
LS mean (SE)	68.82 (2.01)
95% CI of LS mean	(64.76, 72.88)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	2.49 (2.01)
95% CI of LS mean	(-1.57, 6.56)
Week 8 (MMRM)	
n	42
LS mean (SE)	67.35 (2.06)
95% CI of LS mean	(63.19, 71.51)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	1.02 (2.06)
95% CI of LS mean	(-3.14, 5.18)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	72.14 (2.20)
95% CI of LS mean	(67.70, 76.59)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	5.82 (2.20)
95% CI of LS mean	(1.37, 10.26)
Week 16 (MMRM)	
n	42
LS mean (SE)	74.72 (2.15)
95% CI of LS mean	(70.38, 79.05)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	8.39 (2.15)
95% CI of LS mean	(4.06, 12.72)
Week 24	
n	44
Mean (SD)	74.89 (15.04)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	9.07 (17.08)
Week 24 (MMRM)	
n	44
LS mean (SE)	75.40 (2.12)
95% CI of LS mean	(71.10, 79.69)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	9.07 (2.12)
95% CI of LS mean	(4.77, 13.37)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	8.73 (2.01)
95% CI of LS mean	(4.67, 12.79)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	67.82 (22.56)
Week 4 (MMRM)	
n	33
LS mean (SE)	67.24 (2.67)
95% CI of LS mean	(61.79, 72.70)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	-0.58 (2.67)
95% CI of LS mean	(-6.03, 4.88)
Week 8 (MMRM)	
n	33
LS mean (SE)	71.14 (3.26)
95% CI of LS mean	(64.50, 77.78)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	3.32 (3.26)
95% CI of LS mean	(-3.32, 9.96)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	72.73 (2.76)
95% CI of LS mean	(67.09, 78.37)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	4.91 (2.76)
95% CI of LS mean	(-0.73, 10.54)
Week 16 (MMRM)	
n	33
LS mean (SE)	70.13 (3.57)
95% CI of LS mean	(62.85, 77.41)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	2.31 (3.57)
95% CI of LS mean	(-4.97, 9.59)
Week 24	
n	34
Mean (SD)	74.86 (15.96)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	8.15 (23.06)
Week 24 (MMRM)	
n	34
LS mean (SE)	75.97 (2.54)
95% CI of LS mean	(70.76, 81.19)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	8.15 (2.54)
95% CI of LS mean	(2.94, 13.37)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	5.23 (2.74)
95% CI of LS mean	(-0.38, 10.84)
P-value	0.0664

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	66.36 (19.94)
Week 4 (MMRM)	
n	47
LS mean (SE)	69.20 (1.97)
95% CI of LS mean	(65.21, 73.18)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	2.84 (1.97)
95% CI of LS mean	(-1.15, 6.82)
Week 8 (MMRM)	
n	47
LS mean (SE)	69.81 (2.48)
95% CI of LS mean	(64.81, 74.80)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	3.44 (2.48)
95% CI of LS mean	(-1.55, 8.44)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	73.35 (2.25)
95% CI of LS mean	(68.82, 77.88)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	6.99 (2.25)
95% CI of LS mean	(2.46, 11.52)
Week 16 (MMRM)	
n	47
LS mean (SE)	74.47 (2.59)
95% CI of LS mean	(69.25, 79.69)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	8.11 (2.59)
95% CI of LS mean	(2.89, 13.32)
Week 24	
n	47
Mean (SD)	76.44 (13.74)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	10.08 (20.59)
Week 24 (MMRM)	
n	47
LS mean (SE)	76.44 (2.01)
95% CI of LS mean	(72.38, 80.51)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	10.08 (2.01)
95% CI of LS mean	(6.01, 14.15)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	9.09 (2.10)
95% CI of LS mean	(4.85, 13.33)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	68.03 (18.32)
Week 4 (MMRM)	
n	28
LS mean (SE)	66.33 (2.73)
95% CI of LS mean	(60.69, 71.96)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	-1.70 (2.73)
95% CI of LS mean	(-7.33, 3.93)
Week 8 (MMRM)	
n	28
LS mean (SE)	67.69 (2.62)
95% CI of LS mean	(62.29, 73.09)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	-0.34 (2.62)
95% CI of LS mean	(-5.74, 5.06)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	70.71 (2.60)
95% CI of LS mean	(65.37, 76.06)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	2.69 (2.60)
95% CI of LS mean	(-2.66, 8.03)
Week 16 (MMRM)	
n	28
LS mean (SE)	69.73 (3.05)
95% CI of LS mean	(63.47, 75.99)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	1.70 (3.05)
95% CI of LS mean	(-4.56, 7.96)
Week 24	
n	31
Mean (SD)	72.50 (17.46)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	6.29 (18.51)
Week 24 (MMRM)	
n	31
LS mean (SE)	74.32 (2.90)
95% CI of LS mean	(68.36, 80.28)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	6.29 (2.90)
95% CI of LS mean	(0.33, 12.25)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	4.00 (2.72)
95% CI of LS mean	(-1.59, 9.59)
P-value	0.1537

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	67.31 (17.85)
Week 4 (MMRM)	
n	59
LS mean (SE)	68.12 (1.81)
95% CI of LS mean	(64.49, 71.74)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	0.81 (1.81)
95% CI of LS mean	(-2.82, 4.43)
Week 8 (MMRM)	
n	59
LS mean (SE)	70.06 (1.71)
95% CI of LS mean	(66.62, 73.49)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	2.74 (1.71)
95% CI of LS mean	(-0.69, 6.18)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	74.01 (1.82)
95% CI of LS mean	(70.36, 77.65)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	6.69 (1.82)
95% CI of LS mean	(3.04, 10.34)
Week 16 (MMRM)	
n	59
LS mean (SE)	74.01 (2.03)
95% CI of LS mean	(69.94, 78.08)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	6.70 (2.03)
95% CI of LS mean	(2.63, 10.77)
Week 24	
n	62
Mean (SD)	75.92 (14.80)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	9.64 (19.23)
Week 24 (MMRM)	
n	62
LS mean (SE)	76.96 (1.83)
95% CI of LS mean	(73.29, 80.62)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	9.64 (1.83)
95% CI of LS mean	(5.98, 13.31)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	8.17 (1.74)
95% CI of LS mean	(4.68, 11.66)
P-value	<0.0001

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	67.14 (28.87)
Week 4 (MMRM)	
n	10
LS mean (SE)	71.90 (3.63)
95% CI of LS mean	(63.62, 80.19)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	4.76 (3.63)
95% CI of LS mean	(-3.53, 13.05)
Week 8 (MMRM)	
n	10
LS mean (SE)	72.86 (8.01)
95% CI of LS mean	(54.36, 91.36)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	5.71 (8.01)
95% CI of LS mean	(-12.79, 24.21)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	72.86 (4.54)
95% CI of LS mean	(62.38, 83.34)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	5.71 (4.54)
95% CI of LS mean	(-4.77, 16.20)
Week 16 (MMRM)	
n	10
LS mean (SE)	74.29 (7.13)
95% CI of LS mean	(58.00, 90.57)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	7.14 (7.13)
95% CI of LS mean	(-9.15, 23.43)
Week 24	
n	10
Mean (SD)	73.33 (17.56)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	6.19 (26.18)
Week 24 (MMRM)	
n	10
LS mean (SE)	73.33 (5.42)
95% CI of LS mean	(60.40, 86.27)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	6.19 (5.42)
95% CI of LS mean	(-6.75, 19.13)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	6.67 (6.03)
95% CI of LS mean	(-7.28, 20.62)
P-value	0.3018

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	42
Mean (SD)	77.12 (21.75)
Week 4 (MMRM)	
n	42
LS mean (SE)	79.63 (2.39)
95% CI of LS mean	(74.80, 84.46)
Absolute Change at Week 4 (MMRM)	
n	42
LS mean (SE)	2.51 (2.39)
95% CI of LS mean	(-2.31, 7.34)
Week 8 (MMRM)	
n	42
LS mean (SE)	80.69 (2.50)
95% CI of LS mean	(75.64, 85.74)
Absolute Change at Week 8 (MMRM)	
n	42
LS mean (SE)	3.57 (2.50)
95% CI of LS mean	(-1.48, 8.62)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Week 12 (MMRM)	
n	41
LS mean (SE)	81.21 (3.04)
95% CI of LS mean	(75.07, 87.34)
Absolute Change at Week 12 (MMRM)	
n	41
LS mean (SE)	4.09 (3.04)
95% CI of LS mean	(-2.04, 10.22)
Week 16 (MMRM)	
n	42
LS mean (SE)	81.22 (3.33)
95% CI of LS mean	(74.49, 87.94)
Absolute Change at Week 16 (MMRM)	
n	42
LS mean (SE)	4.10 (3.33)
95% CI of LS mean	(-2.63, 10.83)
Week 24	
n	44
Mean (SD)	81.57 (22.34)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 24	
n	42
Mean (SD)	4.63 (22.02)
Week 24 (MMRM)	
n	44
LS mean (SE)	81.75 (3.15)
95% CI of LS mean	(75.37, 88.12)
Absolute Change at Week 24 (MMRM)	
n	42
LS mean (SE)	4.63 (3.15)
95% CI of LS mean	(-1.74, 11.00)
Absolute Change through Week 24 (MMRM)	
n	42
LS mean (SE)	4.37 (2.89)
95% CI of LS mean	(-1.48, 10.21)
P-value	0.1390

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	33
Mean (SD)	75.42 (20.74)
Week 4 (MMRM)	
n	33
LS mean (SE)	78.45 (3.39)
95% CI of LS mean	(71.51, 85.40)
Absolute Change at Week 4 (MMRM)	
n	33
LS mean (SE)	3.03 (3.39)
95% CI of LS mean	(-3.92, 9.98)
Week 8 (MMRM)	
n	33
LS mean (SE)	78.28 (2.82)
95% CI of LS mean	(72.52, 84.04)
Absolute Change at Week 8 (MMRM)	
n	33
LS mean (SE)	2.86 (2.82)
95% CI of LS mean	(-2.90, 8.62)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Week 12 (MMRM)	
n	33
LS mean (SE)	80.47 (2.11)
95% CI of LS mean	(76.16, 84.78)
Absolute Change at Week 12 (MMRM)	
n	33
LS mean (SE)	5.05 (2.11)
95% CI of LS mean	(0.74, 9.36)
Week 16 (MMRM)	
n	33
LS mean (SE)	77.44 (3.67)
95% CI of LS mean	(69.94, 84.94)
Absolute Change at Week 16 (MMRM)	
n	33
LS mean (SE)	2.02 (3.67)
95% CI of LS mean	(-5.48, 9.52)
Week 24	
n	34
Mean (SD)	82.03 (20.29)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 24	
n	33
Mean (SD)	6.40 (16.90)
Week 24 (MMRM)	
n	34
LS mean (SE)	81.82 (2.67)
95% CI of LS mean	(76.36, 87.28)
Absolute Change at Week 24 (MMRM)	
n	33
LS mean (SE)	6.40 (2.67)
95% CI of LS mean	(0.94, 11.86)
Absolute Change through Week 24 (MMRM)	
n	33
LS mean (SE)	4.21 (2.44)
95% CI of LS mean	(-0.77, 9.18)
P-value	0.0943

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	74.82 (21.48)
Week 4 (MMRM)	
n	47
LS mean (SE)	75.41 (2.56)
95% CI of LS mean	(70.26, 80.57)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	0.59 (2.56)
95% CI of LS mean	(-4.56, 5.74)
Week 8 (MMRM)	
n	47
LS mean (SE)	75.30 (2.40)
95% CI of LS mean	(70.47, 80.12)
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	0.47 (2.40)
95% CI of LS mean	(-4.35, 5.30)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 47
Week 12 (MMRM)	
n	47
LS mean (SE)	78.01 (2.52)
95% CI of LS mean	(72.94, 83.08)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	3.19 (2.52)
95% CI of LS mean	(-1.88, 8.26)
Week 16 (MMRM)	
n	47
LS mean (SE)	78.49 (3.00)
95% CI of LS mean	(72.44, 84.54)
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	3.66 (3.00)
95% CI of LS mean	(-2.39, 9.72)
Week 24	
n	47
Mean (SD)	78.72 (23.95)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 24	
n	47
Mean (SD)	3.90 (18.93)
Week 24 (MMRM)	
n	47
LS mean (SE)	78.72 (2.66)
95% CI of LS mean	(73.38, 84.07)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	3.90 (2.66)
95% CI of LS mean	(-1.45, 9.25)
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	3.78 (2.51)
95% CI of LS mean	(-1.28, 8.84)
P-value	0.1390

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	28
Mean (SD)	78.97 (20.81)
Week 4 (MMRM)	
n	28
LS mean (SE)	85.32 (2.52)
95% CI of LS mean	(80.11, 90.52)
Absolute Change at Week 4 (MMRM)	
n	28
LS mean (SE)	6.35 (2.52)
95% CI of LS mean	(1.15, 11.55)
Week 8 (MMRM)	
n	28
LS mean (SE)	86.90 (2.63)
95% CI of LS mean	(81.49, 92.32)
Absolute Change at Week 8 (MMRM)	
n	28
LS mean (SE)	7.94 (2.63)
95% CI of LS mean	(2.52, 13.35)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Week 12 (MMRM)	
n	27
LS mean (SE)	85.72 (2.73)
95% CI of LS mean	(80.11, 91.32)
Absolute Change at Week 12 (MMRM)	
n	27
LS mean (SE)	6.75 (2.73)
95% CI of LS mean	(1.15, 12.35)
Week 16 (MMRM)	
n	28
LS mean (SE)	81.35 (4.28)
95% CI of LS mean	(72.55, 90.15)
Absolute Change at Week 16 (MMRM)	
n	28
LS mean (SE)	2.38 (4.28)
95% CI of LS mean	(-6.42, 11.18)
Week 24	
n	31
Mean (SD)	86.38 (15.90)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 24	
n	28
Mean (SD)	7.94 (21.35)
Week 24 (MMRM)	
n	31
LS mean (SE)	86.90 (3.08)
95% CI of LS mean	(80.56, 93.25)
Absolute Change at Week 24 (MMRM)	
n	28
LS mean (SE)	7.94 (3.08)
95% CI of LS mean	(1.59, 14.29)
Absolute Change through Week 24 (MMRM)	
n	28
LS mean (SE)	5.16 (2.81)
95% CI of LS mean	(-0.64, 10.96)
P-value	0.0789

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	59
Mean (SD)	78.91 (20.50)
Week 4 (MMRM)	
n	59
LS mean (SE)	80.60 (2.05)
95% CI of LS mean	(76.51, 84.70)
Absolute Change at Week 4 (MMRM)	
n	59
LS mean (SE)	1.69 (2.05)
95% CI of LS mean	(-2.40, 5.79)
Week 8 (MMRM)	
n	59
LS mean (SE)	83.33 (1.99)
95% CI of LS mean	(79.35, 87.32)
Absolute Change at Week 8 (MMRM)	
n	59
LS mean (SE)	4.43 (1.99)
95% CI of LS mean	(0.44, 8.41)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Week 12 (MMRM)	
n	58
LS mean (SE)	83.41 (2.04)
95% CI of LS mean	(79.32, 87.50)
Absolute Change at Week 12 (MMRM)	
n	58
LS mean (SE)	4.50 (2.04)
95% CI of LS mean	(0.41, 8.59)
Week 16 (MMRM)	
n	59
LS mean (SE)	83.05 (2.49)
95% CI of LS mean	(78.06, 88.05)
Absolute Change at Week 16 (MMRM)	
n	59
LS mean (SE)	4.14 (2.49)
95% CI of LS mean	(-0.85, 9.14)
Week 24	
n	62
Mean (SD)	85.48 (17.26)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 24	
n	59
Mean (SD)	6.78 (17.99)
Week 24 (MMRM)	
n	62
LS mean (SE)	85.69 (1.90)
95% CI of LS mean	(81.88, 89.49)
Absolute Change at Week 24 (MMRM)	
n	59
LS mean (SE)	6.78 (1.90)
95% CI of LS mean	(2.98, 10.58)
Absolute Change through Week 24 (MMRM)	
n	59
LS mean (SE)	5.46 (1.89)
95% CI of LS mean	(1.69, 9.24)
P-value	0.0053

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	68.33 (22.23)
Week 4 (MMRM)	
n	10
LS mean (SE)	75.56 (4.24)
95% CI of LS mean	(65.92, 85.19)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	7.22 (4.24)
95% CI of LS mean	(-2.41, 16.86)
Week 8 (MMRM)	
n	10
LS mean (SE)	68.89 (3.81)
95% CI of LS mean	(60.14, 77.64)
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	0.56 (3.81)
95% CI of LS mean	(-8.20, 9.31)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Week 12 (MMRM)	
n	10
LS mean (SE)	77.78 (3.91)
95% CI of LS mean	(68.89, 86.67)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	9.44 (3.91)
95% CI of LS mean	(0.56, 18.33)
Week 16 (MMRM)	
n	10
LS mean (SE)	72.22 (4.56)
95% CI of LS mean	(61.74, 82.70)
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	3.89 (4.56)
95% CI of LS mean	(-6.59, 14.37)
Week 24	
n	10
Mean (SD)	73.33 (27.81)

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.3.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 24	
n	10
Mean (SD)	5.00 (13.47)
Week 24 (MMRM)	
n	10
LS mean (SE)	73.33 (4.18)
95% CI of LS mean	(63.80, 82.86)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	5.00 (4.18)
95% CI of LS mean	(-4.53, 14.53)
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	4.44 (3.36)
95% CI of LS mean	(-3.41, 12.30)
P-value	0.2251

- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Body (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1284
Region (North America vs. Rest of the World)	0.6770
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9477

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Body (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.5745
Region (North America vs. Rest of the World)	0.5410
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.1735

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Digestion (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1053
Region (North America vs. Rest of the World)	0.6606
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.2280

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Eat (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1374
Region (North America vs. Rest of the World)	0.8245
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.5137

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Emotion (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.3551
Region (North America vs. Rest of the World)	0.0852
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.8761

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Health Perceptions (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.1374
Region (North America vs. Rest of the World)	0.6299
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9767

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Physical (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: School (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9168
Region (North America vs. Rest of the World)	0.7182
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.2702

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R School (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.6739
Region (North America vs. Rest of the World)	0.5357
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.0712

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Treatment Burden (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.4364
Region (North America vs. Rest of the World)	0.7135
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.1369

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Vitality (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.1
Study VX21-121-105: Subgroup Factor Test for
MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	0.9242
Region (North America vs. Rest of the World)	0.1453
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.4678

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-values are obtained from MMRM with visit and genotype group (F/MF vs rest) as fixed effect and baseline CFQ-R Weight (Parents/Caregivers Form) domain score as covariate.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	80.81 (26.72)
Week 4 (MMRM)	
n	44
LS mean (SE)	84.60 (2.08)
95% CI of LS mean	(80.40, 88.79)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	3.79 (2.08)
95% CI of LS mean	(-0.41, 7.98)
Week 8 (MMRM)	
n	44
LS mean (SE)	81.82 (2.21)
95% CI of LS mean	(77.35, 86.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	1.01 (2.21)
95% CI of LS mean	(-3.46, 5.48)
Week 12 (MMRM)	
n	43
LS mean (SE)	84.80 (2.17)
95% CI of LS mean	(80.42, 89.17)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	3.99 (2.17)
95% CI of LS mean	(-0.38, 8.36)
Week 16 (MMRM)	
n	44
LS mean (SE)	87.88 (2.64)
95% CI of LS mean	(82.54, 93.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	7.07 (2.64)
95% CI of LS mean	(1.73, 12.41)
Week 24	
n	44
Mean (SD)	87.37 (21.24)
Absolute Change at Week 24	
n	44
Mean (SD)	6.57 (15.22)
Week 24 (MMRM)	
n	44
LS mean (SE)	87.37 (1.85)
95% CI of LS mean	(83.64, 91.11)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	6.57 (1.85)
95% CI of LS mean	(2.83, 10.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	6.82 (2.04)
95% CI of LS mean	(2.68, 10.96)
P-value	0.0019

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	79.25 (25.63)
Week 4 (MMRM)	
n	34
LS mean (SE)	77.12 (2.69)
95% CI of LS mean	(71.60, 82.65)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-2.12 (2.69)
95% CI of LS mean	(-7.65, 3.40)
Week 8 (MMRM)	
n	34
LS mean (SE)	83.33 (3.06)
95% CI of LS mean	(77.05, 89.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	4.08 (3.06)
95% CI of LS mean	(-2.20, 10.37)
Week 12 (MMRM)	
n	34
LS mean (SE)	83.33 (2.89)
95% CI of LS mean	(77.43, 89.24)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	4.08 (2.89)
95% CI of LS mean	(-1.82, 9.99)
Week 16 (MMRM)	
n	34
LS mean (SE)	83.33 (2.61)
95% CI of LS mean	(78.01, 88.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	4.08 (2.61)
95% CI of LS mean	(-1.24, 9.41)
Week 24	
n	34
Mean (SD)	78.76 (20.90)
Absolute Change at Week 24	
n	34
Mean (SD)	-0.49 (19.93)
Week 24 (MMRM)	
n	34
LS mean (SE)	78.76 (2.80)
95% CI of LS mean	(73.05, 84.47)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	-0.49 (2.80)
95% CI of LS mean	(-6.20, 5.22)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	1.80 (2.32)
95% CI of LS mean	(-2.95, 6.54)
P-value	0.4451

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	80.14 (25.05)
Week 4 (MMRM)	
n	47
LS mean (SE)	82.03 (2.24)
95% CI of LS mean	(77.51, 86.56)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	1.89 (2.24)
95% CI of LS mean	(-2.63, 6.41)
Week 8 (MMRM)	
n	47
LS mean (SE)	82.03 (1.89)
95% CI of LS mean	(78.23, 85.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	1.89 (1.89)
95% CI of LS mean	(-1.91, 5.70)
Week 12 (MMRM)	
n	47
LS mean (SE)	83.22 (2.35)
95% CI of LS mean	(78.48, 87.95)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	3.07 (2.35)
95% CI of LS mean	(-1.67, 7.81)
Week 16 (MMRM)	
n	47
LS mean (SE)	87.47 (2.69)
95% CI of LS mean	(82.04, 92.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	7.33 (2.69)
95% CI of LS mean	(1.90, 12.75)
Week 24	
n	47
Mean (SD)	82.51 (21.20)
Absolute Change at Week 24	
n	47
Mean (SD)	2.36 (18.53)
Week 24 (MMRM)	
n	47
LS mean (SE)	82.51 (2.25)
95% CI of LS mean	(77.97, 87.04)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	2.36 (2.25)
95% CI of LS mean	(-2.17, 6.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	4.85 (2.24)
95% CI of LS mean	(0.33, 9.36)
P-value	0.0361

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	80.11 (28.03)
Week 4 (MMRM)	
n	31
LS mean (SE)	80.29 (2.31)
95% CI of LS mean	(75.56, 85.01)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	0.18 (2.31)
95% CI of LS mean	(-4.54, 4.90)
Week 8 (MMRM)	
n	31
LS mean (SE)	83.15 (3.82)
95% CI of LS mean	(75.33, 90.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	3.05 (3.82)
95% CI of LS mean	(-4.78, 10.87)
Week 12 (MMRM)	
n	30
LS mean (SE)	85.67 (2.72)
95% CI of LS mean	(80.09, 91.24)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	5.56 (2.72)
95% CI of LS mean	(-0.02, 11.14)
Week 16 (MMRM)	
n	31
LS mean (SE)	83.51 (2.42)
95% CI of LS mean	(78.54, 88.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	3.41 (2.42)
95% CI of LS mean	(-1.57, 8.38)
Week 24	
n	31
Mean (SD)	85.30 (21.92)
Absolute Change at Week 24	
n	31
Mean (SD)	5.20 (16.41)
Week 24 (MMRM)	
n	31
LS mean (SE)	85.30 (2.48)
95% CI of LS mean	(80.21, 90.40)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	5.20 (2.48)
95% CI of LS mean	(0.10, 10.30)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	4.30 (2.10)
95% CI of LS mean	(-0.03, 8.63)
P-value	0.0516

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	76.97 (27.84)
Week 4 (MMRM)	
n	62
LS mean (SE)	78.85 (1.96)
95% CI of LS mean	(74.94, 82.77)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	1.88 (1.96)
95% CI of LS mean	(-2.04, 5.80)
Week 8 (MMRM)	
n	62
LS mean (SE)	81.54 (1.94)
95% CI of LS mean	(77.66, 85.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	4.57 (1.94)
95% CI of LS mean	(0.69, 8.45)
Week 12 (MMRM)	
n	61
LS mean (SE)	82.59 (1.97)
95% CI of LS mean	(78.66, 86.52)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	5.62 (1.97)
95% CI of LS mean	(1.68, 9.55)
Week 16 (MMRM)	
n	62
LS mean (SE)	84.95 (1.98)
95% CI of LS mean	(80.99, 88.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	7.97 (1.98)
95% CI of LS mean	(4.02, 11.93)
Week 24	
n	62
Mean (SD)	81.54 (22.22)
Absolute Change at Week 24	
n	62
Mean (SD)	4.57 (19.02)
Week 24 (MMRM)	
n	62
LS mean (SE)	81.54 (1.98)
95% CI of LS mean	(77.58, 85.50)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	4.57 (1.98)
95% CI of LS mean	(0.61, 8.53)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	6.27 (1.76)
95% CI of LS mean	(2.75, 9.79)
P-value	0.0007

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	91.11 (14.63)
Week 4 (MMRM)	
n	10
LS mean (SE)	91.11 (4.12)
95% CI of LS mean	(82.76, 99.46)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	0.00 (4.12)
95% CI of LS mean	(-8.35, 8.35)
Week 8 (MMRM)	
n	10
LS mean (SE)	84.44 (4.12)
95% CI of LS mean	(76.09, 92.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-6.67 (4.12)
95% CI of LS mean	(-15.02, 1.69)
Week 12 (MMRM)	
n	10
LS mean (SE)	88.89 (4.12)
95% CI of LS mean	(80.54, 97.24)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-2.22 (4.12)
95% CI of LS mean	(-10.57, 6.13)
Week 16 (MMRM)	
n	10
LS mean (SE)	84.44 (4.12)
95% CI of LS mean	(76.09, 92.80)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	-6.67 (4.12)
95% CI of LS mean	(-15.02, 1.69)
Week 24	
n	10
Mean (SD)	88.89 (18.89)
Absolute Change at Week 24	
n	10
Mean (SD)	-2.22 (8.76)
Week 24 (MMRM)	
n	10
LS mean (SE)	88.89 (4.12)
95% CI of LS mean	(80.54, 97.24)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	-2.22 (4.12)
95% CI of LS mean	(-10.57, 6.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	-4.44 (3.13)
95% CI of LS mean	(-10.97, 2.08)
P-value	0.1706

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	80.81 (17.67)
Week 4 (MMRM)	
n	44
LS mean (SE)	80.05 (2.66)
95% CI of LS mean	(74.69, 85.41)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	-0.76 (2.66)
95% CI of LS mean	(-6.12, 4.60)
Week 8 (MMRM)	
n	44
LS mean (SE)	83.33 (2.05)
95% CI of LS mean	(79.19, 87.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	2.53 (2.05)
95% CI of LS mean	(-1.62, 6.67)
Week 12 (MMRM)	
n	43
LS mean (SE)	83.65 (2.12)
95% CI of LS mean	(79.38, 87.92)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	2.85 (2.12)
95% CI of LS mean	(-1.43, 7.12)
Week 16 (MMRM)	
n	44
LS mean (SE)	86.11 (1.65)
95% CI of LS mean	(82.78, 89.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	5.30 (1.65)
95% CI of LS mean	(1.97, 8.64)
Week 24	
n	44
Mean (SD)	82.58 (16.84)
Absolute Change at Week 24	
n	44
Mean (SD)	1.77 (15.52)
Week 24 (MMRM)	
n	44
LS mean (SE)	82.58 (2.08)
95% CI of LS mean	(78.38, 86.78)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	1.77 (2.08)
95% CI of LS mean	(-2.43, 5.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	3.54 (1.64)
95% CI of LS mean	(0.23, 6.85)
P-value	0.0369

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	83.99 (17.12)
Week 4 (MMRM)	
n	34
LS mean (SE)	86.60 (1.90)
95% CI of LS mean	(82.73, 90.47)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	2.61 (1.90)
95% CI of LS mean	(-1.25, 6.48)
Week 8 (MMRM)	
n	34
LS mean (SE)	81.70 (2.56)
95% CI of LS mean	(76.48, 86.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	-2.29 (2.56)
95% CI of LS mean	(-7.50, 2.93)
Week 12 (MMRM)	
n	34
LS mean (SE)	84.31 (2.15)
95% CI of LS mean	(79.92, 88.70)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	0.33 (2.15)
95% CI of LS mean	(-4.06, 4.72)
Week 16 (MMRM)	
n	34
LS mean (SE)	84.64 (2.08)
95% CI of LS mean	(80.41, 88.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	0.65 (2.08)
95% CI of LS mean	(-3.58, 4.88)
Week 24	
n	34
Mean (SD)	80.07 (16.13)
Absolute Change at Week 24	
n	34
Mean (SD)	-3.92 (17.06)
Week 24 (MMRM)	
n	34
LS mean (SE)	80.07 (2.45)
95% CI of LS mean	(75.07, 85.06)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	-3.92 (2.45)
95% CI of LS mean	(-8.92, 1.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	-1.63 (1.94)
95% CI of LS mean	(-5.60, 2.33)
P-value	0.4071

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	80.85 (18.78)
Week 4 (MMRM)	
n	47
LS mean (SE)	83.69 (1.78)
95% CI of LS mean	(80.10, 87.27)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	2.84 (1.78)
95% CI of LS mean	(-0.75, 6.42)
Week 8 (MMRM)	
n	47
LS mean (SE)	81.56 (2.18)
95% CI of LS mean	(77.17, 85.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	0.71 (2.18)
95% CI of LS mean	(-3.68, 5.10)
Week 12 (MMRM)	
n	47
LS mean (SE)	82.74 (1.91)
95% CI of LS mean	(78.90, 86.59)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	1.89 (1.91)
95% CI of LS mean	(-1.95, 5.74)
Week 16 (MMRM)	
n	47
LS mean (SE)	85.34 (1.64)
95% CI of LS mean	(82.04, 88.65)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	4.49 (1.64)
95% CI of LS mean	(1.19, 7.79)
Week 24	
n	47
Mean (SD)	81.56 (14.33)
Absolute Change at Week 24	
n	47
Mean (SD)	0.71 (16.45)
Week 24 (MMRM)	
n	47
LS mean (SE)	81.56 (1.83)
95% CI of LS mean	(77.88, 85.24)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	0.71 (1.83)
95% CI of LS mean	(-2.98, 4.39)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	2.60 (1.52)
95% CI of LS mean	(-0.47, 5.67)
P-value	0.0949

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	84.23 (15.12)
Week 4 (MMRM)	
n	31
LS mean (SE)	81.72 (3.37)
95% CI of LS mean	(74.83, 88.61)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	-2.51 (3.37)
95% CI of LS mean	(-9.40, 4.38)
Week 8 (MMRM)	
n	31
LS mean (SE)	84.23 (2.41)
95% CI of LS mean	(79.30, 89.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	0.00 (2.41)
95% CI of LS mean	(-4.93, 4.93)
Week 12 (MMRM)	
n	30
LS mean (SE)	86.08 (2.58)
95% CI of LS mean	(80.77, 91.39)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	1.85 (2.58)
95% CI of LS mean	(-3.46, 7.16)
Week 16 (MMRM)	
n	31
LS mean (SE)	85.66 (2.12)
95% CI of LS mean	(81.32, 90.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	1.43 (2.12)
95% CI of LS mean	(-2.91, 5.77)
Week 24	
n	31
Mean (SD)	81.36 (19.54)
Absolute Change at Week 24	
n	31
Mean (SD)	-2.87 (16.22)
Week 24 (MMRM)	
n	31
LS mean (SE)	81.36 (3.13)
95% CI of LS mean	(74.93, 87.79)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	-2.87 (3.13)
95% CI of LS mean	(-9.29, 3.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-0.72 (2.32)
95% CI of LS mean	(-5.49, 4.05)
P-value	0.7595

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	80.11 (17.56)
Week 4 (MMRM)	
n	62
LS mean (SE)	82.26 (1.85)
95% CI of LS mean	(78.55, 85.96)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	2.15 (1.85)
95% CI of LS mean	(-1.55, 5.86)
Week 8 (MMRM)	
n	62
LS mean (SE)	80.82 (1.90)
95% CI of LS mean	(77.03, 84.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	0.72 (1.90)
95% CI of LS mean	(-3.08, 4.51)
Week 12 (MMRM)	
n	61
LS mean (SE)	82.60 (1.83)
95% CI of LS mean	(78.95, 86.26)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	2.49 (1.83)
95% CI of LS mean	(-1.16, 6.15)
Week 16 (MMRM)	
n	62
LS mean (SE)	83.51 (1.54)
95% CI of LS mean	(80.43, 86.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	3.41 (1.54)
95% CI of LS mean	(0.33, 6.48)
Week 24	
n	62
Mean (SD)	78.85 (16.43)
Absolute Change at Week 24	
n	62
Mean (SD)	-1.25 (17.78)
Week 24 (MMRM)	
n	62
LS mean (SE)	78.85 (1.87)
95% CI of LS mean	(75.12, 82.58)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	-1.25 (1.87)
95% CI of LS mean	(-4.99, 2.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	1.08 (1.48)
95% CI of LS mean	(-1.88, 4.03)
P-value	0.4694

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	90.00 (17.72)
Week 4 (MMRM)	
n	10
LS mean (SE)	82.22 (7.20)
95% CI of LS mean	(65.83, 98.62)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-7.78 (7.20)
95% CI of LS mean	(-24.17, 8.62)
Week 8 (MMRM)	
n	10
LS mean (SE)	91.11 (4.14)
95% CI of LS mean	(81.62, 100.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	1.11 (4.14)
95% CI of LS mean	(-8.38, 10.60)
Week 12 (MMRM)	
n	10
LS mean (SE)	91.11 (2.50)
95% CI of LS mean	(85.38, 96.84)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	1.11 (2.50)
95% CI of LS mean	(-4.62, 6.84)
Week 16 (MMRM)	
n	10
LS mean (SE)	93.33 (2.31)
95% CI of LS mean	(87.83, 98.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	3.33 (2.31)
95% CI of LS mean	(-2.17, 8.84)
Week 24	
n	10
Mean (SD)	93.33 (11.94)
Absolute Change at Week 24	
n	10
Mean (SD)	3.33 (9.15)
Week 24 (MMRM)	
n	10
LS mean (SE)	93.33 (1.83)
95% CI of LS mean	(88.80, 97.87)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	3.33 (1.83)
95% CI of LS mean	(-1.20, 7.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	3.33 (1.27)
95% CI of LS mean	(0.29, 6.37)
P-value	0.0361

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	81.06 (25.31)
Week 4 (MMRM)	
n	44
LS mean (SE)	82.20 (2.29)
95% CI of LS mean	(77.57, 86.82)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	1.14 (2.29)
95% CI of LS mean	(-3.49, 5.76)
Week 8 (MMRM)	
n	44
LS mean (SE)	82.20 (2.88)
95% CI of LS mean	(76.38, 88.01)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	1.14 (2.88)
95% CI of LS mean	(-4.68, 6.95)
Week 12 (MMRM)	
n	43
LS mean (SE)	82.99 (2.63)
95% CI of LS mean	(77.67, 88.31)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	1.93 (2.63)
95% CI of LS mean	(-3.39, 7.25)
Week 16 (MMRM)	
n	44
LS mean (SE)	83.71 (2.11)
95% CI of LS mean	(79.45, 87.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	2.65 (2.11)
95% CI of LS mean	(-1.61, 6.91)
Week 24	
n	44
Mean (SD)	84.47 (21.98)
Absolute Change at Week 24	
n	44
Mean (SD)	3.41 (17.82)
Week 24 (MMRM)	
n	44
LS mean (SE)	84.47 (2.31)
95% CI of LS mean	(79.80, 89.14)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	3.41 (2.31)
95% CI of LS mean	(-1.26, 8.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	3.03 (1.85)
95% CI of LS mean	(-0.71, 6.77)
P-value	0.1096

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	77.45 (26.23)
Week 4 (MMRM)	
n	34
LS mean (SE)	73.53 (3.09)
95% CI of LS mean	(67.24, 79.82)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-3.92 (3.09)
95% CI of LS mean	(-10.22, 2.37)
Week 8 (MMRM)	
n	34
LS mean (SE)	75.49 (3.11)
95% CI of LS mean	(69.15, 81.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	-1.96 (3.11)
95% CI of LS mean	(-8.30, 4.38)
Week 12 (MMRM)	
n	34
LS mean (SE)	72.06 (3.27)
95% CI of LS mean	(65.41, 78.71)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	-5.39 (3.27)
95% CI of LS mean	(-12.05, 1.26)
Week 16 (MMRM)	
n	34
LS mean (SE)	77.45 (2.66)
95% CI of LS mean	(72.02, 82.88)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	0.00 (2.66)
95% CI of LS mean	(-5.43, 5.43)
Week 24	
n	34
Mean (SD)	78.43 (26.44)
Absolute Change at Week 24	
n	34
Mean (SD)	0.98 (19.65)
Week 24 (MMRM)	
n	34
LS mean (SE)	78.43 (3.20)
95% CI of LS mean	(71.91, 84.95)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	0.98 (3.20)
95% CI of LS mean	(-5.54, 7.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	0.49 (2.70)
95% CI of LS mean	(-5.02, 6.00)
P-value	0.8573

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	75.89 (27.54)
Week 4 (MMRM)	
n	47
LS mean (SE)	76.24 (2.53)
95% CI of LS mean	(71.15, 81.33)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	0.35 (2.53)
95% CI of LS mean	(-4.73, 5.44)
Week 8 (MMRM)	
n	47
LS mean (SE)	77.66 (2.59)
95% CI of LS mean	(72.45, 82.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	1.77 (2.59)
95% CI of LS mean	(-3.44, 6.99)
Week 12 (MMRM)	
n	47
LS mean (SE)	75.53 (2.47)
95% CI of LS mean	(70.54, 80.52)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	-0.35 (2.47)
95% CI of LS mean	(-5.35, 4.64)
Week 16 (MMRM)	
n	47
LS mean (SE)	79.08 (2.16)
95% CI of LS mean	(74.71, 83.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	3.19 (2.16)
95% CI of LS mean	(-1.17, 7.56)
Week 24	
n	47
Mean (SD)	80.85 (25.06)
Absolute Change at Week 24	
n	47
Mean (SD)	4.96 (19.01)
Week 24 (MMRM)	
n	47
LS mean (SE)	80.85 (2.49)
95% CI of LS mean	(75.83, 85.87)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	4.96 (2.49)
95% CI of LS mean	(-0.06, 9.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	4.08 (2.13)
95% CI of LS mean	(-0.21, 8.37)
P-value	0.0620

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	84.95 (21.67)
Week 4 (MMRM)	
n	31
LS mean (SE)	81.72 (2.80)
95% CI of LS mean	(76.00, 87.44)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	-3.23 (2.80)
95% CI of LS mean	(-8.94, 2.49)
Week 8 (MMRM)	
n	31
LS mean (SE)	81.72 (3.54)
95% CI of LS mean	(74.48, 88.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	-3.23 (3.54)
95% CI of LS mean	(-10.47, 4.02)
Week 12 (MMRM)	
n	30
LS mean (SE)	82.58 (3.67)
95% CI of LS mean	(75.07, 90.10)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	-2.36 (3.67)
95% CI of LS mean	(-9.88, 5.15)
Week 16 (MMRM)	
n	31
LS mean (SE)	83.87 (2.68)
95% CI of LS mean	(78.38, 89.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	-1.08 (2.68)
95% CI of LS mean	(-6.56, 4.41)
Week 24	
n	31
Mean (SD)	83.33 (22.77)
Absolute Change at Week 24	
n	31
Mean (SD)	-1.61 (17.40)
Week 24 (MMRM)	
n	31
LS mean (SE)	83.33 (2.96)
95% CI of LS mean	(77.29, 89.38)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	-1.61 (2.96)
95% CI of LS mean	(-7.66, 4.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-1.34 (2.35)
95% CI of LS mean	(-6.15, 3.46)
P-value	0.5713

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	78.49 (26.89)
Week 4 (MMRM)	
n	62
LS mean (SE)	76.88 (2.29)
95% CI of LS mean	(72.30, 81.47)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	-1.61 (2.29)
95% CI of LS mean	(-6.20, 2.97)
Week 8 (MMRM)	
n	62
LS mean (SE)	78.23 (2.53)
95% CI of LS mean	(73.16, 83.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	-0.27 (2.53)
95% CI of LS mean	(-5.34, 4.80)
Week 12 (MMRM)	
n	61
LS mean (SE)	76.31 (2.51)
95% CI of LS mean	(71.29, 81.33)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	-2.19 (2.51)
95% CI of LS mean	(-7.21, 2.83)
Week 16 (MMRM)	
n	62
LS mean (SE)	79.84 (1.91)
95% CI of LS mean	(76.02, 83.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	1.34 (1.91)
95% CI of LS mean	(-2.48, 5.16)
Week 24	
n	62
Mean (SD)	79.84 (25.27)
Absolute Change at Week 24	
n	62
Mean (SD)	1.34 (19.86)
Week 24 (MMRM)	
n	62
LS mean (SE)	79.84 (2.26)
95% CI of LS mean	(75.31, 84.37)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	1.34 (2.26)
95% CI of LS mean	(-3.18, 5.87)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	1.34 (1.83)
95% CI of LS mean	(-2.32, 5.01)
P-value	0.4661

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	91.67 (14.16)
Week 4 (MMRM)	
n	10
LS mean (SE)	90.00 (2.01)
95% CI of LS mean	(85.93, 94.07)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-1.67 (2.01)
95% CI of LS mean	(-5.74, 2.40)
Week 8 (MMRM)	
n	10
LS mean (SE)	90.00 (2.01)
95% CI of LS mean	(85.93, 94.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-1.67 (2.01)
95% CI of LS mean	(-5.74, 2.40)
Week 12 (MMRM)	
n	10
LS mean (SE)	91.67 (2.01)
95% CI of LS mean	(87.60, 95.74)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	0.00 (2.01)
95% CI of LS mean	(-4.07, 4.07)
Week 16 (MMRM)	
n	10
LS mean (SE)	93.33 (2.01)
95% CI of LS mean	(89.26, 97.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	1.67 (2.01)
95% CI of LS mean	(-2.40, 5.74)
Week 24	
n	10
Mean (SD)	96.67 (7.03)
Absolute Change at Week 24	
n	10
Mean (SD)	5.00 (8.05)
Week 24 (MMRM)	
n	10
LS mean (SE)	96.67 (2.01)
95% CI of LS mean	(92.60, 100.74)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	5.00 (2.01)
95% CI of LS mean	(0.93, 9.07)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	3.33 (1.24)
95% CI of LS mean	(0.83, 5.84)
P-value	0.0105

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	86.82 (12.41)
Week 4 (MMRM)	
n	44
LS mean (SE)	88.48 (1.29)
95% CI of LS mean	(85.87, 91.10)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	1.67 (1.29)
95% CI of LS mean	(-0.95, 4.28)
Week 8 (MMRM)	
n	44
LS mean (SE)	87.58 (1.50)
95% CI of LS mean	(84.55, 90.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	0.76 (1.50)
95% CI of LS mean	(-2.27, 3.78)
Week 12 (MMRM)	
n	43
LS mean (SE)	89.92 (1.37)
95% CI of LS mean	(87.15, 92.68)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	3.10 (1.37)
95% CI of LS mean	(0.33, 5.86)
Week 16 (MMRM)	
n	44
LS mean (SE)	90.45 (1.56)
95% CI of LS mean	(87.32, 93.59)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	3.64 (1.56)
95% CI of LS mean	(0.50, 6.77)
Week 24	
n	44
Mean (SD)	89.85 (9.48)
Absolute Change at Week 24	
n	44
Mean (SD)	3.03 (11.72)
Week 24 (MMRM)	
n	44
LS mean (SE)	89.85 (1.32)
95% CI of LS mean	(87.18, 92.52)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	3.03 (1.32)
95% CI of LS mean	(0.36, 5.70)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	3.33 (1.04)
95% CI of LS mean	(1.23, 5.44)
P-value	0.0027

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	86.13 (13.63)
Week 4 (MMRM)	
n	34
LS mean (SE)	85.10 (1.83)
95% CI of LS mean	(81.37, 88.83)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-1.03 (1.83)
95% CI of LS mean	(-4.76, 2.70)
Week 8 (MMRM)	
n	34
LS mean (SE)	85.59 (1.25)
95% CI of LS mean	(83.04, 88.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	-0.54 (1.25)
95% CI of LS mean	(-3.09, 2.01)
Week 12 (MMRM)	
n	34
LS mean (SE)	88.63 (1.57)
95% CI of LS mean	(85.43, 91.83)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	2.50 (1.57)
95% CI of LS mean	(-0.70, 5.70)
Week 16 (MMRM)	
n	34
LS mean (SE)	88.24 (1.42)
95% CI of LS mean	(85.34, 91.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	2.11 (1.42)
95% CI of LS mean	(-0.79, 5.00)
Week 24	
n	34
Mean (SD)	86.47 (12.66)
Absolute Change at Week 24	
n	34
Mean (SD)	0.34 (12.68)
Week 24 (MMRM)	
n	34
LS mean (SE)	86.47 (1.86)
95% CI of LS mean	(82.68, 90.26)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	0.34 (1.86)
95% CI of LS mean	(-3.45, 4.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	1.23 (1.35)
95% CI of LS mean	(-1.55, 4.00)
P-value	0.3727

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	86.84 (13.76)
Week 4 (MMRM)	
n	47
LS mean (SE)	87.52 (1.37)
95% CI of LS mean	(84.75, 90.28)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	0.67 (1.37)
95% CI of LS mean	(-2.09, 3.44)
Week 8 (MMRM)	
n	47
LS mean (SE)	86.88 (1.19)
95% CI of LS mean	(84.48, 89.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	0.04 (1.19)
95% CI of LS mean	(-2.37, 2.44)
Week 12 (MMRM)	
n	47
LS mean (SE)	89.08 (1.32)
95% CI of LS mean	(86.42, 91.73)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	2.23 (1.32)
95% CI of LS mean	(-0.42, 4.89)
Week 16 (MMRM)	
n	47
LS mean (SE)	90.78 (1.19)
95% CI of LS mean	(88.39, 93.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	3.94 (1.19)
95% CI of LS mean	(1.55, 6.33)
Week 24	
n	47
Mean (SD)	88.51 (10.65)
Absolute Change at Week 24	
n	47
Mean (SD)	1.67 (10.97)
Week 24 (MMRM)	
n	47
LS mean (SE)	88.51 (1.24)
95% CI of LS mean	(86.00, 91.02)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	1.67 (1.24)
95% CI of LS mean	(-0.84, 4.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	2.80 (1.02)
95% CI of LS mean	(0.75, 4.85)
P-value	0.0085

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	86.02 (11.59)
Week 4 (MMRM)	
n	31
LS mean (SE)	86.24 (1.80)
95% CI of LS mean	(82.55, 89.92)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	0.22 (1.80)
95% CI of LS mean	(-3.47, 3.90)
Week 8 (MMRM)	
n	31
LS mean (SE)	86.45 (1.81)
95% CI of LS mean	(82.74, 90.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	0.43 (1.81)
95% CI of LS mean	(-3.29, 4.15)
Week 12 (MMRM)	
n	30
LS mean (SE)	89.96 (1.73)
95% CI of LS mean	(86.41, 93.51)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	3.94 (1.73)
95% CI of LS mean	(0.38, 7.49)
Week 16 (MMRM)	
n	31
LS mean (SE)	87.53 (1.94)
95% CI of LS mean	(83.55, 91.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	1.51 (1.94)
95% CI of LS mean	(-2.47, 5.49)
Week 24	
n	31
Mean (SD)	88.17 (11.76)
Absolute Change at Week 24	
n	31
Mean (SD)	2.15 (13.92)
Week 24 (MMRM)	
n	31
LS mean (SE)	88.17 (2.15)
95% CI of LS mean	(83.76, 92.58)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	2.15 (2.15)
95% CI of LS mean	(-2.26, 6.56)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	1.83 (1.47)
95% CI of LS mean	(-1.18, 4.83)
P-value	0.2231

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	85.30 (13.80)
Week 4 (MMRM)	
n	62
LS mean (SE)	85.70 (1.13)
95% CI of LS mean	(83.45, 87.95)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	0.40 (1.13)
95% CI of LS mean	(-1.85, 2.66)
Week 8 (MMRM)	
n	62
LS mean (SE)	86.08 (1.07)
95% CI of LS mean	(83.94, 88.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	0.78 (1.07)
95% CI of LS mean	(-1.35, 2.91)
Week 12 (MMRM)	
n	61
LS mean (SE)	88.21 (1.14)
95% CI of LS mean	(85.93, 90.48)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	2.91 (1.14)
95% CI of LS mean	(0.63, 5.19)
Week 16 (MMRM)	
n	62
LS mean (SE)	88.60 (1.11)
95% CI of LS mean	(86.37, 90.83)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	3.31 (1.11)
95% CI of LS mean	(1.08, 5.54)
Week 24	
n	62
Mean (SD)	87.31 (11.50)
Absolute Change at Week 24	
n	62
Mean (SD)	2.02 (13.19)
Week 24 (MMRM)	
n	62
LS mean (SE)	87.31 (1.29)
95% CI of LS mean	(84.72, 89.90)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	2.02 (1.29)
95% CI of LS mean	(-0.57, 4.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	2.66 (0.91)
95% CI of LS mean	(0.84, 4.49)
P-value	0.0050

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	91.33 (7.06)
Week 4 (MMRM)	
n	10
LS mean (SE)	92.00 (5.43)
95% CI of LS mean	(76.64, 107.36)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	0.67 (5.43)
95% CI of LS mean	(-14.69, 16.03)
Week 8 (MMRM)	
n	10
LS mean (SE)	88.00 (4.64)
95% CI of LS mean	(71.39, 104.61)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-3.33 (4.64)
95% CI of LS mean	(-19.95, 13.28)
Week 12 (MMRM)	
n	10
LS mean (SE)	92.67 (3.88)
95% CI of LS mean	(80.30, 105.03)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	1.33 (3.88)
95% CI of LS mean	(-11.03, 13.70)
Week 16 (MMRM)	
n	10
LS mean (SE)	92.00 (4.51)
95% CI of LS mean	(77.83, 106.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	0.67 (4.51)
95% CI of LS mean	(-13.51, 14.84)
Week 24	
n	10
Mean (SD)	92.67 (9.14)
Absolute Change at Week 24	
n	10
Mean (SD)	1.33 (5.26)
Week 24 (MMRM)	
n	10
LS mean (SE)	92.67 (1.97)
95% CI of LS mean	(83.18, 102.15)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	1.33 (1.97)
95% CI of LS mean	(-8.15, 10.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	1.00 (2.61)
95% CI of LS mean	(-24.19, 26.19)
P-value	0.7611

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	86.36 (14.94)
Week 4 (MMRM)	
n	44
LS mean (SE)	82.83 (2.33)
95% CI of LS mean	(78.11, 87.54)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	-3.54 (2.33)
95% CI of LS mean	(-8.25, 1.18)
Week 8 (MMRM)	
n	44
LS mean (SE)	83.84 (2.11)
95% CI of LS mean	(79.59, 88.09)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	-2.53 (2.11)
95% CI of LS mean	(-6.78, 1.73)
Week 12 (MMRM)	
n	43
LS mean (SE)	87.30 (1.51)
95% CI of LS mean	(84.25, 90.36)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	0.94 (1.51)
95% CI of LS mean	(-2.12, 3.99)
Week 16 (MMRM)	
n	44
LS mean (SE)	89.14 (1.69)
95% CI of LS mean	(85.74, 92.54)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	2.78 (1.69)
95% CI of LS mean	(-0.62, 6.18)
Week 24	
n	44
Mean (SD)	89.65 (14.85)
Absolute Change at Week 24	
n	44
Mean (SD)	3.28 (14.29)
Week 24 (MMRM)	
n	44
LS mean (SE)	89.65 (1.90)
95% CI of LS mean	(85.81, 93.48)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	3.28 (1.90)
95% CI of LS mean	(-0.55, 7.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	3.03 (1.34)
95% CI of LS mean	(0.32, 5.74)
P-value	0.0291

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	87.25 (12.27)
Week 4 (MMRM)	
n	34
LS mean (SE)	82.03 (2.17)
95% CI of LS mean	(77.61, 86.44)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-5.23 (2.17)
95% CI of LS mean	(-9.65, -0.81)
Week 8 (MMRM)	
n	34
LS mean (SE)	88.56 (1.60)
95% CI of LS mean	(85.31, 91.82)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	1.31 (1.60)
95% CI of LS mean	(-1.95, 4.56)
Week 12 (MMRM)	
n	34
LS mean (SE)	86.27 (2.36)
95% CI of LS mean	(81.46, 91.09)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	-0.98 (2.36)
95% CI of LS mean	(-5.79, 3.83)
Week 16 (MMRM)	
n	34
LS mean (SE)	87.58 (1.68)
95% CI of LS mean	(84.16, 91.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	0.33 (1.68)
95% CI of LS mean	(-3.10, 3.75)
Week 24	
n	34
Mean (SD)	84.64 (18.56)
Absolute Change at Week 24	
n	34
Mean (SD)	-2.61 (18.56)
Week 24 (MMRM)	
n	34
LS mean (SE)	84.64 (3.08)
95% CI of LS mean	(78.36, 90.92)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	-2.61 (3.08)
95% CI of LS mean	(-8.89, 3.66)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	-1.14 (1.94)
95% CI of LS mean	(-5.11, 2.82)
P-value	0.5606

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	87.23 (12.69)
Week 4 (MMRM)	
n	47
LS mean (SE)	82.74 (1.91)
95% CI of LS mean	(78.88, 86.60)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-4.49 (1.91)
95% CI of LS mean	(-8.35, -0.63)
Week 8 (MMRM)	
n	47
LS mean (SE)	86.76 (1.58)
95% CI of LS mean	(83.58, 89.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	-0.47 (1.58)
95% CI of LS mean	(-3.65, 2.71)
Week 12 (MMRM)	
n	47
LS mean (SE)	87.94 (1.77)
95% CI of LS mean	(84.38, 91.50)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	0.71 (1.77)
95% CI of LS mean	(-2.85, 4.27)
Week 16 (MMRM)	
n	47
LS mean (SE)	91.25 (1.33)
95% CI of LS mean	(88.57, 93.94)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	4.02 (1.33)
95% CI of LS mean	(1.33, 6.71)
Week 24	
n	47
Mean (SD)	89.60 (15.09)
Absolute Change at Week 24	
n	47
Mean (SD)	2.36 (13.89)
Week 24 (MMRM)	
n	47
LS mean (SE)	89.60 (1.89)
95% CI of LS mean	(85.80, 93.39)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	2.36 (1.89)
95% CI of LS mean	(-1.43, 6.16)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	3.19 (1.29)
95% CI of LS mean	(0.59, 5.79)
P-value	0.0173

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	86.02 (15.44)
Week 4 (MMRM)	
n	31
LS mean (SE)	82.08 (2.86)
95% CI of LS mean	(76.24, 87.92)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	-3.94 (2.86)
95% CI of LS mean	(-9.78, 1.90)
Week 8 (MMRM)	
n	31
LS mean (SE)	84.59 (2.50)
95% CI of LS mean	(79.46, 89.71)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	-1.43 (2.50)
95% CI of LS mean	(-6.56, 3.69)
Week 12 (MMRM)	
n	30
LS mean (SE)	85.23 (2.09)
95% CI of LS mean	(80.96, 89.50)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	-0.79 (2.09)
95% CI of LS mean	(-5.07, 3.48)
Week 16 (MMRM)	
n	31
LS mean (SE)	84.23 (2.13)
95% CI of LS mean	(79.88, 88.57)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	-1.79 (2.13)
95% CI of LS mean	(-6.14, 2.55)
Week 24	
n	31
Mean (SD)	84.23 (18.54)
Absolute Change at Week 24	
n	31
Mean (SD)	-1.79 (19.69)
Week 24 (MMRM)	
n	31
LS mean (SE)	84.23 (3.30)
95% CI of LS mean	(77.45, 91.01)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	-1.79 (3.30)
95% CI of LS mean	(-8.57, 4.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-1.79 (2.05)
95% CI of LS mean	(-6.01, 2.43)
P-value	0.3903

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	86.38 (13.85)
Week 4 (MMRM)	
n	62
LS mean (SE)	83.33 (1.70)
95% CI of LS mean	(79.93, 86.74)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	-3.05 (1.70)
95% CI of LS mean	(-6.45, 0.36)
Week 8 (MMRM)	
n	62
LS mean (SE)	86.20 (1.50)
95% CI of LS mean	(83.20, 89.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	-0.18 (1.50)
95% CI of LS mean	(-3.18, 2.82)
Week 12 (MMRM)	
n	61
LS mean (SE)	86.72 (1.55)
95% CI of LS mean	(83.61, 89.83)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	0.34 (1.55)
95% CI of LS mean	(-2.77, 3.45)
Week 16 (MMRM)	
n	62
LS mean (SE)	89.07 (1.25)
95% CI of LS mean	(86.56, 91.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	2.69 (1.25)
95% CI of LS mean	(0.18, 5.20)
Week 24	
n	62
Mean (SD)	87.46 (17.01)
Absolute Change at Week 24	
n	62
Mean (SD)	1.08 (17.16)
Week 24 (MMRM)	
n	62
LS mean (SE)	87.46 (2.06)
95% CI of LS mean	(83.33, 91.58)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	1.08 (2.06)
95% CI of LS mean	(-3.05, 5.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	1.88 (1.34)
95% CI of LS mean	(-0.81, 4.57)
P-value	0.1669

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	86.67 (14.63)
Week 4 (MMRM)	
n	10
LS mean (SE)	78.89 (3.67)
95% CI of LS mean	(70.58, 87.20)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-7.78 (3.67)
95% CI of LS mean	(-16.09, 0.53)
Week 8 (MMRM)	
n	10
LS mean (SE)	86.67 (2.38)
95% CI of LS mean	(81.13, 92.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	0.00 (2.38)
95% CI of LS mean	(-5.54, 5.54)
Week 12 (MMRM)	
n	10
LS mean (SE)	87.78 (4.33)
95% CI of LS mean	(77.60, 97.96)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	1.11 (4.33)
95% CI of LS mean	(-9.07, 11.29)
Week 16 (MMRM)	
n	10
LS mean (SE)	87.78 (3.83)
95% CI of LS mean	(78.63, 96.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	1.11 (3.83)
95% CI of LS mean	(-8.04, 10.26)
Week 24	
n	10
Mean (SD)	87.78 (16.10)
Absolute Change at Week 24	
n	10
Mean (SD)	1.11 (8.20)
Week 24 (MMRM)	
n	10
LS mean (SE)	87.78 (2.95)
95% CI of LS mean	(80.94, 94.61)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	1.11 (2.95)
95% CI of LS mean	(-5.72, 7.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	1.11 (2.35)
95% CI of LS mean	(-5.01, 7.23)
P-value	0.6567

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	92.99 (10.28)
Week 4 (MMRM)	
n	44
LS mean (SE)	91.76 (1.73)
95% CI of LS mean	(88.27, 95.25)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	-1.23 (1.73)
95% CI of LS mean	(-4.72, 2.26)
Week 8 (MMRM)	
n	44
LS mean (SE)	89.20 (1.86)
95% CI of LS mean	(85.45, 92.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	-3.79 (1.86)
95% CI of LS mean	(-7.54, -0.03)
Week 12 (MMRM)	
n	43
LS mean (SE)	93.27 (1.33)
95% CI of LS mean	(90.59, 95.95)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	0.28 (1.33)
95% CI of LS mean	(-2.40, 2.96)
Week 16 (MMRM)	
n	44
LS mean (SE)	93.47 (1.84)
95% CI of LS mean	(89.76, 97.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	0.47 (1.84)
95% CI of LS mean	(-3.24, 4.18)
Week 24	
n	44
Mean (SD)	93.47 (12.43)
Absolute Change at Week 24	
n	44
Mean (SD)	0.47 (8.91)
Week 24 (MMRM)	
n	44
LS mean (SE)	93.47 (1.38)
95% CI of LS mean	(90.68, 96.25)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	0.47 (1.38)
95% CI of LS mean	(-2.31, 3.26)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	0.47 (1.24)
95% CI of LS mean	(-2.02, 2.97)
P-value	0.7038

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	90.44 (16.56)
Week 4 (MMRM)	
n	34
LS mean (SE)	90.07 (2.16)
95% CI of LS mean	(85.67, 94.48)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-0.37 (2.16)
95% CI of LS mean	(-4.77, 4.04)
Week 8 (MMRM)	
n	34
LS mean (SE)	91.32 (1.87)
95% CI of LS mean	(87.48, 95.15)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	0.88 (1.87)
95% CI of LS mean	(-2.96, 4.71)
Week 12 (MMRM)	
n	34
LS mean (SE)	95.83 (0.74)
95% CI of LS mean	(94.32, 97.35)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	5.39 (0.74)
95% CI of LS mean	(3.88, 6.91)
Week 16 (MMRM)	
n	34
LS mean (SE)	95.10 (1.45)
95% CI of LS mean	(92.15, 98.05)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	4.66 (1.45)
95% CI of LS mean	(1.71, 7.61)
Week 24	
n	34
Mean (SD)	90.44 (17.36)
Absolute Change at Week 24	
n	34
Mean (SD)	0.00 (14.29)
Week 24 (MMRM)	
n	34
LS mean (SE)	90.44 (2.52)
95% CI of LS mean	(85.32, 95.57)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	0.00 (2.52)
95% CI of LS mean	(-5.13, 5.13)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	2.33 (1.59)
95% CI of LS mean	(-0.92, 5.58)
P-value	0.1541

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	92.02 (14.11)
Week 4 (MMRM)	
n	47
LS mean (SE)	91.31 (1.44)
95% CI of LS mean	(88.41, 94.22)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-0.71 (1.44)
95% CI of LS mean	(-3.61, 2.19)
Week 8 (MMRM)	
n	47
LS mean (SE)	90.26 (1.67)
95% CI of LS mean	(86.88, 93.64)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	-1.76 (1.67)
95% CI of LS mean	(-5.14, 1.62)
Week 12 (MMRM)	
n	47
LS mean (SE)	94.59 (1.07)
95% CI of LS mean	(92.45, 96.74)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	2.57 (1.07)
95% CI of LS mean	(0.42, 4.72)
Week 16 (MMRM)	
n	47
LS mean (SE)	96.28 (0.86)
95% CI of LS mean	(94.52, 98.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	4.26 (0.86)
95% CI of LS mean	(2.50, 6.01)
Week 24	
n	47
Mean (SD)	93.09 (13.83)
Absolute Change at Week 24	
n	47
Mean (SD)	1.06 (8.58)
Week 24 (MMRM)	
n	47
LS mean (SE)	93.09 (1.31)
95% CI of LS mean	(90.43, 95.74)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	1.06 (1.31)
95% CI of LS mean	(-1.59, 3.72)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	2.66 (0.83)
95% CI of LS mean	(0.99, 4.33)
P-value	0.0024

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	91.67 (12.31)
Week 4 (MMRM)	
n	31
LS mean (SE)	90.59 (2.37)
95% CI of LS mean	(85.75, 95.43)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	-1.08 (2.37)
95% CI of LS mean	(-5.92, 3.77)
Week 8 (MMRM)	
n	31
LS mean (SE)	89.92 (1.93)
95% CI of LS mean	(85.98, 93.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	-1.75 (1.93)
95% CI of LS mean	(-5.68, 2.19)
Week 12 (MMRM)	
n	30
LS mean (SE)	94.25 (1.38)
95% CI of LS mean	(91.43, 97.07)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	2.58 (1.38)
95% CI of LS mean	(-0.24, 5.40)
Week 16 (MMRM)	
n	31
LS mean (SE)	90.99 (2.74)
95% CI of LS mean	(85.39, 96.60)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	-0.67 (2.74)
95% CI of LS mean	(-6.27, 4.93)
Week 24	
n	31
Mean (SD)	90.73 (16.20)
Absolute Change at Week 24	
n	31
Mean (SD)	-0.94 (14.93)
Week 24 (MMRM)	
n	31
LS mean (SE)	90.73 (2.64)
95% CI of LS mean	(85.34, 96.12)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	-0.94 (2.64)
95% CI of LS mean	(-6.33, 4.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-0.81 (2.04)
95% CI of LS mean	(-4.98, 3.36)
P-value	0.6954

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	90.32 (14.49)
Week 4 (MMRM)	
n	62
LS mean (SE)	90.12 (1.46)
95% CI of LS mean	(87.19, 93.05)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	-0.20 (1.46)
95% CI of LS mean	(-3.13, 2.73)
Week 8 (MMRM)	
n	62
LS mean (SE)	88.72 (1.48)
95% CI of LS mean	(85.75, 91.69)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	-1.60 (1.48)
95% CI of LS mean	(-4.57, 1.37)
Week 12 (MMRM)	
n	61
LS mean (SE)	93.68 (0.98)
95% CI of LS mean	(91.72, 95.65)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	3.36 (0.98)
95% CI of LS mean	(1.39, 5.32)
Week 16 (MMRM)	
n	62
LS mean (SE)	93.68 (1.33)
95% CI of LS mean	(91.02, 96.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	3.36 (1.33)
95% CI of LS mean	(0.70, 6.02)
Week 24	
n	62
Mean (SD)	90.32 (16.05)
Absolute Change at Week 24	
n	62
Mean (SD)	0.00 (12.83)
Week 24 (MMRM)	
n	62
LS mean (SE)	90.32 (1.61)
95% CI of LS mean	(87.09, 93.55)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	0.00 (1.61)
95% CI of LS mean	(-3.23, 3.23)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	1.68 (1.12)
95% CI of LS mean	(-0.56, 3.92)
P-value	0.1383

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	97.50 (4.03)
Week 4 (MMRM)	
n	10
LS mean (SE)	91.25 (3.12)
95% CI of LS mean	(84.66, 97.84)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-6.25 (3.12)
95% CI of LS mean	(-12.84, 0.34)
Week 8 (MMRM)	
n	10
LS mean (SE)	95.42 (3.12)
95% CI of LS mean	(88.83, 102.00)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-2.08 (3.12)
95% CI of LS mean	(-8.67, 4.50)
Week 12 (MMRM)	
n	10
LS mean (SE)	95.83 (3.12)
95% CI of LS mean	(89.25, 102.42)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-1.67 (3.12)
95% CI of LS mean	(-8.25, 4.92)
Week 16 (MMRM)	
n	10
LS mean (SE)	93.75 (3.12)
95% CI of LS mean	(87.16, 100.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	-3.75 (3.12)
95% CI of LS mean	(-10.34, 2.84)
Week 24	
n	10
Mean (SD)	98.75 (2.01)
Absolute Change at Week 24	
n	10
Mean (SD)	1.25 (2.81)
Week 24 (MMRM)	
n	10
LS mean (SE)	98.75 (3.12)
95% CI of LS mean	(92.16, 105.34)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	1.25 (3.12)
95% CI of LS mean	(-5.34, 7.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	-1.25 (2.73)
95% CI of LS mean	(-7.28, 4.78)
P-value	0.6558

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	82.77 (17.65)
Week 4 (MMRM)	
n	44
LS mean (SE)	84.09 (2.11)
95% CI of LS mean	(79.83, 88.35)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	1.33 (2.11)
95% CI of LS mean	(-2.93, 5.58)
Week 8 (MMRM)	
n	44
LS mean (SE)	81.82 (2.32)
95% CI of LS mean	(77.14, 86.49)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	-0.95 (2.32)
95% CI of LS mean	(-5.62, 3.73)
Week 12 (MMRM)	
n	43
LS mean (SE)	84.63 (1.62)
95% CI of LS mean	(81.34, 87.92)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	1.87 (1.62)
95% CI of LS mean	(-1.42, 5.16)
Week 16 (MMRM)	
n	44
LS mean (SE)	84.66 (2.27)
95% CI of LS mean	(80.08, 89.24)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	1.89 (2.27)
95% CI of LS mean	(-2.69, 6.47)
Week 24	
n	44
Mean (SD)	86.17 (15.56)
Absolute Change at Week 24	
n	44
Mean (SD)	3.41 (14.64)
Week 24 (MMRM)	
n	44
LS mean (SE)	86.17 (1.90)
95% CI of LS mean	(82.33, 90.01)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	3.41 (1.90)
95% CI of LS mean	(-0.43, 7.25)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	2.65 (1.83)
95% CI of LS mean	(-1.05, 6.35)
P-value	0.1550

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	77.45 (16.86)
Week 4 (MMRM)	
n	34
LS mean (SE)	80.39 (2.50)
95% CI of LS mean	(75.28, 85.50)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	2.94 (2.50)
95% CI of LS mean	(-2.17, 8.05)
Week 8 (MMRM)	
n	34
LS mean (SE)	80.88 (2.65)
95% CI of LS mean	(75.45, 86.32)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	3.43 (2.65)
95% CI of LS mean	(-2.00, 8.87)
Week 12 (MMRM)	
n	34
LS mean (SE)	83.58 (2.52)
95% CI of LS mean	(78.45, 88.71)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	6.13 (2.52)
95% CI of LS mean	(1.00, 11.26)
Week 16 (MMRM)	
n	34
LS mean (SE)	85.54 (2.23)
95% CI of LS mean	(81.00, 90.08)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	8.09 (2.23)
95% CI of LS mean	(3.55, 12.63)
Week 24	
n	34
Mean (SD)	78.19 (18.00)
Absolute Change at Week 24	
n	34
Mean (SD)	0.74 (16.46)
Week 24 (MMRM)	
n	34
LS mean (SE)	78.19 (2.60)
95% CI of LS mean	(72.89, 83.48)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	0.74 (2.60)
95% CI of LS mean	(-4.56, 6.03)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	4.41 (2.04)
95% CI of LS mean	(0.25, 8.58)
P-value	0.0386

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	78.90 (18.78)
Week 4 (MMRM)	
n	47
LS mean (SE)	82.09 (1.80)
95% CI of LS mean	(78.45, 85.73)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	3.19 (1.80)
95% CI of LS mean	(-0.45, 6.83)
Week 8 (MMRM)	
n	47
LS mean (SE)	79.96 (2.39)
95% CI of LS mean	(75.15, 84.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	1.06 (2.39)
95% CI of LS mean	(-3.75, 5.88)
Week 12 (MMRM)	
n	47
LS mean (SE)	83.57 (1.87)
95% CI of LS mean	(79.78, 87.36)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	4.67 (1.87)
95% CI of LS mean	(0.88, 8.46)
Week 16 (MMRM)	
n	47
LS mean (SE)	85.99 (2.08)
95% CI of LS mean	(81.80, 90.19)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	7.09 (2.08)
95% CI of LS mean	(2.90, 11.29)
Week 24	
n	47
Mean (SD)	82.62 (16.92)
Absolute Change at Week 24	
n	47
Mean (SD)	3.72 (15.43)
Week 24 (MMRM)	
n	47
LS mean (SE)	82.62 (1.93)
95% CI of LS mean	(78.73, 86.52)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	3.72 (1.93)
95% CI of LS mean	(-0.17, 7.62)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	5.41 (1.85)
95% CI of LS mean	(1.67, 9.14)
P-value	0.0056

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	82.80 (15.05)
Week 4 (MMRM)	
n	31
LS mean (SE)	83.06 (3.04)
95% CI of LS mean	(76.85, 89.28)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	0.27 (3.04)
95% CI of LS mean	(-5.94, 6.48)
Week 8 (MMRM)	
n	31
LS mean (SE)	83.60 (2.36)
95% CI of LS mean	(78.76, 88.44)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	0.81 (2.36)
95% CI of LS mean	(-4.03, 5.65)
Week 12 (MMRM)	
n	30
LS mean (SE)	85.09 (2.18)
95% CI of LS mean	(80.63, 89.54)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	2.29 (2.18)
95% CI of LS mean	(-2.17, 6.75)
Week 16 (MMRM)	
n	31
LS mean (SE)	83.60 (2.52)
95% CI of LS mean	(78.46, 88.75)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	0.81 (2.52)
95% CI of LS mean	(-4.34, 5.95)
Week 24	
n	31
Mean (SD)	82.80 (17.47)
Absolute Change at Week 24	
n	31
Mean (SD)	0.00 (15.37)
Week 24 (MMRM)	
n	31
LS mean (SE)	82.80 (2.67)
95% CI of LS mean	(77.34, 88.25)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	0.00 (2.67)
95% CI of LS mean	(-5.46, 5.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	0.40 (1.90)
95% CI of LS mean	(-3.49, 4.30)
P-value	0.8334

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	79.84 (18.02)
Week 4 (MMRM)	
n	62
LS mean (SE)	81.59 (1.92)
95% CI of LS mean	(77.74, 85.43)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	1.75 (1.92)
95% CI of LS mean	(-2.10, 5.60)
Week 8 (MMRM)	
n	62
LS mean (SE)	80.78 (2.04)
95% CI of LS mean	(76.71, 84.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	0.94 (2.04)
95% CI of LS mean	(-3.13, 5.01)
Week 12 (MMRM)	
n	61
LS mean (SE)	83.20 (1.68)
95% CI of LS mean	(79.83, 86.57)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	3.36 (1.68)
95% CI of LS mean	(-0.01, 6.73)
Week 16 (MMRM)	
n	62
LS mean (SE)	84.14 (1.76)
95% CI of LS mean	(80.61, 87.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	4.30 (1.76)
95% CI of LS mean	(0.77, 7.83)
Week 24	
n	62
Mean (SD)	81.32 (17.83)
Absolute Change at Week 24	
n	62
Mean (SD)	1.48 (16.22)
Week 24 (MMRM)	
n	62
LS mean (SE)	81.32 (1.82)
95% CI of LS mean	(77.68, 84.96)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	1.48 (1.82)
95% CI of LS mean	(-2.16, 5.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	2.89 (1.50)
95% CI of LS mean	(-0.12, 5.90)
P-value	0.0592

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	81.67 (18.76)
Week 4 (MMRM)	
n	10
LS mean (SE)	86.67 (3.36)
95% CI of LS mean	(78.62, 94.71)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	5.00 (3.36)
95% CI of LS mean	(-3.04, 13.04)
Week 8 (MMRM)	
n	10
LS mean (SE)	83.33 (3.95)
95% CI of LS mean	(74.38, 92.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	1.67 (3.95)
95% CI of LS mean	(-7.29, 10.62)
Week 12 (MMRM)	
n	10
LS mean (SE)	85.83 (2.36)
95% CI of LS mean	(80.18, 91.49)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	4.17 (2.36)
95% CI of LS mean	(-1.49, 9.82)
Week 16 (MMRM)	
n	10
LS mean (SE)	87.50 (6.25)
95% CI of LS mean	(73.09, 101.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	5.83 (6.25)
95% CI of LS mean	(-8.58, 20.25)
Week 24	
n	10
Mean (SD)	86.67 (15.32)
Absolute Change at Week 24	
n	10
Mean (SD)	5.00 (14.27)
Week 24 (MMRM)	
n	10
LS mean (SE)	86.67 (4.23)
95% CI of LS mean	(76.80, 96.53)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	5.00 (4.23)
95% CI of LS mean	(-4.86, 14.86)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	5.42 (4.71)
95% CI of LS mean	(-5.63, 16.46)
P-value	0.2862

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	72.73 (23.17)
Week 4 (MMRM)	
n	44
LS mean (SE)	77.53 (1.91)
95% CI of LS mean	(73.67, 81.38)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	4.80 (1.91)
95% CI of LS mean	(0.94, 8.65)
Week 8 (MMRM)	
n	44
LS mean (SE)	80.56 (2.74)
95% CI of LS mean	(75.01, 86.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	7.83 (2.74)
95% CI of LS mean	(2.28, 13.38)
Week 12 (MMRM)	
n	43
LS mean (SE)	78.67 (2.61)
95% CI of LS mean	(73.40, 83.94)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	5.94 (2.61)
95% CI of LS mean	(0.67, 11.22)
Week 16 (MMRM)	
n	44
LS mean (SE)	78.79 (2.08)
95% CI of LS mean	(74.60, 82.98)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	6.06 (2.08)
95% CI of LS mean	(1.87, 10.25)
Week 24	
n	44
Mean (SD)	80.56 (21.85)
Absolute Change at Week 24	
n	44
Mean (SD)	7.83 (20.97)
Week 24 (MMRM)	
n	44
LS mean (SE)	80.56 (2.64)
95% CI of LS mean	(75.21, 85.90)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	7.83 (2.64)
95% CI of LS mean	(2.49, 13.17)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	6.94 (1.99)
95% CI of LS mean	(2.91, 10.98)
P-value	0.0012

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	65.03 (17.76)
Week 4 (MMRM)	
n	34
LS mean (SE)	74.51 (2.41)
95% CI of LS mean	(69.60, 79.42)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	9.48 (2.41)
95% CI of LS mean	(4.57, 14.39)
Week 8 (MMRM)	
n	34
LS mean (SE)	74.84 (3.19)
95% CI of LS mean	(68.33, 81.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	9.80 (3.19)
95% CI of LS mean	(3.29, 16.31)
Week 12 (MMRM)	
n	34
LS mean (SE)	71.90 (3.26)
95% CI of LS mean	(65.27, 78.52)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	6.86 (3.26)
95% CI of LS mean	(0.23, 13.49)
Week 16 (MMRM)	
n	34
LS mean (SE)	74.84 (2.51)
95% CI of LS mean	(69.71, 79.96)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	9.80 (2.51)
95% CI of LS mean	(4.68, 14.93)
Week 24	
n	34
Mean (SD)	75.16 (19.92)
Absolute Change at Week 24	
n	34
Mean (SD)	10.13 (16.50)
Week 24 (MMRM)	
n	34
LS mean (SE)	75.16 (2.63)
95% CI of LS mean	(69.81, 80.52)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	10.13 (2.63)
95% CI of LS mean	(4.78, 15.48)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	9.97 (2.35)
95% CI of LS mean	(5.17, 14.76)
P-value	0.0002

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	70.21 (21.12)
Week 4 (MMRM)	
n	47
LS mean (SE)	77.07 (2.00)
95% CI of LS mean	(73.04, 81.10)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	6.86 (2.00)
95% CI of LS mean	(2.83, 10.88)
Week 8 (MMRM)	
n	47
LS mean (SE)	78.01 (2.69)
95% CI of LS mean	(72.60, 83.43)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	7.80 (2.69)
95% CI of LS mean	(2.39, 13.21)
Week 12 (MMRM)	
n	47
LS mean (SE)	74.47 (2.73)
95% CI of LS mean	(68.97, 79.97)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	4.26 (2.73)
95% CI of LS mean	(-1.25, 9.76)
Week 16 (MMRM)	
n	47
LS mean (SE)	80.14 (2.23)
95% CI of LS mean	(75.66, 84.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	9.93 (2.23)
95% CI of LS mean	(5.44, 14.41)
Week 24	
n	47
Mean (SD)	79.20 (19.33)
Absolute Change at Week 24	
n	47
Mean (SD)	8.98 (20.15)
Week 24 (MMRM)	
n	47
LS mean (SE)	79.20 (2.50)
95% CI of LS mean	(74.16, 84.23)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	8.98 (2.50)
95% CI of LS mean	(3.95, 14.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	9.46 (2.12)
95% CI of LS mean	(5.17, 13.74)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	68.10 (21.61)
Week 4 (MMRM)	
n	31
LS mean (SE)	74.91 (2.30)
95% CI of LS mean	(70.18, 79.64)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	6.81 (2.30)
95% CI of LS mean	(2.08, 11.54)
Week 8 (MMRM)	
n	31
LS mean (SE)	78.14 (3.81)
95% CI of LS mean	(70.31, 85.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	10.04 (3.81)
95% CI of LS mean	(2.21, 17.87)
Week 12 (MMRM)	
n	30
LS mean (SE)	77.68 (3.17)
95% CI of LS mean	(71.20, 84.16)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	9.58 (3.17)
95% CI of LS mean	(3.10, 16.06)
Week 16 (MMRM)	
n	31
LS mean (SE)	72.40 (1.99)
95% CI of LS mean	(68.31, 76.50)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	4.30 (1.99)
95% CI of LS mean	(0.21, 8.40)
Week 24	
n	31
Mean (SD)	76.70 (23.72)
Absolute Change at Week 24	
n	31
Mean (SD)	8.60 (17.62)
Week 24 (MMRM)	
n	31
LS mean (SE)	76.70 (3.11)
95% CI of LS mean	(70.34, 83.07)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	8.60 (3.11)
95% CI of LS mean	(2.24, 14.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	6.45 (2.19)
95% CI of LS mean	(1.97, 10.93)
P-value	0.0064

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	67.20 (21.05)
Week 4 (MMRM)	
n	62
LS mean (SE)	75.45 (1.71)
95% CI of LS mean	(72.02, 78.87)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	8.24 (1.71)
95% CI of LS mean	(4.82, 11.67)
Week 8 (MMRM)	
n	62
LS mean (SE)	77.96 (2.48)
95% CI of LS mean	(72.98, 82.93)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	10.75 (2.48)
95% CI of LS mean	(5.78, 15.73)
Week 12 (MMRM)	
n	61
LS mean (SE)	74.78 (2.33)
95% CI of LS mean	(70.13, 79.43)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	7.58 (2.33)
95% CI of LS mean	(2.93, 12.23)
Week 16 (MMRM)	
n	62
LS mean (SE)	76.70 (1.90)
95% CI of LS mean	(72.89, 80.51)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	9.50 (1.90)
95% CI of LS mean	(5.69, 13.31)
Week 24	
n	62
Mean (SD)	77.42 (21.57)
Absolute Change at Week 24	
n	62
Mean (SD)	10.22 (18.14)
Week 24 (MMRM)	
n	62
LS mean (SE)	77.42 (2.13)
95% CI of LS mean	(73.16, 81.68)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	10.22 (2.13)
95% CI of LS mean	(5.96, 14.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	9.86 (1.81)
95% CI of LS mean	(6.24, 13.47)
P-value	<0.0001

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	77.78 (20.95)
Week 4 (MMRM)	
n	10
LS mean (SE)	75.56 (4.33)
95% CI of LS mean	(65.42, 85.69)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-2.22 (4.33)
95% CI of LS mean	(-12.35, 7.91)
Week 8 (MMRM)	
n	10
LS mean (SE)	73.33 (5.26)
95% CI of LS mean	(61.30, 85.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	-4.44 (5.26)
95% CI of LS mean	(-16.47, 7.58)
Week 12 (MMRM)	
n	10
LS mean (SE)	74.44 (6.30)
95% CI of LS mean	(59.99, 88.90)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-3.33 (6.30)
95% CI of LS mean	(-17.79, 11.12)
Week 16 (MMRM)	
n	10
LS mean (SE)	73.33 (3.09)
95% CI of LS mean	(66.26, 80.40)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	-4.44 (3.09)
95% CI of LS mean	(-11.52, 2.63)
Week 24	
n	10
Mean (SD)	76.67 (22.50)
Absolute Change at Week 24	
n	10
Mean (SD)	-1.11 (21.24)
Week 24 (MMRM)	
n	10
LS mean (SE)	76.67 (7.11)
95% CI of LS mean	(60.22, 93.11)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	-1.11 (7.11)
95% CI of LS mean	(-17.56, 15.34)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	-2.78 (4.45)
95% CI of LS mean	(-13.23, 7.67)
P-value	0.5513

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	78.18 (12.15)
Week 4 (MMRM)	
n	44
LS mean (SE)	76.82 (1.79)
95% CI of LS mean	(73.21, 80.43)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	-1.36 (1.79)
95% CI of LS mean	(-4.97, 2.25)
Week 8 (MMRM)	
n	44
LS mean (SE)	76.82 (1.71)
95% CI of LS mean	(73.37, 80.27)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	-1.36 (1.71)
95% CI of LS mean	(-4.81, 2.09)
Week 12 (MMRM)	
n	43
LS mean (SE)	78.85 (1.46)
95% CI of LS mean	(75.89, 81.80)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	0.66 (1.46)
95% CI of LS mean	(-2.29, 3.62)
Week 16 (MMRM)	
n	44
LS mean (SE)	80.15 (1.79)
95% CI of LS mean	(76.53, 83.77)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	1.97 (1.79)
95% CI of LS mean	(-1.65, 5.59)
Week 24	
n	44
Mean (SD)	78.79 (12.88)
Absolute Change at Week 24	
n	44
Mean (SD)	0.61 (12.76)
Week 24 (MMRM)	
n	44
LS mean (SE)	78.79 (1.74)
95% CI of LS mean	(75.27, 82.30)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	0.61 (1.74)
95% CI of LS mean	(-2.91, 4.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	1.29 (1.42)
95% CI of LS mean	(-1.58, 4.15)
P-value	0.3694

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	74.71 (12.80)
Week 4 (MMRM)	
n	34
LS mean (SE)	73.14 (2.27)
95% CI of LS mean	(68.52, 77.75)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	-1.57 (2.27)
95% CI of LS mean	(-6.18, 3.04)
Week 8 (MMRM)	
n	34
LS mean (SE)	73.33 (1.32)
95% CI of LS mean	(70.65, 76.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	-1.37 (1.32)
95% CI of LS mean	(-4.05, 1.31)
Week 12 (MMRM)	
n	34
LS mean (SE)	75.88 (2.08)
95% CI of LS mean	(71.65, 80.12)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	1.18 (2.08)
95% CI of LS mean	(-3.06, 5.41)
Week 16 (MMRM)	
n	34
LS mean (SE)	76.67 (1.73)
95% CI of LS mean	(73.14, 80.20)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	1.96 (1.73)
95% CI of LS mean	(-1.57, 5.49)
Week 24	
n	34
Mean (SD)	71.96 (14.93)
Absolute Change at Week 24	
n	34
Mean (SD)	-2.75 (15.32)
Week 24 (MMRM)	
n	34
LS mean (SE)	71.96 (2.38)
95% CI of LS mean	(67.12, 76.80)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	-2.75 (2.38)
95% CI of LS mean	(-7.59, 2.10)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	-0.39 (1.76)
95% CI of LS mean	(-3.97, 3.19)
P-value	0.8250

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	75.60 (12.91)
Week 4 (MMRM)	
n	47
LS mean (SE)	75.18 (1.80)
95% CI of LS mean	(71.56, 78.80)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	-0.43 (1.80)
95% CI of LS mean	(-4.05, 3.19)
Week 8 (MMRM)	
n	47
LS mean (SE)	74.33 (1.39)
95% CI of LS mean	(71.53, 77.12)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	-1.28 (1.39)
95% CI of LS mean	(-4.07, 1.52)
Week 12 (MMRM)	
n	47
LS mean (SE)	76.03 (1.54)
95% CI of LS mean	(72.92, 79.14)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	0.43 (1.54)
95% CI of LS mean	(-2.68, 3.53)
Week 16 (MMRM)	
n	47
LS mean (SE)	79.15 (1.38)
95% CI of LS mean	(76.38, 81.92)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	3.55 (1.38)
95% CI of LS mean	(0.78, 6.32)
Week 24	
n	47
Mean (SD)	75.60 (12.99)
Absolute Change at Week 24	
n	47
Mean (SD)	0.00 (12.20)
Week 24 (MMRM)	
n	47
LS mean (SE)	75.60 (1.59)
95% CI of LS mean	(72.40, 78.81)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	0.00 (1.59)
95% CI of LS mean	(-3.21, 3.21)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	1.77 (1.18)
95% CI of LS mean	(-0.60, 4.15)
P-value	0.1401

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	78.28 (11.80)
Week 4 (MMRM)	
n	31
LS mean (SE)	75.27 (2.24)
95% CI of LS mean	(70.68, 79.86)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	-3.01 (2.24)
95% CI of LS mean	(-7.60, 1.58)
Week 8 (MMRM)	
n	31
LS mean (SE)	76.77 (1.88)
95% CI of LS mean	(72.92, 80.63)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	-1.51 (1.88)
95% CI of LS mean	(-5.36, 2.35)
Week 12 (MMRM)	
n	30
LS mean (SE)	79.91 (2.04)
95% CI of LS mean	(75.74, 84.09)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	1.63 (2.04)
95% CI of LS mean	(-2.54, 5.81)
Week 16 (MMRM)	
n	31
LS mean (SE)	77.85 (2.36)
95% CI of LS mean	(73.02, 82.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	-0.43 (2.36)
95% CI of LS mean	(-5.26, 4.40)
Week 24	
n	31
Mean (SD)	76.13 (15.94)
Absolute Change at Week 24	
n	31
Mean (SD)	-2.15 (16.37)
Week 24 (MMRM)	
n	31
LS mean (SE)	76.13 (2.75)
95% CI of LS mean	(70.51, 81.74)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	-2.15 (2.75)
95% CI of LS mean	(-7.77, 3.46)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	-1.29 (2.16)
95% CI of LS mean	(-5.71, 3.13)
P-value	0.5549

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	75.59 (12.07)
Week 4 (MMRM)	
n	62
LS mean (SE)	73.87 (1.41)
95% CI of LS mean	(71.04, 76.70)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	-1.72 (1.41)
95% CI of LS mean	(-4.55, 1.11)
Week 8 (MMRM)	
n	62
LS mean (SE)	74.41 (1.22)
95% CI of LS mean	(71.98, 76.84)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	-1.18 (1.22)
95% CI of LS mean	(-3.62, 1.25)
Week 12 (MMRM)	
n	61
LS mean (SE)	76.19 (1.32)
95% CI of LS mean	(73.55, 78.83)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	0.60 (1.32)
95% CI of LS mean	(-2.04, 3.24)
Week 16 (MMRM)	
n	62
LS mean (SE)	76.34 (1.30)
95% CI of LS mean	(73.74, 78.95)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	0.75 (1.30)
95% CI of LS mean	(-1.85, 3.36)
Week 24	
n	62
Mean (SD)	73.98 (13.43)
Absolute Change at Week 24	
n	62
Mean (SD)	-1.61 (14.32)
Week 24 (MMRM)	
n	62
LS mean (SE)	73.98 (1.59)
95% CI of LS mean	(70.79, 77.17)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	-1.61 (1.59)
95% CI of LS mean	(-4.80, 1.58)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	-0.43 (1.21)
95% CI of LS mean	(-2.86, 2.00)
P-value	0.7240

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	79.33 (12.75)
Week 4 (MMRM)	
n	10
LS mean (SE)	77.33 (5.81)
95% CI of LS mean	(64.15, 90.52)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	-2.00 (5.81)
95% CI of LS mean	(-15.19, 11.19)
Week 8 (MMRM)	
n	10
LS mean (SE)	79.33 (3.13)
95% CI of LS mean	(71.70, 86.97)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	0.00 (3.13)
95% CI of LS mean	(-7.63, 7.63)
Week 12 (MMRM)	
n	10
LS mean (SE)	82.00 (4.91)
95% CI of LS mean	(70.16, 93.84)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	2.67 (4.91)
95% CI of LS mean	(-9.17, 14.50)
Week 16 (MMRM)	
n	10
LS mean (SE)	87.33 (3.33)
95% CI of LS mean	(79.76, 94.91)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Zusatzanalysen zur Studie VX21-121-105

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	8.00 (3.33)
95% CI of LS mean	(0.42, 15.58)
Week 24	
n	10
Mean (SD)	81.33 (16.87)
Absolute Change at Week 24	
n	10
Mean (SD)	2.00 (13.35)
Week 24 (MMRM)	
n	10
LS mean (SE)	81.33 (4.46)
95% CI of LS mean	(71.05, 91.61)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	2.00 (4.46)
95% CI of LS mean	(-8.28, 12.28)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	5.00 (2.12)
95% CI of LS mean	(-0.19, 10.19)
P-value	0.0563

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Baseline	
n	44
Mean (SD)	70.45 (35.38)
Week 4 (MMRM)	
n	44
LS mean (SE)	70.45 (3.70)
95% CI of LS mean	(62.99, 77.92)
Absolute Change at Week 4 (MMRM)	
n	44
LS mean (SE)	0.00 (3.70)
95% CI of LS mean	(-7.46, 7.46)
Week 8 (MMRM)	
n	44
LS mean (SE)	78.03 (3.54)
95% CI of LS mean	(70.88, 85.18)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 8 (MMRM)	
n	44
LS mean (SE)	7.58 (3.54)
95% CI of LS mean	(0.43, 14.72)
Week 12 (MMRM)	
n	43
LS mean (SE)	75.82 (3.42)
95% CI of LS mean	(68.91, 82.74)
Absolute Change at Week 12 (MMRM)	
n	43
LS mean (SE)	5.37 (3.42)
95% CI of LS mean	(-1.54, 12.28)
Week 16 (MMRM)	
n	44
LS mean (SE)	75.00 (3.64)
95% CI of LS mean	(67.65, 82.35)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change at Week 16 (MMRM)	
n	44
LS mean (SE)	4.55 (3.64)
95% CI of LS mean	(-2.81, 11.90)
Week 24	
n	44
Mean (SD)	71.21 (35.65)
Absolute Change at Week 24	
n	44
Mean (SD)	0.76 (22.14)
Week 24 (MMRM)	
n	44
LS mean (SE)	71.21 (3.27)
95% CI of LS mean	(64.61, 77.82)
Absolute Change at Week 24 (MMRM)	
n	44
LS mean (SE)	0.76 (3.27)
95% CI of LS mean	(-5.85, 7.36)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Male

	VNZ/TEZ/D-IVA N = 44
Absolute Change through Week 24 (MMRM)	
n	44
LS mean (SE)	2.65 (2.79)
95% CI of LS mean	(-2.99, 8.29)
P-value	0.3478

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Baseline	
n	34
Mean (SD)	67.65 (36.22)
Week 4 (MMRM)	
n	34
LS mean (SE)	70.59 (4.61)
95% CI of LS mean	(61.18, 80.00)
Absolute Change at Week 4 (MMRM)	
n	34
LS mean (SE)	2.94 (4.61)
95% CI of LS mean	(-6.47, 12.35)
Week 8 (MMRM)	
n	34
LS mean (SE)	71.57 (4.03)
95% CI of LS mean	(63.36, 79.78)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 8 (MMRM)	
n	34
LS mean (SE)	3.92 (4.03)
95% CI of LS mean	(-4.29, 12.13)
Week 12 (MMRM)	
n	34
LS mean (SE)	70.59 (4.16)
95% CI of LS mean	(62.10, 79.07)
Absolute Change at Week 12 (MMRM)	
n	34
LS mean (SE)	2.94 (4.16)
95% CI of LS mean	(-5.54, 11.42)
Week 16 (MMRM)	
n	34
LS mean (SE)	73.53 (4.00)
95% CI of LS mean	(65.38, 81.67)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change at Week 16 (MMRM)	
n	34
LS mean (SE)	5.88 (4.00)
95% CI of LS mean	(-2.26, 14.03)
Week 24	
n	34
Mean (SD)	78.43 (31.66)
Absolute Change at Week 24	
n	34
Mean (SD)	10.78 (33.56)
Week 24 (MMRM)	
n	34
LS mean (SE)	78.43 (4.75)
95% CI of LS mean	(68.75, 88.11)
Absolute Change at Week 24 (MMRM)	
n	34
LS mean (SE)	10.78 (4.75)
95% CI of LS mean	(1.10, 20.47)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Sex = Female

	VNZ/TEZ/D-IVA N = 34
Absolute Change through Week 24 (MMRM)	
n	34
LS mean (SE)	8.33 (4.03)
95% CI of LS mean	(0.13, 16.54)
P-value	0.0468

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Baseline	
n	47
Mean (SD)	71.63 (35.43)
Week 4 (MMRM)	
n	47
LS mean (SE)	72.34 (4.10)
95% CI of LS mean	(64.09, 80.59)
Absolute Change at Week 4 (MMRM)	
n	47
LS mean (SE)	0.71 (4.10)
95% CI of LS mean	(-7.54, 8.96)
Week 8 (MMRM)	
n	47
LS mean (SE)	79.43 (3.40)
95% CI of LS mean	(72.57, 86.29)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 8 (MMRM)	
n	47
LS mean (SE)	7.80 (3.40)
95% CI of LS mean	(0.94, 14.66)
Week 12 (MMRM)	
n	47
LS mean (SE)	76.60 (3.55)
95% CI of LS mean	(69.44, 83.75)
Absolute Change at Week 12 (MMRM)	
n	47
LS mean (SE)	4.96 (3.55)
95% CI of LS mean	(-2.19, 12.12)
Week 16 (MMRM)	
n	47
LS mean (SE)	80.14 (3.41)
95% CI of LS mean	(73.26, 87.02)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change at Week 16 (MMRM)	
n	47
LS mean (SE)	8.51 (3.41)
95% CI of LS mean	(1.63, 15.39)
Week 24	
n	47
Mean (SD)	80.14 (29.21)
Absolute Change at Week 24	
n	47
Mean (SD)	8.51 (29.87)
Week 24 (MMRM)	
n	47
LS mean (SE)	80.14 (3.50)
95% CI of LS mean	(73.10, 87.18)
Absolute Change at Week 24 (MMRM)	
n	47
LS mean (SE)	8.51 (3.50)
95% CI of LS mean	(1.47, 15.55)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = North America

	VNZ/TEZ/D-IVA N = 47
Absolute Change through Week 24 (MMRM)	
n	47
LS mean (SE)	8.51 (2.98)
95% CI of LS mean	(2.51, 14.51)
P-value	0.0064

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24
by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Baseline	
n	31
Mean (SD)	65.59 (35.99)
Week 4 (MMRM)	
n	31
LS mean (SE)	67.74 (3.35)
95% CI of LS mean	(60.89, 74.60)
Absolute Change at Week 4 (MMRM)	
n	31
LS mean (SE)	2.15 (3.35)
95% CI of LS mean	(-4.70, 9.01)
Week 8 (MMRM)	
n	31
LS mean (SE)	68.82 (3.99)
95% CI of LS mean	(60.64, 76.99)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 8 (MMRM)	
n	31
LS mean (SE)	3.23 (3.99)
95% CI of LS mean	(-4.95, 11.40)
Week 12 (MMRM)	
n	30
LS mean (SE)	68.88 (4.33)
95% CI of LS mean	(60.02, 77.73)
Absolute Change at Week 12 (MMRM)	
n	30
LS mean (SE)	3.28 (4.33)
95% CI of LS mean	(-5.57, 12.14)
Week 16 (MMRM)	
n	31
LS mean (SE)	65.59 (4.30)
95% CI of LS mean	(56.76, 74.42)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change at Week 16 (MMRM)	
n	31
LS mean (SE)	0.00 (4.30)
95% CI of LS mean	(-8.83, 8.83)
Week 24	
n	31
Mean (SD)	65.59 (38.95)
Absolute Change at Week 24	
n	31
Mean (SD)	0.00 (24.34)
Week 24 (MMRM)	
n	31
LS mean (SE)	65.59 (4.31)
95% CI of LS mean	(56.78, 74.40)
Absolute Change at Week 24 (MMRM)	
n	31
LS mean (SE)	0.00 (4.31)
95% CI of LS mean	(-8.81, 8.81)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
Region = Rest of World

	VNZ/TEZ/D-IVA N = 31
Absolute Change through Week 24 (MMRM)	
n	31
LS mean (SE)	0.00 (3.63)
95% CI of LS mean	(-7.43, 7.43)
P-value	>0.9999

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Baseline	
n	62
Mean (SD)	65.05 (37.90)
Week 4 (MMRM)	
n	62
LS mean (SE)	68.28 (3.16)
95% CI of LS mean	(61.96, 74.60)
Absolute Change at Week 4 (MMRM)	
n	62
LS mean (SE)	3.23 (3.16)
95% CI of LS mean	(-3.10, 9.55)
Week 8 (MMRM)	
n	62
LS mean (SE)	72.58 (3.13)
95% CI of LS mean	(66.31, 78.85)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 8 (MMRM)	
n	62
LS mean (SE)	7.53 (3.13)
95% CI of LS mean	(1.25, 13.80)
Week 12 (MMRM)	
n	61
LS mean (SE)	71.50 (3.07)
95% CI of LS mean	(65.36, 77.64)
Absolute Change at Week 12 (MMRM)	
n	61
LS mean (SE)	6.44 (3.07)
95% CI of LS mean	(0.30, 12.59)
Week 16 (MMRM)	
n	62
LS mean (SE)	70.97 (3.24)
95% CI of LS mean	(64.49, 77.45)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change at Week 16 (MMRM)	
n	62
LS mean (SE)	5.91 (3.24)
95% CI of LS mean	(-0.57, 12.39)
Week 24	
n	62
Mean (SD)	70.43 (36.27)
Absolute Change at Week 24	
n	62
Mean (SD)	5.38 (29.69)
Week 24 (MMRM)	
n	62
LS mean (SE)	70.43 (3.38)
95% CI of LS mean	(63.67, 77.19)
Absolute Change at Week 24 (MMRM)	
n	62
LS mean (SE)	5.38 (3.38)
95% CI of LS mean	(-1.39, 12.14)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62
Absolute Change through Week 24 (MMRM)	
n	62
LS mean (SE)	5.65 (2.87)
95% CI of LS mean	(-0.10, 11.39)
P-value	0.0540

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Baseline	
n	10
Mean (SD)	80.00 (17.21)
Week 4 (MMRM)	
n	10
LS mean (SE)	80.00 (9.31)
95% CI of LS mean	(58.85, 101.15)
Absolute Change at Week 4 (MMRM)	
n	10
LS mean (SE)	0.00 (9.31)
95% CI of LS mean	(-21.15, 21.15)
Week 8 (MMRM)	
n	10
LS mean (SE)	86.67 (5.39)
95% CI of LS mean	(74.43, 98.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 8 (MMRM)	
n	10
LS mean (SE)	6.67 (5.39)
95% CI of LS mean	(-5.57, 18.90)
Week 12 (MMRM)	
n	10
LS mean (SE)	76.67 (8.84)
95% CI of LS mean	(56.59, 96.74)
Absolute Change at Week 12 (MMRM)	
n	10
LS mean (SE)	-3.33 (8.84)
95% CI of LS mean	(-23.41, 16.74)
Week 16 (MMRM)	
n	10
LS mean (SE)	86.67 (4.78)
95% CI of LS mean	(75.43, 97.90)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change at Week 16 (MMRM)	
n	10
LS mean (SE)	6.67 (4.78)
95% CI of LS mean	(-4.57, 17.90)
Week 24	
n	10
Mean (SD)	90.00 (16.10)
Absolute Change at Week 24	
n	10
Mean (SD)	10.00 (16.10)
Week 24 (MMRM)	
n	10
LS mean (SE)	90.00 (4.26)
95% CI of LS mean	(80.32, 99.68)
Absolute Change at Week 24 (MMRM)	
n	10
LS mean (SE)	10.00 (4.26)
95% CI of LS mean	(0.32, 19.68)

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.10.4.2
Study VX21-121-105: MMRM Analysis of Absolute Change from Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) through Week 24 by Subgroups
Full Analysis Set

Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10
Absolute Change through Week 24 (MMRM)	
n	10
LS mean (SE)	8.33 (3.39)
95% CI of LS mean	(0.28, 16.39)
P-value	0.0444

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- CI: Confidence interval; LS Mean: Least Squares Mean; SD: Standard deviation; SE: Standard error.
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Treatment effect through Week 24 is estimated by averaging Weeks 16 and 24.
- N/C: model does not converge.

Table 3.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Any Pulmonary Exacerbation	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 3.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring Hospitalization	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 3.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring IV Antibiotic Therapy	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 3.2.2.13.1
Study VX21-121-105: Subgroup Factor Test for
Pulmonary Exacerbations during the PEx Analysis Period
Full Analysis Set

Type of Pulmonary Exacerbations Subgroup	P-value for Subgroup Factor[1]
Pulmonary Exacerbation Requiring Hospitalization or IV Antibiotic Therapy	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on negative binomial regression with the number of events as the dependent variable, corresponding subgroup factor as a fixed effect, and log(PEx analysis period in days/336) as an offset.

Table 3.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.2.13.2
Study VX21-121-105: Summary of Pulmonary Exacerbations during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Total number of days = sum of the individual duration (actual number of days) of the PEx analysis period across all subjects. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days of the PEx analysis period.

Table 3.2.2.14.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation during the PEx Analysis Period
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 3.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.14.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.15.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 3.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.15.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring Hospitalization during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.16.1
Study VX21-121-105: Subgroup Factor Test for
Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period
Full Analysis Set

Subgroup	P-value for Subgroup Factor[1]
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	-

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- P-values are reported for each subgroup factor only when Subgroup Criteria are fulfilled. If not, display '-'.
- [1] P-value based on Log-rank test.

Table 3.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Table 3.2.2.16.2
Study VX21-121-105: Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics during the PEx Analysis Period by Subgroups
Full Analysis Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for time-to-event endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.
- Subjects without any protocol-defined pulmonary exacerbation during the PEx analysis period were censored at the PEx analysis period end date.

Zusatzanalysen zur Studie VX21-121-105

Table 3.3.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any TEAEs	72 (92.31)
Respiratory, thoracic and mediastinal disorders	51 (65.38)
Cough	36 (46.15)
Oropharyngeal pain	13 (16.67)
Nasal congestion	9 (11.54)
Rhinorrhoea	9 (11.54)
Infections and infestations	35 (44.87)
Gastrointestinal disorders	25 (32.05)
Abdominal pain	9 (11.54)
Vomiting	8 (10.26)
General disorders and administration site conditions	22 (28.21)
Pyrexia	16 (20.51)
Investigations	22 (28.21)
Nervous system disorders	17 (21.79)
Headache	14 (17.95)
Injury, poisoning and procedural complications	11 (14.10)
Skin and subcutaneous tissue disorders	9 (11.54)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any TEAEs	72 (92.31)
Grade 1/Mild	39 (50.00)
Grade 2/Moderate	33 (42.31)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Respiratory, thoracic and mediastinal disorders	51 (65.38)
Grade 1/Mild	35 (44.87)
Grade 2/Moderate	16 (20.51)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Cough	36 (46.15)
Grade 1/Mild	24 (30.77)
Grade 2/Moderate	12 (15.38)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Oropharyngeal pain	13 (16.67)
Grade 1/Mild	13 (16.67)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 78 n (%)
Nasal congestion	9 (11.54)
Grade 1/Mild	9 (11.54)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Rhinorrhoea	9 (11.54)
Grade 1/Mild	9 (11.54)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0
Infections and infestations	35 (44.87)
Grade 1/Mild	22 (28.21)
Grade 2/Moderate	13 (16.67)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Gastrointestinal disorders	25 (32.05)
Grade 1/Mild	21 (26.92)
Grade 2/Moderate	4 (5.13)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 78 n (%)
Abdominal pain	9 (11.54)
Grade 1/Mild	8 (10.26)
Grade 2/Moderate	1 (1.28)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Vomiting	8 (10.26)
Grade 1/Mild	6 (7.69)
Grade 2/Moderate	2 (2.56)
Grade 3/Severe	0
Grade 4/Life Threatening	0
General disorders and administration site conditions	22 (28.21)
Grade 1/Mild	19 (24.36)
Grade 2/Moderate	3 (3.85)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Pyrexia	16 (20.51)
Grade 1/Mild	14 (17.95)
Grade 2/Moderate	2 (2.56)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 78 n (%)
Investigations	22 (28.21)
Grade 1/Mild	17 (21.79)
Grade 2/Moderate	5 (6.41)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Nervous system disorders	17 (21.79)
Grade 1/Mild	13 (16.67)
Grade 2/Moderate	4 (5.13)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Headache	14 (17.95)
Grade 1/Mild	12 (15.38)
Grade 2/Moderate	2 (2.56)
Grade 3/Severe	0
Grade 4/Life Threatening	0
Injury, poisoning and procedural complications	11 (14.10)
Grade 1/Mild	10 (12.82)
Grade 2/Moderate	1 (1.28)
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.1.1
Study VX21-121-105: Summary of TEAEs by SOC and PT, and by Maximum Severity
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 78 n (%)
Skin and subcutaneous tissue disorders	9 (11.54)
Grade 1/Mild	9 (11.54)
Grade 2/Moderate	0
Grade 3/Severe	0
Grade 4/Life Threatening	0

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once with the maximum severity in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 10% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Zusatzanalysen zur Studie VX21-121-105

Table 3.3.1.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 78 n (%)

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Zusatzanalysen zur Studie VX21-121-105

Table 3.3.1.3
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any Serious TEAEs	5 (6.41)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- SOCs and PTs are reported only if corresponding events are either 1) occurring in at least 5% of patients in any treatment group; OR 2) occurring in at least 10 patients in the total study population and also occurring in at least 1% of patients in any treatment group.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Zusatzanalysen zur Studie VX21-121-105

Table 3.3.1.4
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any TEAEs leading to treatment discontinuation	1 (1.28)
General disorders and administration site conditions	1 (1.28)
Fatigue	1 (1.28)
Respiratory, thoracic and mediastinal disorders	1 (1.28)
Cough	1 (1.28)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.1.11
Study VX21-121-105: Summary of Death
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.

Table 3.3.1.12
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

	VNZ/TEZ/D-IVA N = 78 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	13 (16.67)
Subjects with non-severe events (Maximum Grade 1/2)	13 (16.67)
Subjects with severe events (Maximum Grade 3/4/5)	0
Subjects with serious events	2 (2.56)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.

Table 3.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Subjects with any TEAEs	
Sex (Male vs. Female)	0.7417
Region (North America vs. Rest of the World)	0.0384
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.3519
Respiratory, thoracic and mediastinal disorders	
Sex (Male vs. Female)	0.5547
Region (North America vs. Rest of the World)	0.3999
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.3351

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Cough	
Sex (Male vs. Female)	0.5492
Region (North America vs. Rest of the World)	0.5439
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.4374
Oropharyngeal pain	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.4754

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Infections and infestations	
Sex (Male vs. Female)	0.1349
Region (North America vs. Rest of the World)	0.1506
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.2436
Gastrointestinal disorders	
Sex (Male vs. Female)	0.9600
Region (North America vs. Rest of the World)	0.5978
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.5560

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
General disorders and administration site conditions	
Sex (Male vs. Female)	0.4742
Region (North America vs. Rest of the World)	0.1583
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9502
Pyrexia	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	0.4362
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.9443

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Investigations	
Sex (Male vs. Female)	0.7647
Region (North America vs. Rest of the World)	0.5183
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.0208
Nervous system disorders	
Sex (Male vs. Female)	0.0111
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.1451

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.1
Study VX21-121-105: Subgroup Factor Test for TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]
Headache	
Sex (Male vs. Female)	0.0204
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.2900
Injury, poisoning and procedural complications	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.6171

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test. If the overall rate or any SOC/PT level rate is 100%, display "NA" because Chi-square statistics are undefined in this case.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 44 n (%)
Subjects with any TEAEs	41 (93.18)
Respiratory, thoracic and mediastinal disorders	30 (68.18)
Cough	19 (43.18)
Infections and infestations	23 (52.27)
Gastrointestinal disorders	14 (31.82)
Investigations	13 (29.55)
General disorders and administration site conditions	11 (25.00)
Nervous system disorders	5 (11.36)
Headache	4 (9.09)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 34 n (%)
Subjects with any TEAEs	31 (91.18)
Respiratory, thoracic and mediastinal disorders	21 (61.76)
Cough	17 (50.00)
Infections and infestations	12 (35.29)
Nervous system disorders	12 (35.29)
Headache	10 (29.41)
Gastrointestinal disorders	11 (32.35)
General disorders and administration site conditions	11 (32.35)
Investigations	9 (26.47)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)
Subjects with any TEAEs	41 (87.23)
Respiratory, thoracic and mediastinal disorders	29 (61.70)
Cough	23 (48.94)
Infections and infestations	18 (38.30)
General disorders and administration site conditions	16 (34.04)
Pyrexia	11 (23.40)
Gastrointestinal disorders	14 (29.79)
Investigations	12 (25.53)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 31 n (%)
Subjects with any TEAEs	31 (100.00)
Respiratory, thoracic and mediastinal disorders	22 (70.97)
Cough	13 (41.94)
Infections and infestations	17 (54.84)
Gastrointestinal disorders	11 (35.48)
Investigations	10 (32.26)
General disorders and administration site conditions	6 (19.35)
Pyrexia	5 (16.13)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 62 n (%)
Subjects with any TEAEs	57 (91.94)
Respiratory, thoracic and mediastinal disorders	40 (64.52)
Cough	29 (46.77)
Oropharyngeal pain	12 (19.35)
Infections and infestations	25 (40.32)
Gastrointestinal disorders	19 (30.65)
General disorders and administration site conditions	18 (29.03)
Pyrexia	13 (20.97)
Investigations	15 (24.19)
Nervous system disorders	12 (19.35)
Headache	10 (16.13)
Injury, poisoning and procedural complications	10 (16.13)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.1.2
Study VX21-121-105: Summary of TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 10 n (%)
Subjects with any TEAEs	10 (100.00)
Respiratory, thoracic and mediastinal disorders	8 (80.00)
Cough	6 (60.00)
Oropharyngeal pain	1 (10.00)
Infections and infestations	6 (60.00)
Investigations	6 (60.00)
Gastrointestinal disorders	4 (40.00)
Nervous system disorders	4 (40.00)
Headache	3 (30.00)
General disorders and administration site conditions	3 (30.00)
Pyrexia	2 (20.00)
Injury, poisoning and procedural complications	1 (10.00)

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.1
Study VX21-121-105: Subgroup Factor Test for Grade 3/4/5 TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 62 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.2.2
Study VX21-121-105: Summary of Grade 3/4/5 TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 10 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Zusatzanalysen zur Studie VX21-121-105

Table 3.3.2.3.1
Study VX21-121-105: Subgroup Factor Test for Serious TEAEs by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 62 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.3.2
Study VX21-121-105: Summary of Serious TEAEs by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 10 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.1
Study VX21-121-105: Subgroup Factor Test for TEAEs Leading to Treatment Discontinuation by SOC and PT
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set

System Organ Class Preferred Term Subgroup	P-value[1]

No data met the criteria for this table.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, p-value will be reported if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Male

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Sex = Female

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = North America

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
Region = Rest of the World

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline <7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 62 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.4.2
Study VX21-121-105: Summary of TEAEs Leading to Treatment Discontinuation by SOC and PT by Each Applicable Subgroup Factor
(Excluding Infective Pulmonary Exacerbation of Cystic Fibrosis)
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

System Organ Class Preferred Term	VNZ/TEZ/D-IVA N = 10 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup analyses are performed at SOC/PT level only if 1) Respective analysis on the study level is done; 2) there are at least 10 subjects in each subgroup (per factor); and 3) there are at least 10 subjects with events in at least one of the subgroups (per factor). For the overall rate, it is performed if conditions (2) and (3) are met.
- Table is sorted in descending order of frequency of the VNZ/TEZ/D-IVA column by System Organ Class, and by Preferred Term within each System Organ Class.

Table 3.3.2.11.1
Study VX21-121-105: Subgroup Factor Test for Death
Safety Set

Subgroup	P-value[1]

No data met the criteria for this table.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.11.2
Study VX21-121-105: Summary of Death by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)

Subgroup criteria are not met for this subgroup factor.

- Include death during Treatment-emergent Period for the Treatment Period from two sources: 1) treatment/study discontinuation due to death; 2) TEAEs leading to death.
- Subgroup Analysis will be performed if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Zusatzanalysen zur Studie VX21-121-105

Table 3.3.2.12.1
Study VX21-121-105: Subgroup Factor Test for Treatment-emergent Infective Pulmonary Exacerbation Events
Safety Set

Subgroup	P-value[1]
Subjects with non-severe events (Maximum Grade 1/2)	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.7605
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	
Sex (Male vs. Female)	-
Region (North America vs. Rest of the World)	-
$LCI_{2.5}$ at baseline (<7.5 vs. ≥7.5)	0.7605

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- [1] P-value based on Chi-square test.
- P-values are reported only if 1) there are at least 10 subjects in each subgroup (per factor); and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set
Sex = Male

	VNZ/TEZ/D-IVA N = 44 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set
Sex = Female

	VNZ/TEZ/D-IVA N = 34 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set
Region = North America

	VNZ/TEZ/D-IVA N = 47 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set
Region = Rest of the World

	VNZ/TEZ/D-IVA N = 31 n (%)

Subgroup criteria are not met for this subgroup factor.

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline <7.5

	VNZ/TEZ/D-IVA N = 62 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	10 (16.13)
Subjects with non-severe events (Maximum Grade 1/2)	10 (16.13)
Subjects with severe events (Maximum Grade 3/4/5)	-
Subjects with serious events	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 3.3.2.12.2
Study VX21-121-105: Summary of Treatment-emergent Infective Pulmonary Exacerbation Events by Each Applicable Subgroup Factor
Safety Set
$LCI_{2.5}$ at baseline ≥7.5

	VNZ/TEZ/D-IVA N = 10 n (%)
Subjects with any Treatment-emergent Infective Pulmonary Exacerbation Events	2 (20.00)
Subjects with non-severe events (Maximum Grade 1/2)	2 (20.00)
Subjects with severe events (Maximum Grade 3/4/5)	-
Subjects with serious events	-

- MedDRA version 26.1.
- A subject with multiple events within a category is counted only once in that category.
- Subgroup Analysis will be performed only if 1) there are at least 10 subjects in each subgroup (per factor), and 2) there are at least 10 subjects with events in at least one of the subgroups (per factor).

Table 14.2.5.1.1b1
Summary of CFQ-R Respiratory Domain Score (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	75
	Mean (SD)	84.8 (16.1)
	Median	91.7
	Min, max	16.7, 100.0
Week 4	n	75
	Mean (SD)	85.4 (15.9)
	Median	91.7
	Min, max	25.0, 100.0
Change at Week 4	n	75
	Mean (SD)	0.7 (17.5)
	Median	0.0
	Min, max	-75.0, 58.3
Week 8	n	75
	Mean (SD)	86.4 (16.0)
	Median	91.7
	Min, max	41.7, 100.0
Change at Week 8	n	75
	Mean (SD)	1.7 (18.4)
	Median	0.0
	Min, max	-50.0, 66.7

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.1.1b1
Summary of CFQ-R Respiratory Domain Score (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	74
	Mean (SD)	90.3 (11.7)
	Median	91.7
	Min, max	41.7, 100.0
Change at Week 12	n	74
	Mean (SD)	5.6 (16.8)
	Median	8.3
	Min, max	-33.3, 75.0
Week 16	n	75
	Mean (SD)	90.9 (12.0)
	Median	91.7
	Min, max	41.7, 100.0
Change at Week 16	n	75
	Mean (SD)	6.1 (17.1)
	Median	8.3
	Min, max	-41.7, 75.0
Week 24	n	78
	Mean (SD)	85.8 (15.6)
	Median	91.7
	Min, max	33.3, 100.0
Change at Week 24	n	75
	Mean (SD)	1.8 (18.7)
	Median	0.0
	Min, max	-50.0, 75.0

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.4b1
Summary of CFQ-R Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	78
	Mean (SD)	87.4 (15.8)
	Median	93.9
	Min, max	16.7, 100.0
Week 4	n	78
	Mean (SD)	84.6 (17.6)
	Median	88.9
	Min, max	27.8, 100.0
Change at Week 4	n	78
	Mean (SD)	-2.8 (21.9)
	Median	0.0
	Min, max	-72.2, 72.2
Week 8	n	78
	Mean (SD)	86.8 (16.7)
	Median	94.4
	Min, max	33.3, 100.0
Change at Week 8	n	78
	Mean (SD)	-0.6 (19.5)
	Median	0.0
	Min, max	-55.6, 72.2

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.4b1
Summary of CFQ-R Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	77
	Mean (SD)	92.1 (11.3)
	Median	94.4
	Min, max	38.9, 100.0
Change at Week 12	n	77
	Mean (SD)	4.8 (17.4)
	Median	0.0
	Min, max	-44.4, 83.3
Week 16	n	78
	Mean (SD)	91.4 (13.7)
	Median	100.0
	Min, max	20.0, 100.0
Change at Week 16	n	78
	Mean (SD)	4.0 (18.7)
	Median	0.0
	Min, max	-63.3, 83.3
Week 24	n	78
	Mean (SD)	87.0 (16.1)
	Median	94.4
	Min, max	33.3, 100.0
Change at Week 24	n	78
	Mean (SD)	-0.4 (21.0)
	Median	0.0
	Min, max	-55.6, 77.8

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Physical

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	75
	Mean (SD)	87.3 (13.0)
	Median	88.9
	Min, max	50.0, 100.0
Week 4	n	75
	Mean (SD)	87.0 (15.0)
	Median	94.4
	Min, max	38.9, 100.0
Change at Week 4	n	75
	Mean (SD)	-0.3 (12.5)
	Median	0.0
	Min, max	-33.3, 33.3
Week 8	n	75
	Mean (SD)	85.5 (18.1)
	Median	94.4
	Min, max	27.8, 100.0
Change at Week 8	n	75
	Mean (SD)	-1.7 (15.8)
	Median	0.0
	Min, max	-66.7, 27.8

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Physical

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	74
	Mean (SD)	86.3 (16.8)
	Median	91.7
	Min, max	22.2, 100.0
Change at Week 12	n	74
	Mean (SD)	-1.1 (17.3)
	Median	0.0
	Min, max	-77.8, 33.3
Week 16	n	75
	Mean (SD)	88.5 (16.1)
	Median	100.0
	Min, max	38.9, 100.0
Change at Week 16	n	75
	Mean (SD)	1.3 (15.6)
	Median	0.0
	Min, max	-38.9, 27.8
Week 24	n	78
	Mean (SD)	90.4 (14.4)
	Median	97.2
	Min, max	16.7, 100.0
Change at Week 24	n	75
	Mean (SD)	3.3 (14.3)
	Median	0.0
	Min, max	-66.7, 27.8

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Emotion

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	75
	Mean (SD)	76.5 (14.7)
	Median	79.2
	Min, max	45.8, 100.0
Week 4	n	75
	Mean (SD)	76.5 (16.8)
	Median	79.2
	Min, max	41.7, 100.0
Change at Week 4	n	75
	Mean (SD)	0.0 (13.3)
	Median	0.0
	Min, max	-41.7, 29.2
Week 8	n	75
	Mean (SD)	77.9 (16.0)
	Median	79.2
	Min, max	29.2, 100.0
Change at Week 8	n	75
	Mean (SD)	1.4 (13.7)
	Median	0.0
	Min, max	-37.5, 29.2

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Emotion

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	74
	Mean (SD)	79.3 (16.3)
	Median	83.3
	Min, max	33.3, 100.0
Change at Week 12	n	74
	Mean (SD)	3.0 (15.2)
	Median	4.2
	Min, max	-45.8, 33.3
Week 16	n	75
	Mean (SD)	80.2 (17.3)
	Median	83.3
	Min, max	29.2, 100.0
Change at Week 16	n	75
	Mean (SD)	3.7 (15.2)
	Median	4.2
	Min, max	-54.2, 33.3
Week 24	n	78
	Mean (SD)	79.8 (15.0)
	Median	83.3
	Min, max	45.8, 100.0
Change at Week 24	n	75
	Mean (SD)	3.8 (12.4)
	Median	4.2
	Min, max	-33.3, 29.2

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Body

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	75
	Mean (SD)	82.7 (23.5)
	Median	100.0
	Min, max	0.0, 100.0
Week 4	n	75
	Mean (SD)	84.9 (21.7)
	Median	100.0
	Min, max	33.3, 100.0
Change at Week 4	n	75
	Mean (SD)	2.2 (22.1)
	Median	0.0
	Min, max	-66.7, 100.0
Week 8	n	75
	Mean (SD)	87.6 (20.3)
	Median	100.0
	Min, max	0.0, 100.0
Change at Week 8	n	75
	Mean (SD)	4.9 (21.6)
	Median	0.0
	Min, max	-44.4, 88.9

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Body

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	74
	Mean (SD)	88.4 (17.0)
	Median	100.0
	Min, max	33.3, 100.0
Change at Week 12	n	74
	Mean (SD)	6.0 (21.5)
	Median	0.0
	Min, max	-44.4, 88.9
Week 16	n	75
	Mean (SD)	91.3 (14.8)
	Median	100.0
	Min, max	33.3, 100.0
Change at Week 16	n	75
	Mean (SD)	8.6 (20.7)
	Median	0.0
	Min, max	-33.3, 100.0
Week 24	n	78
	Mean (SD)	88.0 (20.9)
	Median	100.0
	Min, max	0.0, 100.0
Change at Week 24	n	75
	Mean (SD)	5.6 (24.2)
	Median	0.0
	Min, max	-88.9, 100.0

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Eat

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	75
	Mean (SD)	81.5 (21.4)
	Median	88.9
	Min, max	11.1, 100.0
Week 4	n	75
	Mean (SD)	81.8 (23.8)
	Median	88.9
	Min, max	11.1, 100.0
Change at Week 4	n	75
	Mean (SD)	0.3 (18.3)
	Median	0.0
	Min, max	-55.6, 66.7
Week 8	n	75
	Mean (SD)	79.9 (25.6)
	Median	88.9
	Min, max	0.0, 100.0
Change at Week 8	n	75
	Mean (SD)	-1.6 (19.3)
	Median	0.0
	Min, max	-88.9, 33.3

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Eat

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	74
	Mean (SD)	83.2 (23.1)
	Median	88.9
	Min, max	0.0, 100.0
Change at Week 12	n	74
	Mean (SD)	1.8 (21.2)
	Median	0.0
	Min, max	-66.7, 66.7
Week 16	n	75
	Mean (SD)	84.4 (23.2)
	Median	100.0
	Min, max	0.0, 100.0
Change at Week 16	n	75
	Mean (SD)	3.0 (20.4)
	Median	0.0
	Min, max	-88.9, 66.7
Week 24	n	78
	Mean (SD)	88.9 (18.2)
	Median	100.0
	Min, max	22.2, 100.0
Change at Week 24	n	75
	Mean (SD)	7.3 (17.2)
	Median	0.0
	Min, max	-33.3, 55.6

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Treatment Burden

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	75
	Mean (SD)	76.4 (21.2)
	Median	77.8
	Min, max	33.3, 100.0
Week 4	n	75
	Mean (SD)	79.1 (20.3)
	Median	77.8
	Min, max	33.3, 100.0
Change at Week 4	n	75
	Mean (SD)	2.7 (19.2)
	Median	0.0
	Min, max	-44.4, 55.6
Week 8	n	75
	Mean (SD)	79.6 (21.4)
	Median	88.9
	Min, max	22.2, 100.0
Change at Week 8	n	75
	Mean (SD)	3.3 (17.4)
	Median	0.0
	Min, max	-55.6, 44.4

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Treatment Burden

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	74
	Mean (SD)	80.6 (21.9)
	Median	88.9
	Min, max	11.1, 100.0
Change at Week 12	n	74
	Mean (SD)	4.6 (17.8)
	Median	0.0
	Min, max	-33.3, 55.6
Week 16	n	75
	Mean (SD)	79.6 (25.4)
	Median	88.9
	Min, max	0.0, 100.0
Change at Week 16	n	75
	Mean (SD)	3.2 (21.9)
	Median	0.0
	Min, max	-66.7, 55.6
Week 24	n	78
	Mean (SD)	81.8 (21.3)
	Median	88.9
	Min, max	22.2, 100.0
Change at Week 24	n	75
	Mean (SD)	5.4 (19.8)
	Median	0.0
	Min, max	-77.8, 55.6

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Digestion

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	74
	Mean (SD)	79.7 (21.2)
	Median	66.7
	Min, max	33.3, 100.0
Week 4	n	75
	Mean (SD)	77.8 (28.1)
	Median	100.0
	Min, max	0.0, 100.0
Change at Week 4	n	74
	Mean (SD)	-2.3 (28.8)
	Median	0.0
	Min, max	-100.0, 66.7
Week 8	n	75
	Mean (SD)	80.0 (25.1)
	Median	100.0
	Min, max	0.0, 100.0
Change at Week 8	n	74
	Mean (SD)	0.0 (25.9)
	Median	0.0
	Min, max	-66.7, 66.7

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Digestion

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	74
	Mean (SD)	80.2 (20.6)
	Median	66.7
	Min, max	33.3, 100.0
Change at Week 12	n	73
	Mean (SD)	0.5 (22.6)
	Median	0.0
	Min, max	-66.7, 66.7
Week 16	n	75
	Mean (SD)	84.0 (22.2)
	Median	100.0
	Min, max	33.3, 100.0
Change at Week 16	n	74
	Mean (SD)	4.1 (25.3)
	Median	0.0
	Min, max	-33.3, 66.7
Week 24	n	78
	Mean (SD)	84.6 (21.9)
	Median	100.0
	Min, max	33.3, 100.0
Change at Week 24	n	74
	Mean (SD)	5.0 (26.3)
	Median	0.0
	Min, max	-33.3, 66.7

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Social

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	75
	Mean (SD)	67.0 (19.2)
	Median	66.7
	Min, max	0.0, 100.0
Week 4	n	75
	Mean (SD)	68.1 (17.6)
	Median	71.4
	Min, max	19.0, 100.0
Change at Week 4	n	75
	Mean (SD)	1.1 (15.5)
	Median	0.0
	Min, max	-38.1, 38.1
Week 8	n	75
	Mean (SD)	69.0 (17.4)
	Median	71.4
	Min, max	23.8, 100.0
Change at Week 8	n	75
	Mean (SD)	2.0 (19.7)
	Median	0.0
	Min, max	-57.1, 100.0

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.5b1
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit
Full Analysis Set

Social

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	74
	Mean (SD)	72.1 (17.0)
	Median	73.8
	Min, max	33.3, 100.0
Change at Week 12	n	74
	Mean (SD)	5.3 (17.9)
	Median	4.8
	Min, max	-33.3, 61.9
Week 16	n	75
	Mean (SD)	72.7 (18.6)
	Median	76.2
	Min, max	28.6, 100.0
Change at Week 16	n	75
	Mean (SD)	5.7 (21.0)
	Median	4.8
	Min, max	-47.6, 85.7
Week 24	n	78
	Mean (SD)	74.9 (15.3)
	Median	76.2
	Min, max	38.1, 100.0
Change at Week 24	n	75
	Mean (SD)	8.7 (19.8)
	Median	4.8
	Min, max	-38.1, 66.7

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Physical (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	78
	Mean (SD)	91.9 (13.3)
	Median	95.8
	Min, max	41.7, 100.0
Week 4	n	78
	Mean (SD)	91.0 (13.9)
	Median	100.0
	Min, max	37.5, 100.0
Change at Week 4	n	78
	Mean (SD)	-0.9 (12.2)
	Median	0.0
	Min, max	-41.7, 45.8
Week 8	n	78
	Mean (SD)	90.1 (14.4)
	Median	95.8
	Min, max	38.1, 100.0
Change at Week 8	n	78
	Mean (SD)	-1.8 (11.5)
	Median	0.0
	Min, max	-41.7, 37.5

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Physical (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	77
	Mean (SD)	94.4 (9.1)
	Median	100.0
	Min, max	62.5, 100.0
Change at Week 12	n	77
	Mean (SD)	2.6 (10.7)
	Median	0.0
	Min, max	-25.0, 45.8
Week 16	n	78
	Mean (SD)	94.2 (11.7)
	Median	100.0
	Min, max	33.3, 100.0
Change at Week 16	n	78
	Mean (SD)	2.3 (13.6)
	Median	0.0
	Min, max	-45.8, 50.0
Week 24	n	78
	Mean (SD)	92.1 (14.8)
	Median	100.0
	Min, max	33.3, 100.0
Change at Week 24	n	78
	Mean (SD)	0.3 (11.5)
	Median	0.0
	Min, max	-50.0, 29.2

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Vitality (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	78
	Mean (SD)	76.7 (12.5)
	Median	73.3
	Min, max	40.0, 100.0
Week 4	n	78
	Mean (SD)	75.2 (14.7)
	Median	73.3
	Min, max	33.3, 100.0
Change at Week 4	n	78
	Mean (SD)	-1.5 (13.2)
	Median	0.0
	Min, max	-40.0, 26.7
Week 8	n	78
	Mean (SD)	75.3 (12.4)
	Median	73.3
	Min, max	33.3, 100.0
Change at Week 8	n	78
	Mean (SD)	-1.4 (11.1)
	Median	0.0
	Min, max	-33.3, 26.7

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Vitality (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	77
	Mean (SD)	77.6 (12.8)
	Median	80.0
	Min, max	40.0, 100.0
Change at Week 12	n	77
	Mean (SD)	0.9 (11.9)
	Median	0.0
	Min, max	-26.7, 33.3
Week 16	n	78
	Mean (SD)	78.6 (13.2)
	Median	80.0
	Min, max	40.0, 100.0
Change at Week 16	n	78
	Mean (SD)	2.0 (12.2)
	Median	0.0
	Min, max	-26.7, 40.0
Week 24	n	78
	Mean (SD)	75.8 (14.1)
	Median	73.3
	Min, max	40.0, 100.0
Change at Week 24	n	78
	Mean (SD)	-0.9 (13.9)
	Median	0.0
	Min, max	-40.0, 26.7

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Emotion (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	78
	Mean (SD)	86.5 (12.9)
	Median	86.7
	Min, max	40.0, 100.0
Week 4	n	78
	Mean (SD)	87.0 (12.5)
	Median	93.3
	Min, max	53.3, 100.0
Change at Week 4	n	78
	Mean (SD)	0.5 (10.5)
	Median	0.0
	Min, max	-33.3, 20.0
Week 8	n	78
	Mean (SD)	86.7 (11.7)
	Median	86.7
	Min, max	46.7, 100.0
Change at Week 8	n	78
	Mean (SD)	0.2 (10.5)
	Median	0.0
	Min, max	-26.7, 26.7

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Emotion (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	77
	Mean (SD)	89.4 (11.5)
	Median	93.3
	Min, max	46.7, 100.0
Change at Week 12	n	77
	Mean (SD)	2.9 (10.6)
	Median	0.0
	Min, max	-20.0, 46.7
Week 16	n	78
	Mean (SD)	89.5 (11.7)
	Median	93.3
	Min, max	53.3, 100.0
Change at Week 16	n	78
	Mean (SD)	3.0 (11.1)
	Median	0.0
	Min, max	-26.7, 33.3
Week 24	n	78
	Mean (SD)	88.4 (11.0)
	Median	86.7
	Min, max	53.3, 100.0
Change at Week 24	n	78
	Mean (SD)	1.9 (12.1)
	Median	0.0
	Min, max	-33.3, 46.7

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

School (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	78
	Mean (SD)	80.4 (17.4)
	Median	83.3
	Min, max	16.7, 100.0
Week 4	n	78
	Mean (SD)	82.5 (15.9)
	Median	83.3
	Min, max	33.3, 100.0
Change at Week 4	n	78
	Mean (SD)	2.0 (17.3)
	Median	0.0
	Min, max	-41.7, 50.0
Week 8	n	78
	Mean (SD)	81.4 (18.3)
	Median	83.3
	Min, max	25.0, 100.0
Change at Week 8	n	78
	Mean (SD)	1.0 (16.6)
	Median	0.0
	Min, max	-50.0, 41.7

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

School (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	77
	Mean (SD)	84.0 (17.0)
	Median	91.7
	Min, max	25.0, 100.0
Change at Week 12	n	77
	Mean (SD)	3.8 (14.1)
	Median	0.0
	Min, max	-41.7, 50.0
Week 16	n	78
	Mean (SD)	85.0 (15.7)
	Median	91.7
	Min, max	50.0, 100.0
Change at Week 16	n	78
	Mean (SD)	4.6 (16.6)
	Median	0.0
	Min, max	-41.7, 50.0
Week 24	n	78
	Mean (SD)	82.7 (17.0)
	Median	91.7
	Min, max	33.3, 100.0
Change at Week 24	n	78
	Mean (SD)	2.2 (15.4)
	Median	0.0
	Min, max	-41.7, 41.7

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Body (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	78
	Mean (SD)	80.1 (26.1)
	Median	88.9
	Min, max	0.0, 100.0
Week 4	n	78
	Mean (SD)	81.3 (24.5)
	Median	88.9
	Min, max	0.0, 100.0
Change at Week 4	n	78
	Mean (SD)	1.2 (15.9)
	Median	0.0
	Min, max	-33.3, 44.4
Week 8	n	78
	Mean (SD)	82.5 (22.0)
	Median	88.9
	Min, max	22.2, 100.0
Change at Week 8	n	78
	Mean (SD)	2.4 (19.2)
	Median	0.0
	Min, max	-55.6, 100.0

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Body (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	77
	Mean (SD)	84.0 (22.3)
	Median	100.0
	Min, max	22.2, 100.0
Change at Week 12	n	77
	Mean (SD)	4.1 (18.3)
	Median	0.0
	Min, max	-44.4, 66.7
Week 16	n	78
	Mean (SD)	85.9 (21.3)
	Median	100.0
	Min, max	22.2, 100.0
Change at Week 16	n	78
	Mean (SD)	5.8 (19.9)
	Median	0.0
	Min, max	-44.4, 100.0
Week 24	n	78
	Mean (SD)	83.6 (21.4)
	Median	100.0
	Min, max	22.2, 100.0
Change at Week 24	n	78
	Mean (SD)	3.5 (17.7)
	Median	0.0
	Min, max	-33.3, 66.7

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Eat (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	78
	Mean (SD)	79.5 (25.6)
	Median	83.3
	Min, max	0.0, 100.0
Week 4	n	78
	Mean (SD)	78.4 (24.6)
	Median	83.3
	Min, max	0.0, 100.0
Change at Week 4	n	78
	Mean (SD)	-1.1 (17.9)
	Median	0.0
	Min, max	-50.0, 50.0
Week 8	n	78
	Mean (SD)	79.3 (26.3)
	Median	91.7
	Min, max	0.0, 100.0
Change at Week 8	n	78
	Mean (SD)	-0.2 (19.5)
	Median	0.0
	Min, max	-66.7, 50.0

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Eat (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	77
	Mean (SD)	77.9 (27.4)
	Median	83.3
	Min, max	0.0, 100.0
Change at Week 12	n	77
	Mean (SD)	-1.5 (18.4)
	Median	0.0
	Min, max	-66.7, 50.0
Week 16	n	78
	Mean (SD)	81.0 (21.9)
	Median	83.3
	Min, max	16.7, 100.0
Change at Week 16	n	78
	Mean (SD)	1.5 (17.0)
	Median	0.0
	Min, max	-50.0, 66.7
Week 24	n	78
	Mean (SD)	81.8 (24.1)
	Median	100.0
	Min, max	0.0, 100.0
Change at Week 24	n	78
	Mean (SD)	2.4 (18.6)
	Median	0.0
	Min, max	-50.0, 50.0

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Treatment Burden (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	78
	Mean (SD)	69.4 (21.2)
	Median	66.7
	Min, max	11.1, 100.0
Week 4	n	78
	Mean (SD)	76.2 (21.1)
	Median	77.8
	Min, max	11.1, 100.0
Change at Week 4	n	78
	Mean (SD)	6.8 (14.4)
	Median	5.6
	Min, max	-22.2, 33.3
Week 8	n	78
	Mean (SD)	78.1 (21.0)
	Median	77.8
	Min, max	11.1, 100.0
Change at Week 8	n	78
	Mean (SD)	8.7 (21.3)
	Median	5.6
	Min, max	-33.3, 66.7

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Treatment Burden (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	77
	Mean (SD)	75.5 (24.5)
	Median	77.8
	Min, max	11.1, 100.0
Change at Week 12	n	77
	Mean (SD)	6.3 (18.7)
	Median	11.1
	Min, max	-44.4, 55.6
Week 16	n	78
	Mean (SD)	77.1 (20.2)
	Median	77.8
	Min, max	22.2, 100.0
Change at Week 16	n	78
	Mean (SD)	7.7 (15.7)
	Median	11.1
	Min, max	-22.2, 66.7
Week 24	n	78
	Mean (SD)	78.2 (21.1)
	Median	77.8
	Min, max	22.2, 100.0
Change at Week 24	n	78
	Mean (SD)	8.8 (19.1)
	Median	11.1
	Min, max	-33.3, 55.6

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Health Perceptions (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	78
	Mean (SD)	86.8 (13.8)
	Median	88.9
	Min, max	55.6, 100.0
Week 4	n	78
	Mean (SD)	82.5 (17.9)
	Median	88.9
	Min, max	22.2, 100.0
Change at Week 4	n	78
	Mean (SD)	-4.3 (14.1)
	Median	0.0
	Min, max	-44.4, 33.3
Week 8	n	78
	Mean (SD)	85.9 (16.0)
	Median	88.9
	Min, max	22.2, 100.0
Change at Week 8	n	78
	Mean (SD)	-0.9 (12.5)
	Median	0.0
	Min, max	-44.4, 22.2

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Health Perceptions (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	77
	Mean (SD)	86.7 (14.5)
	Median	88.9
	Min, max	44.4, 100.0
Change at Week 12	n	77
	Mean (SD)	0.1 (12.7)
	Median	0.0
	Min, max	-33.3, 33.3
Week 16	n	78
	Mean (SD)	88.5 (13.1)
	Median	88.9
	Min, max	55.6, 100.0
Change at Week 16	n	78
	Mean (SD)	1.7 (12.2)
	Median	0.0
	Min, max	-33.3, 33.3
Week 24	n	78
	Mean (SD)	87.5 (16.6)
	Median	94.4
	Min, max	33.3, 100.0
Change at Week 24	n	78
	Mean (SD)	0.7 (16.4)
	Median	0.0
	Min, max	-66.7, 33.3

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Weight (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	78
	Mean (SD)	69.2 (35.5)
	Median	83.3
	Min, max	0.0, 100.0
Week 4	n	78
	Mean (SD)	70.5 (34.0)
	Median	83.3
	Min, max	0.0, 100.0
Change at Week 4	n	78
	Mean (SD)	1.3 (28.1)
	Median	0.0
	Min, max	-66.7, 100.0
Week 8	n	78
	Mean (SD)	75.2 (30.6)
	Median	100.0
	Min, max	0.0, 100.0
Change at Week 8	n	78
	Mean (SD)	6.0 (27.8)
	Median	0.0
	Min, max	-66.7, 100.0

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Weight (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	77
	Mean (SD)	73.2 (33.8)
	Median	100.0
	Min, max	0.0, 100.0
Change at Week 12	n	77
	Mean (SD)	4.3 (26.1)
	Median	0.0
	Min, max	-66.7, 66.7
Week 16	n	78
	Mean (SD)	74.4 (31.7)
	Median	100.0
	Min, max	0.0, 100.0
Change at Week 16	n	78
	Mean (SD)	5.1 (27.4)
	Median	0.0
	Min, max	-66.7, 66.7
Week 24	n	78
	Mean (SD)	74.4 (33.9)
	Median	100.0
	Min, max	0.0, 100.0
Change at Week 24	n	78
	Mean (SD)	5.1 (28.0)
	Median	0.0
	Min, max	-66.7, 100.0

- Baseline is defined as the pre-dose Day 1 value.

Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Digestion (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Baseline	n	78
	Mean (SD)	82.2 (17.4)
	Median	88.9
	Min, max	22.2, 100.0
Week 4	n	78
	Mean (SD)	82.9 (17.7)
	Median	88.9
	Min, max	22.2, 100.0
Change at Week 4	n	78
	Mean (SD)	0.7 (17.3)
	Median	0.0
	Min, max	-55.6, 55.6
Week 8	n	78
	Mean (SD)	82.6 (15.7)
	Median	88.9
	Min, max	22.2, 100.0
Change at Week 8	n	78
	Mean (SD)	0.4 (17.7)
	Median	0.0
	Min, max	-44.4, 66.7

- Baseline is defined as the pre-dose Day 1 value.

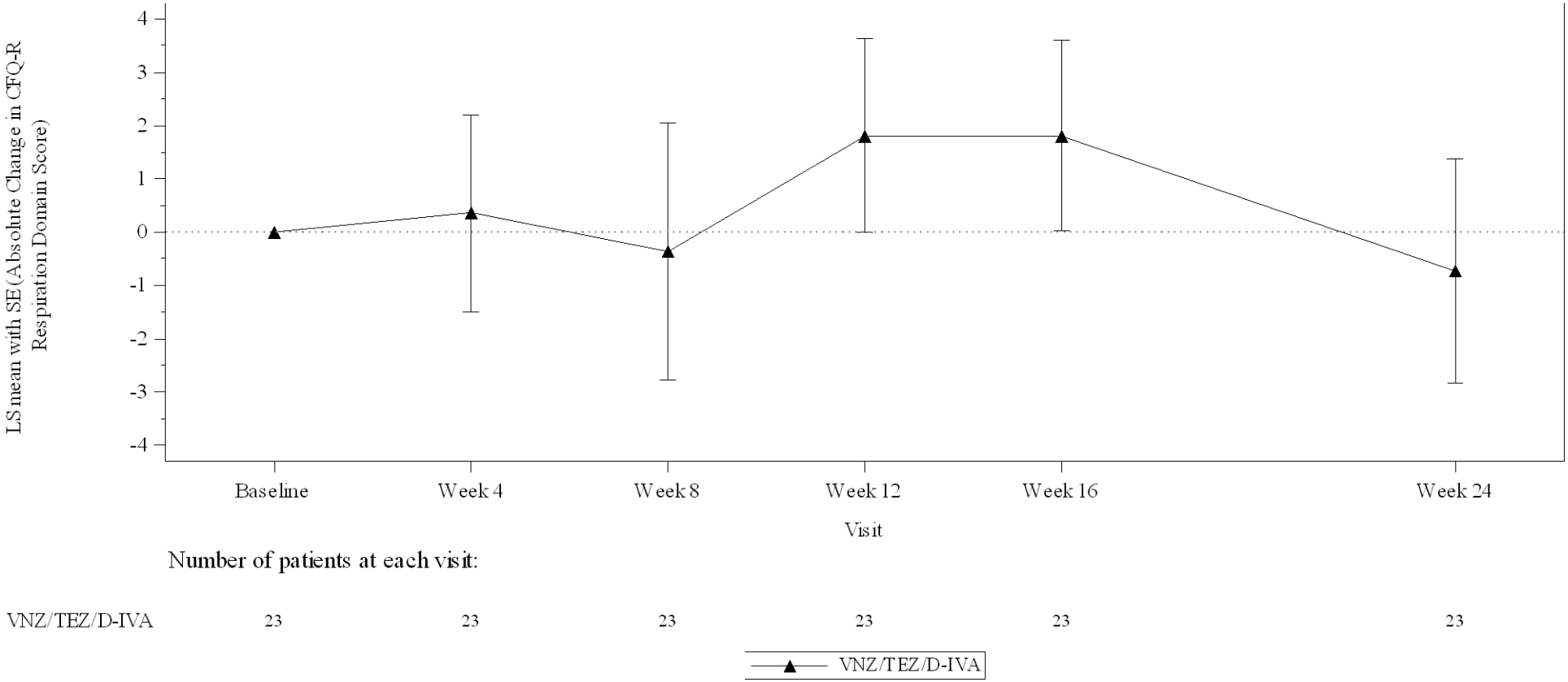
Table 14.2.5.6b1
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit
Full Analysis Set

Digestion (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 78
Week 12	n	77
	Mean (SD)	83.8 (15.7)
	Median	88.9
	Min, max	44.4, 100.0
Change at Week 12	n	77
	Mean (SD)	1.7 (16.2)
	Median	0.0
	Min, max	-44.4, 66.7
Week 16	n	78
	Mean (SD)	85.5 (13.8)
	Median	88.9
	Min, max	55.6, 100.0
Change at Week 16	n	78
	Mean (SD)	3.3 (14.7)
	Median	0.0
	Min, max	-33.3, 44.4
Week 24	n	78
	Mean (SD)	81.5 (16.5)
	Median	83.3
	Min, max	33.3, 100.0
Change at Week 24	n	78
	Mean (SD)	-0.7 (16.3)
	Median	0.0
	Min, max	-33.3, 66.7

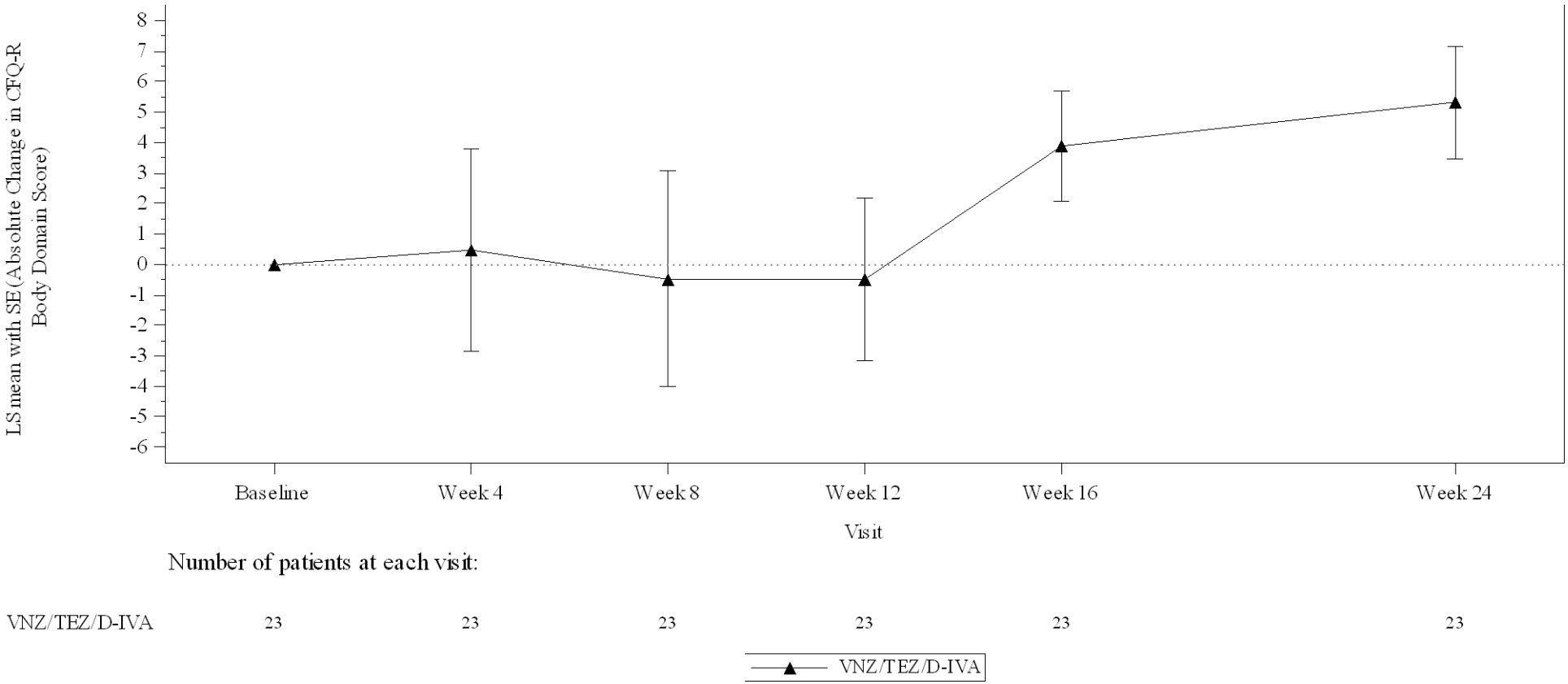
- Baseline is defined as the pre-dose Day 1 value.

Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Respiration



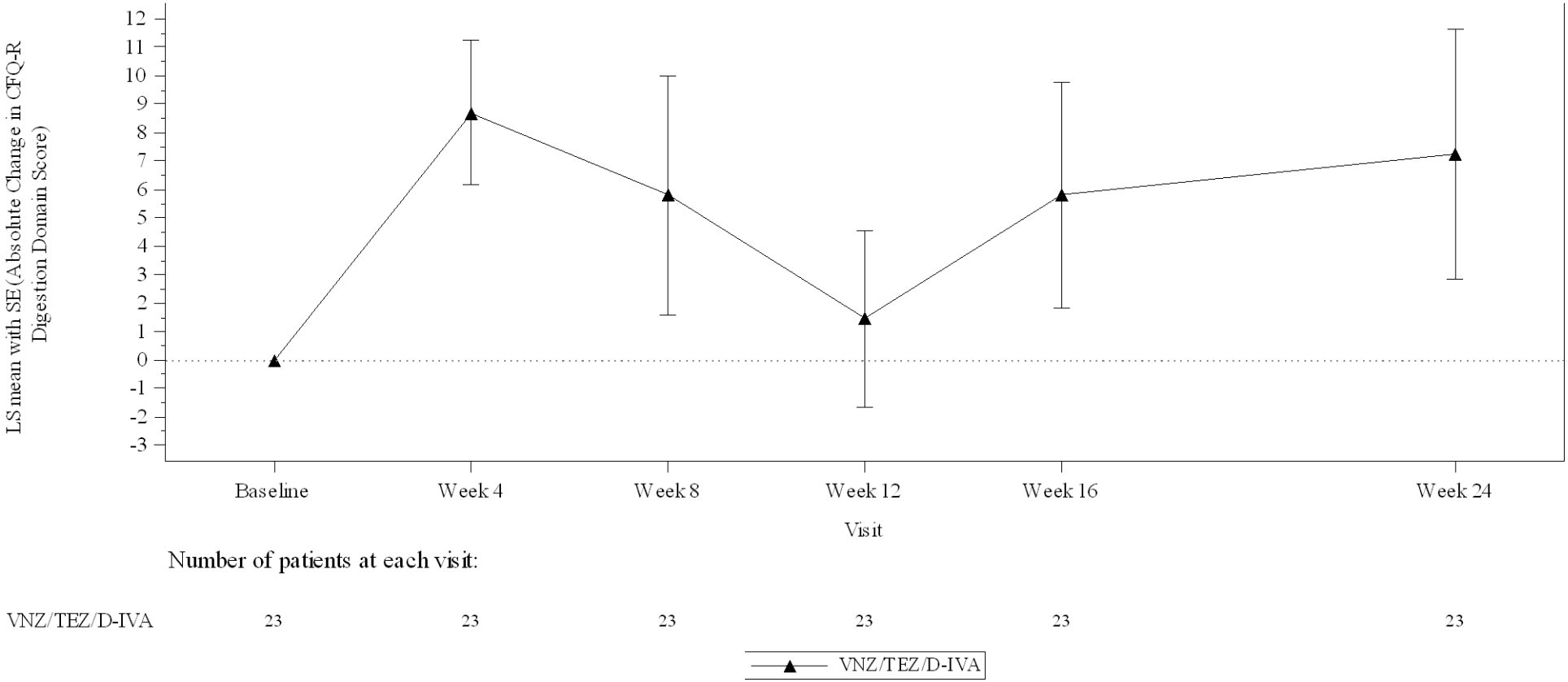
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Body



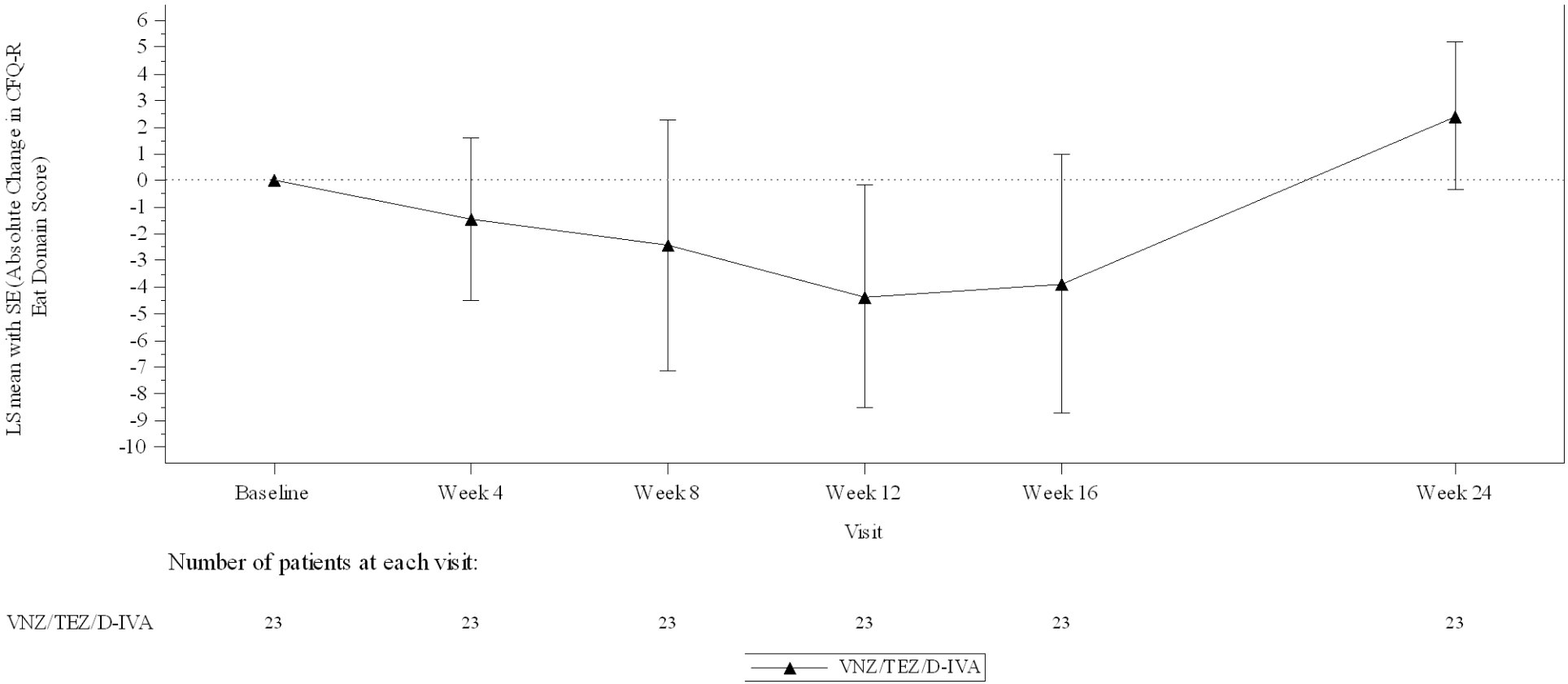
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Digestion



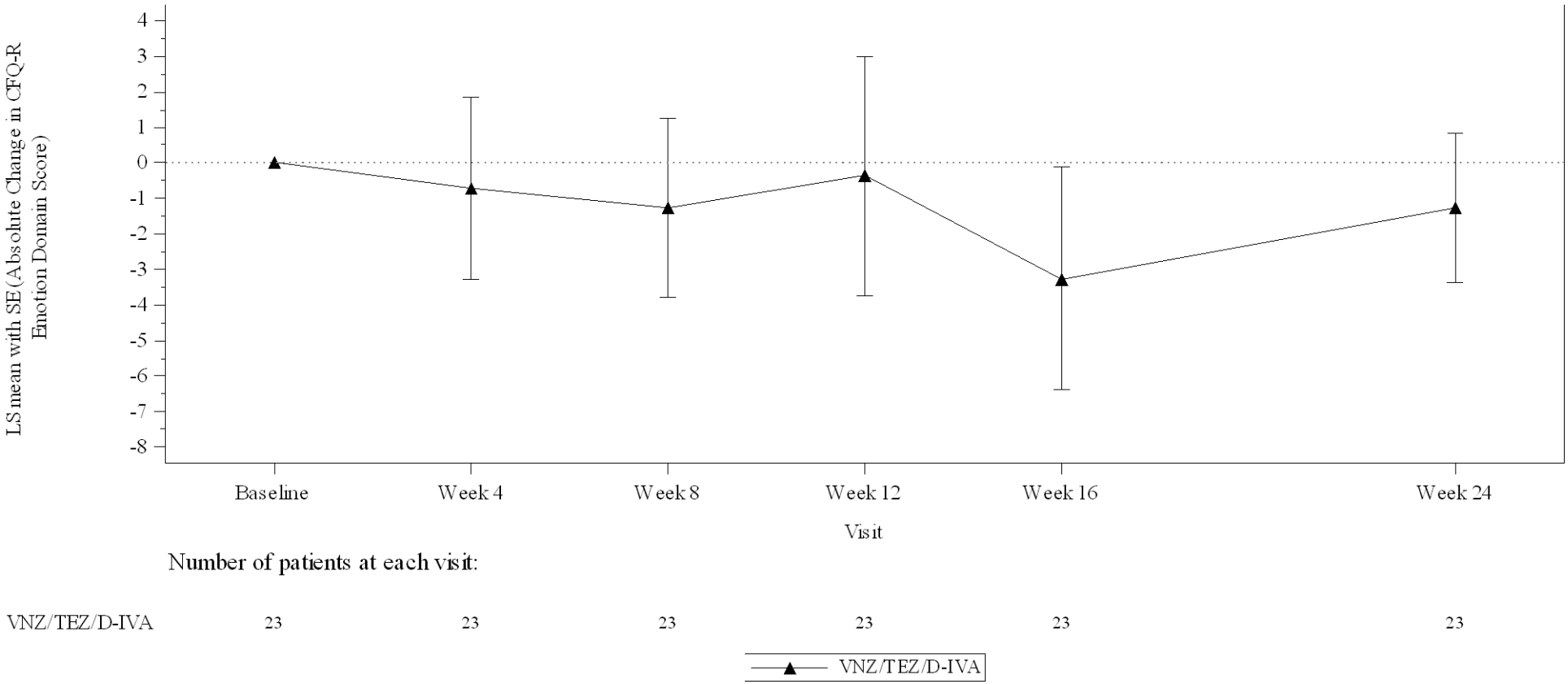
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Eat



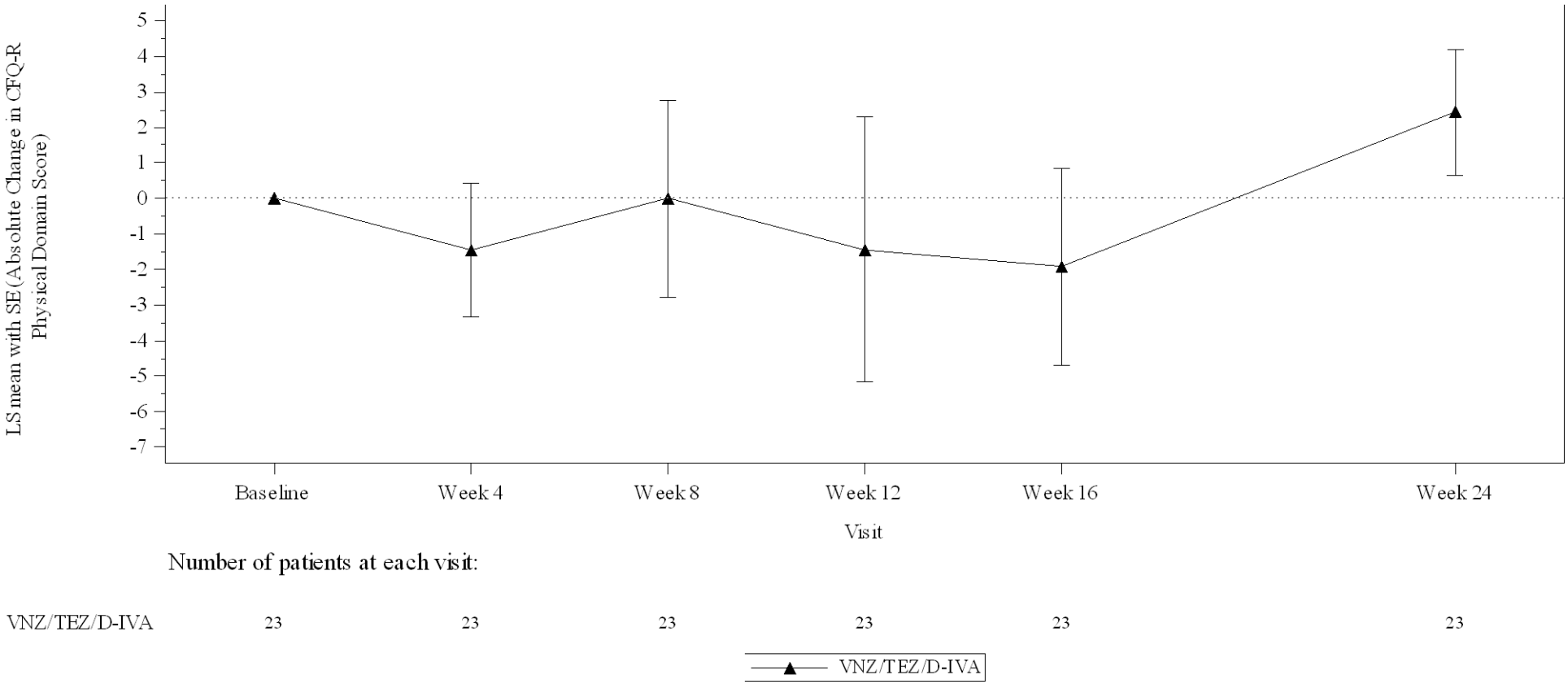
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Emotion



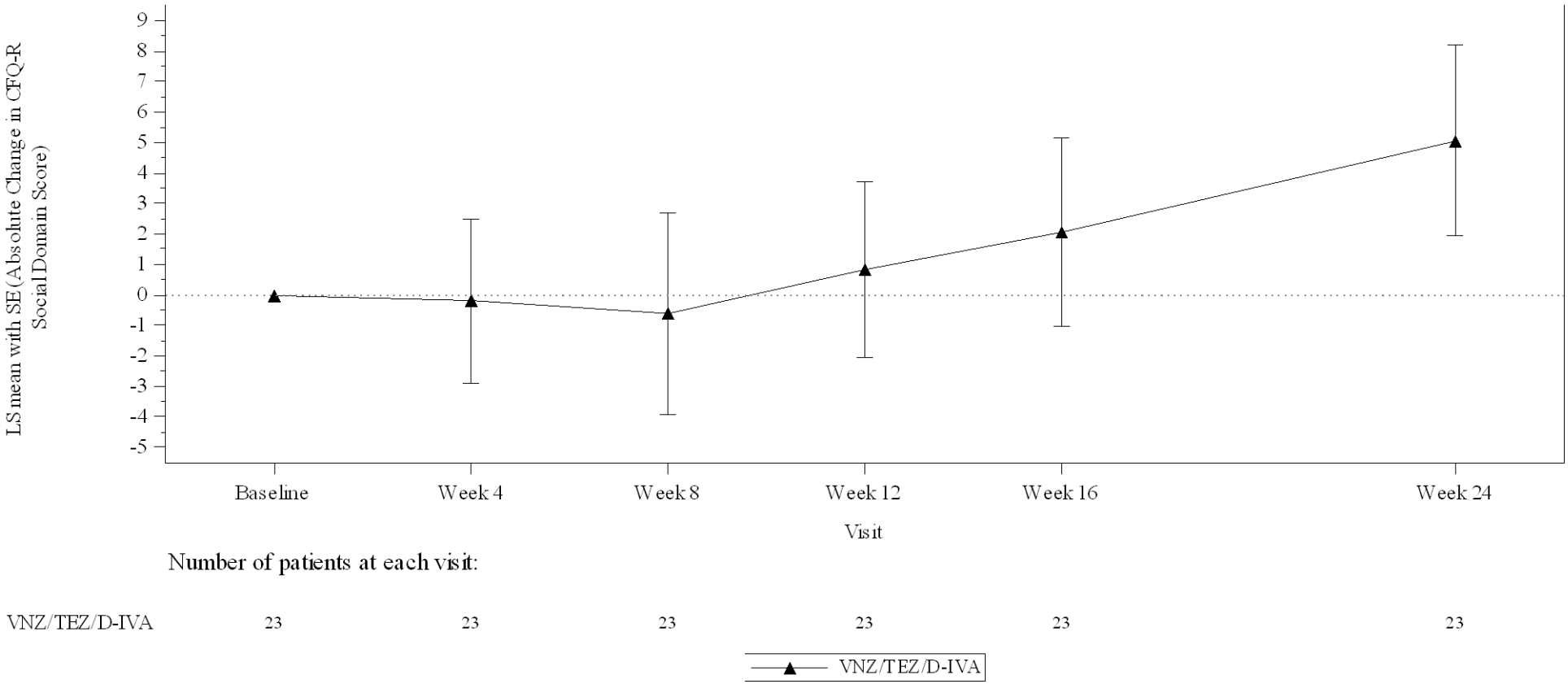
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Physical



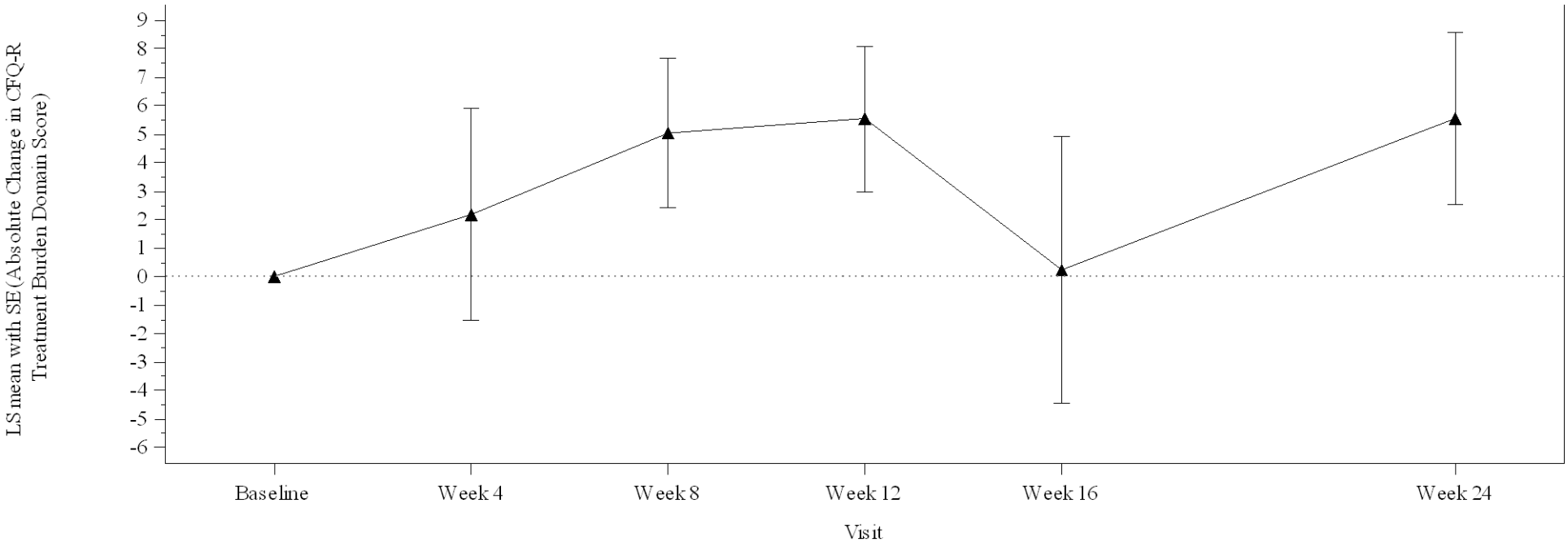
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Social



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Treatment Burden



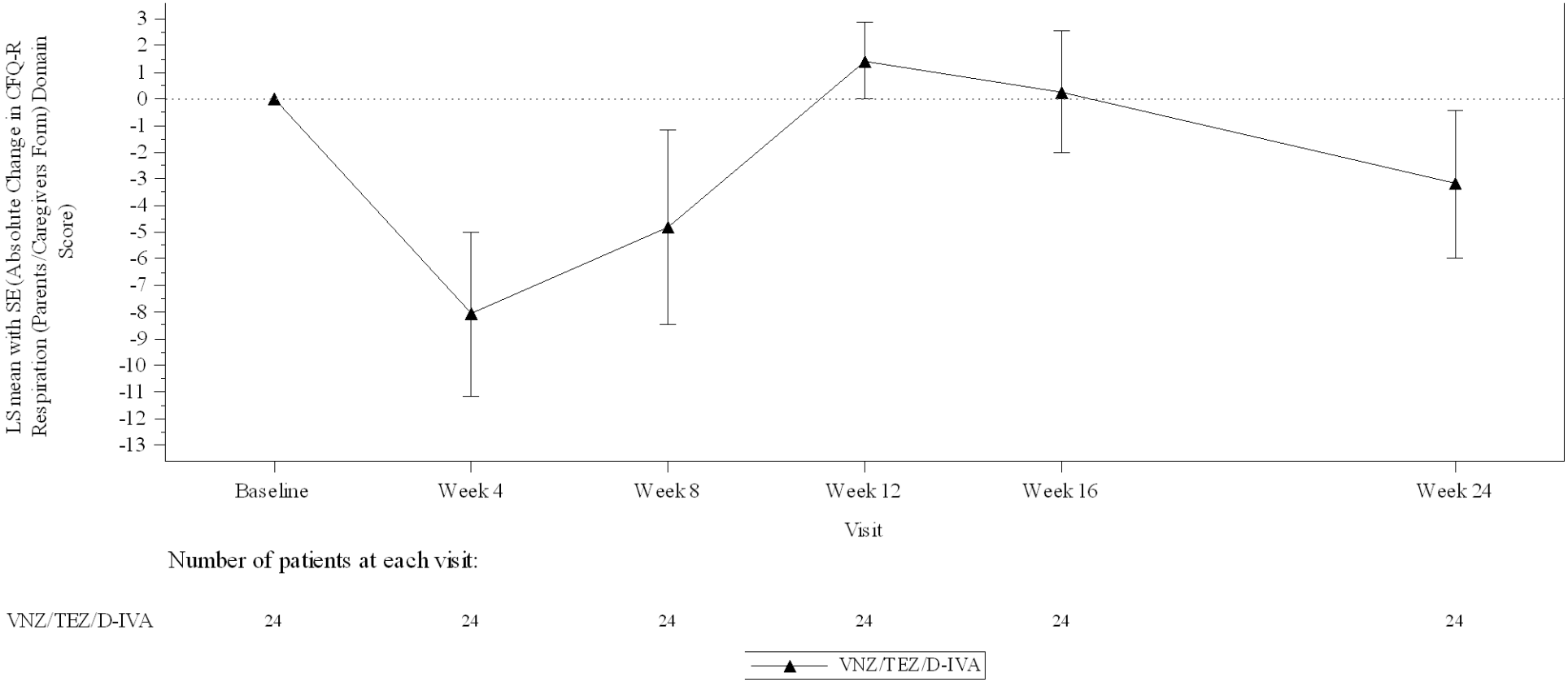
Number of patients at each visit:

	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	23	23	23	23	23	23

VNZ/TEZ/D-IVA

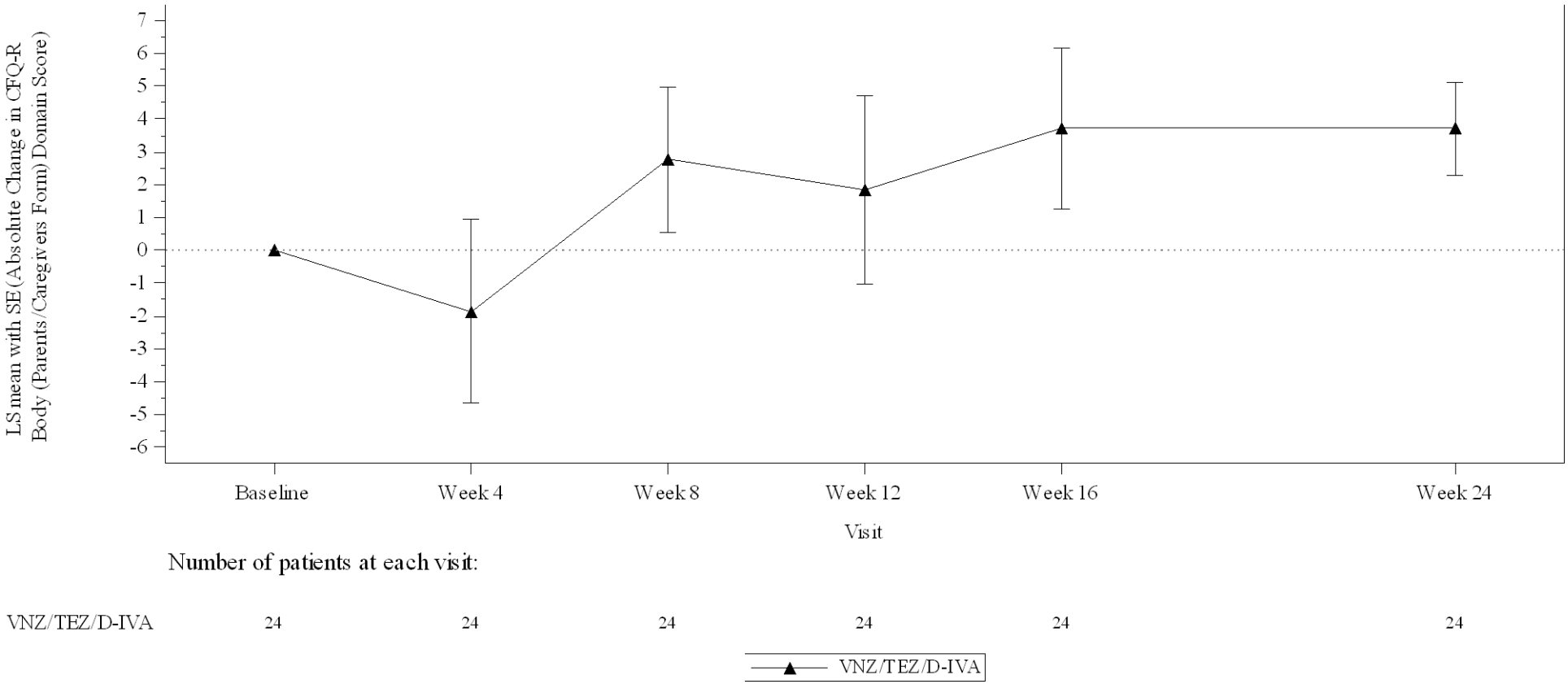
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)



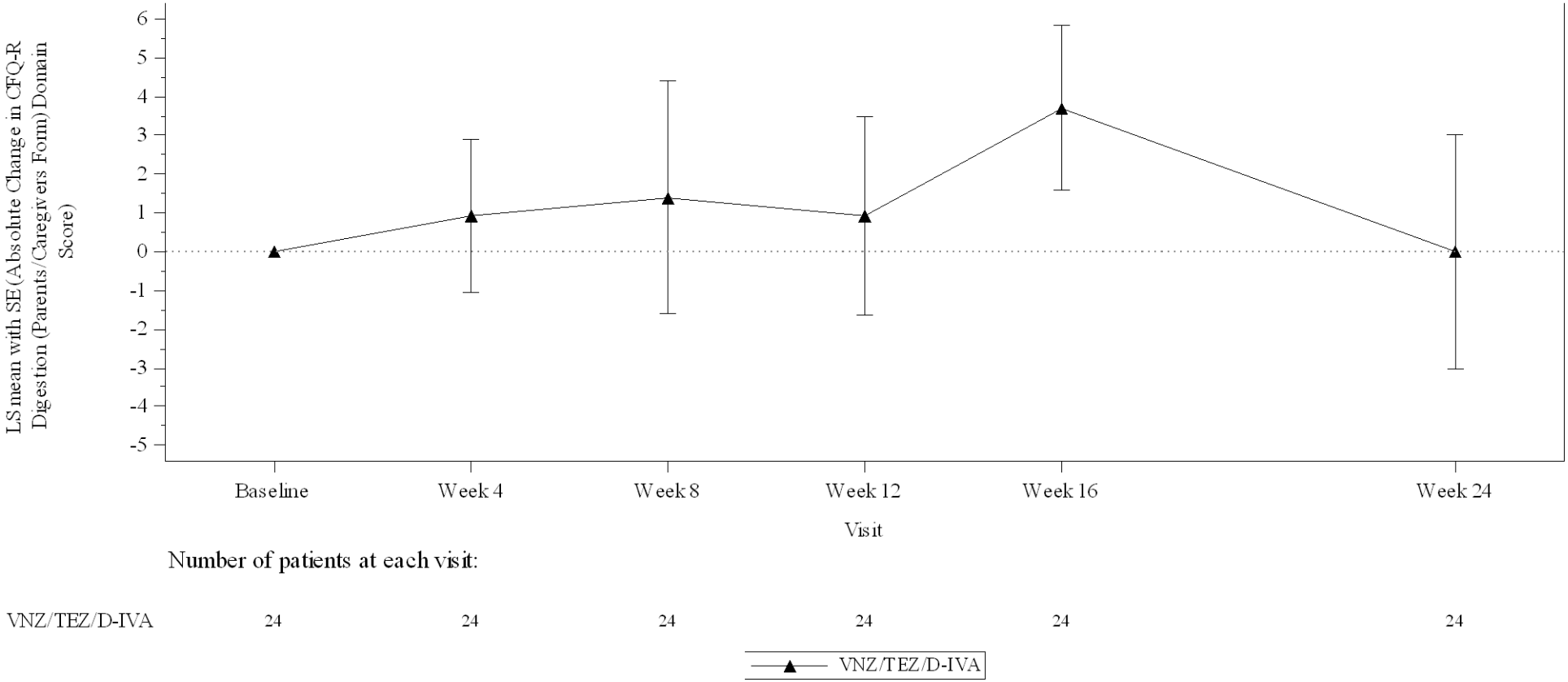
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)



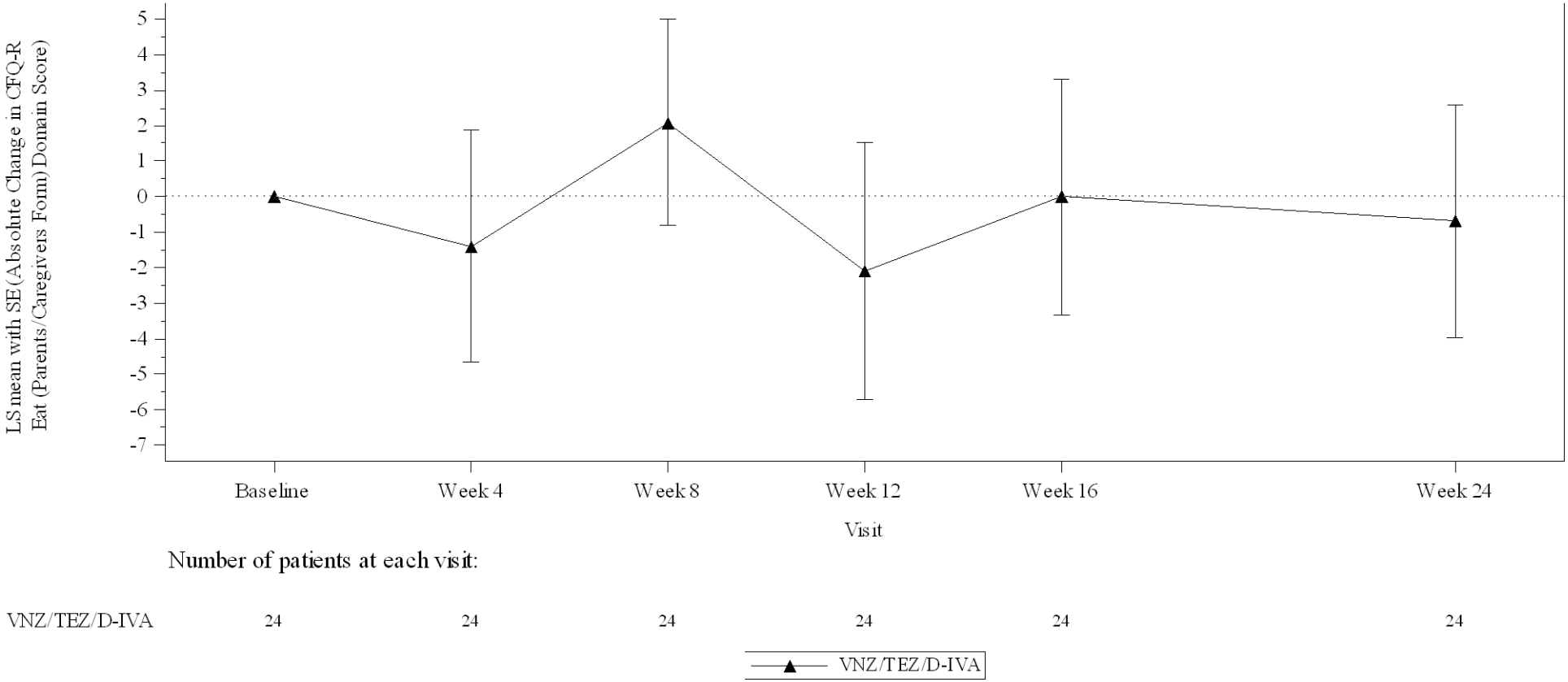
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)



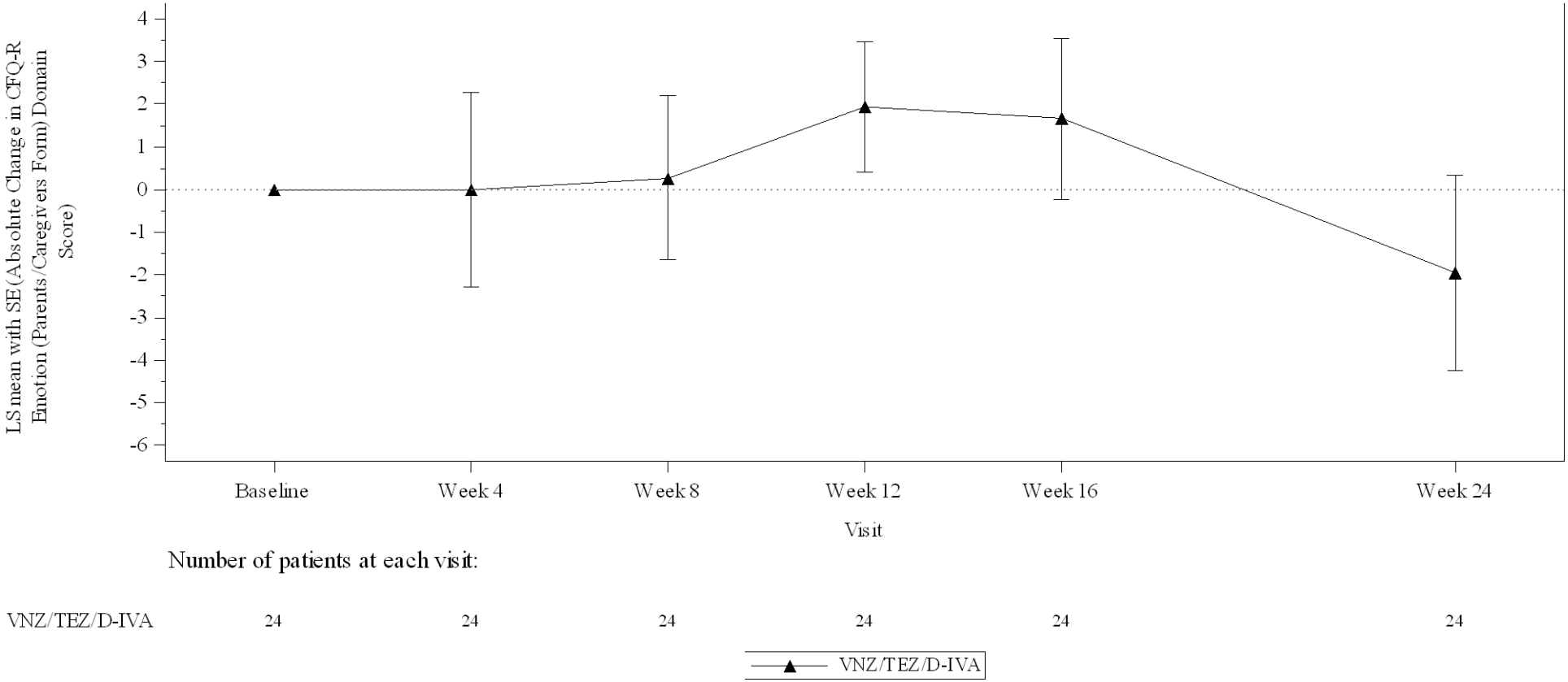
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)



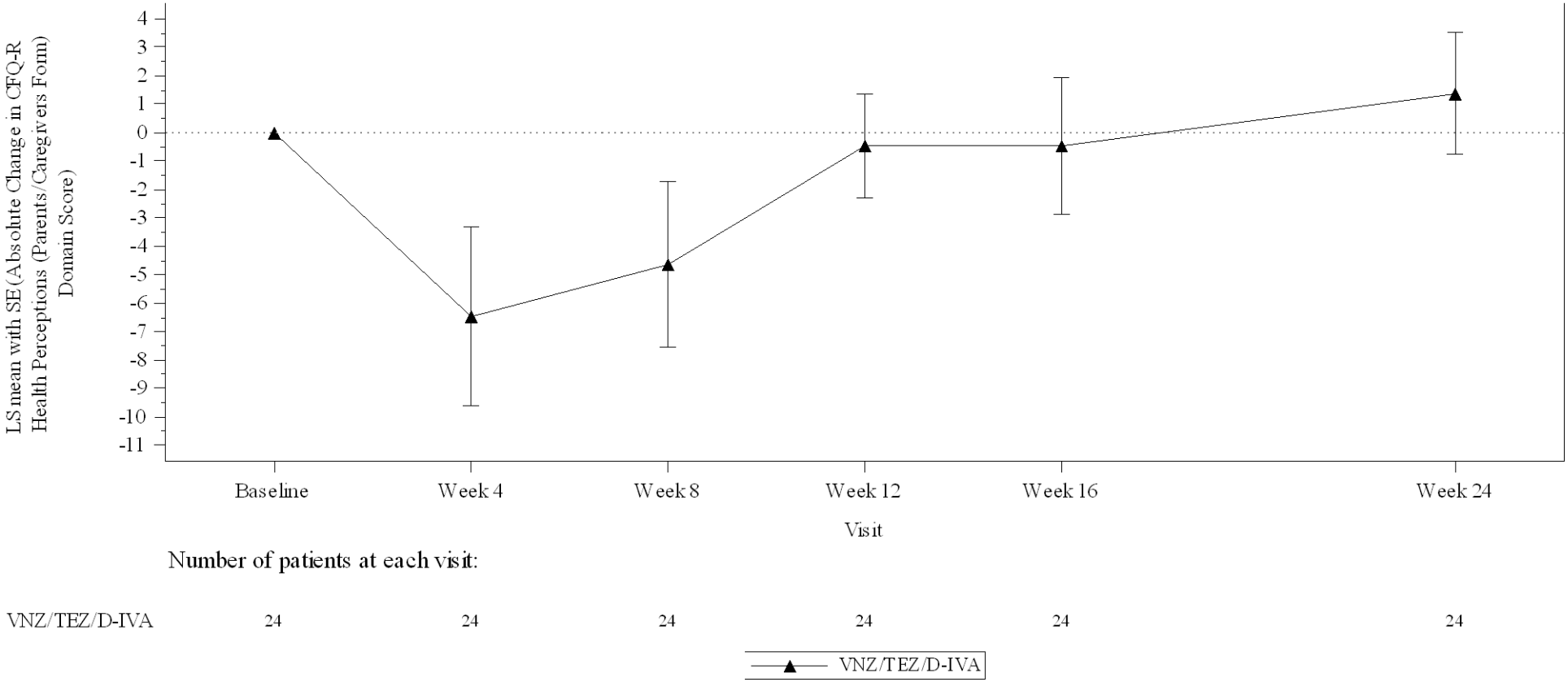
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)



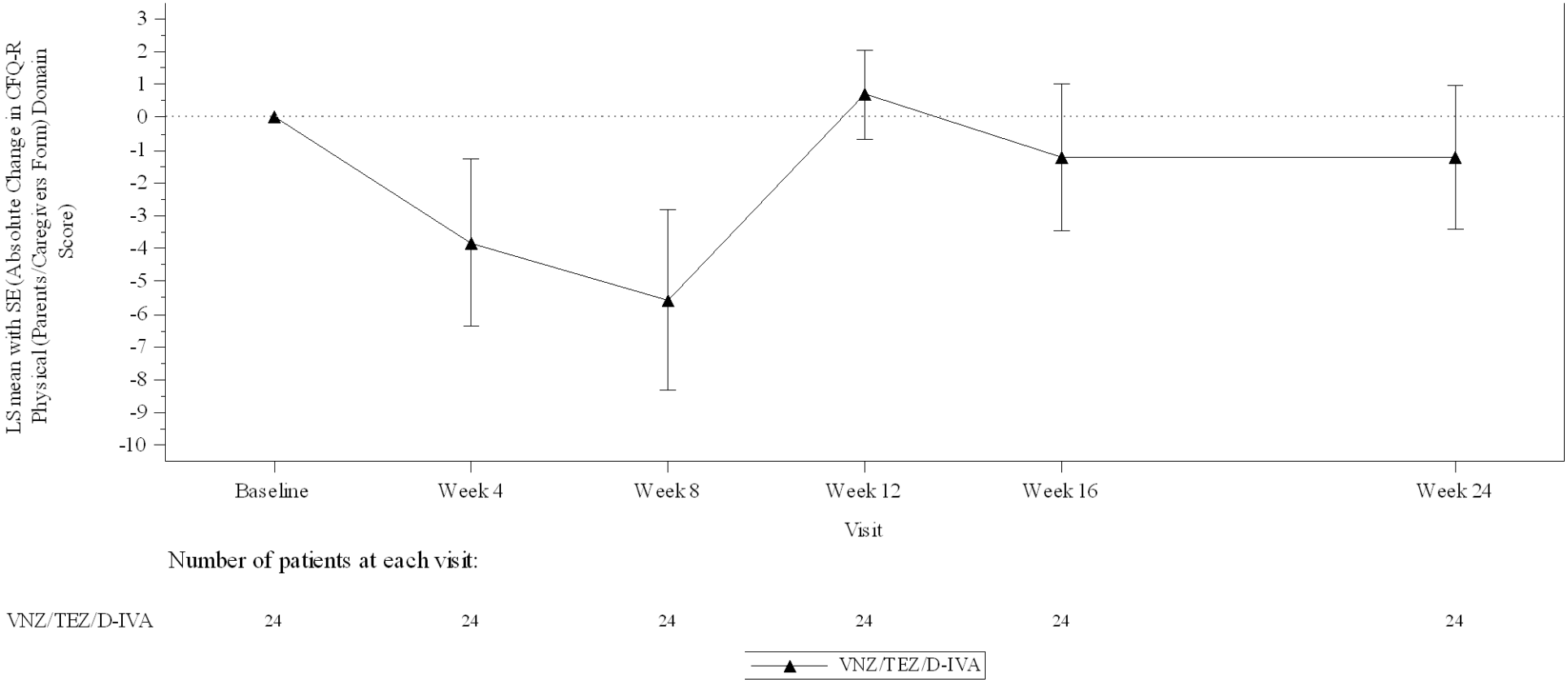
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)



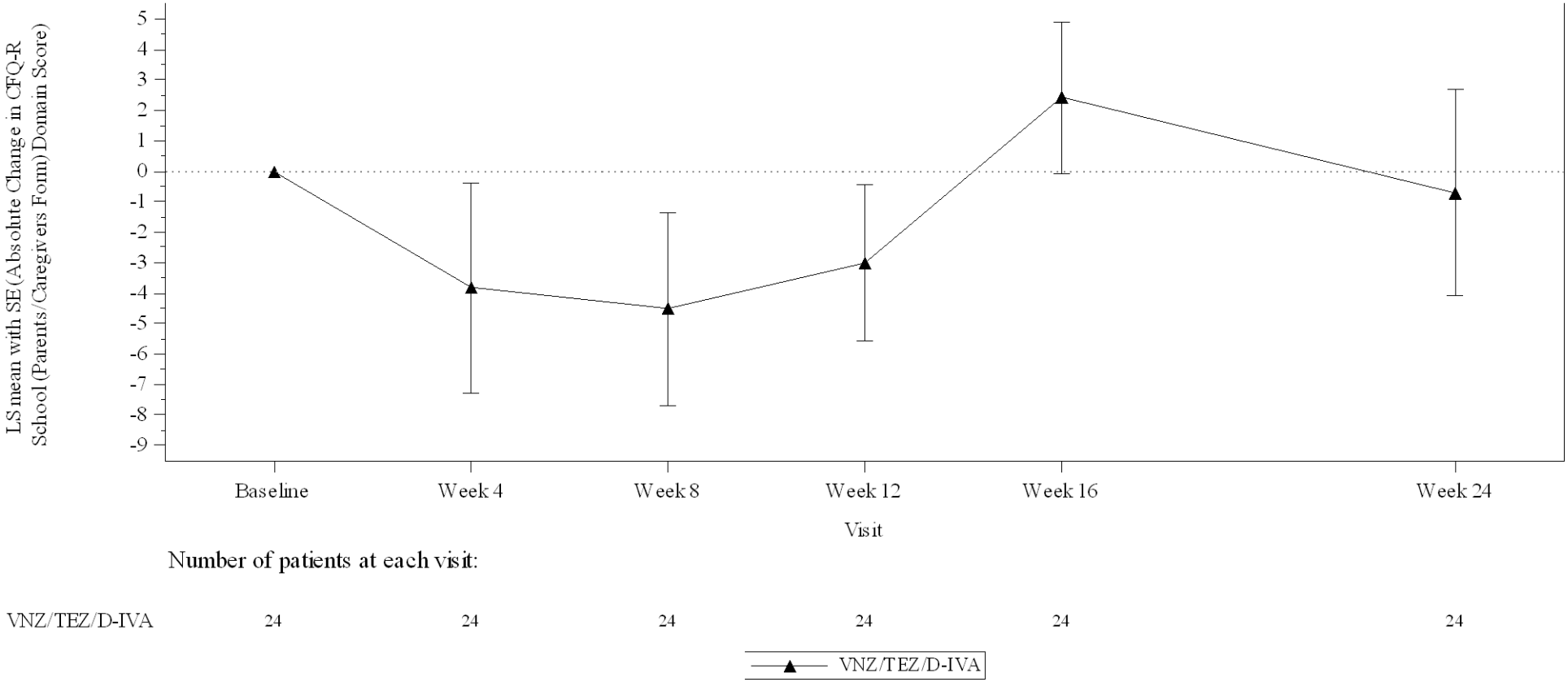
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)



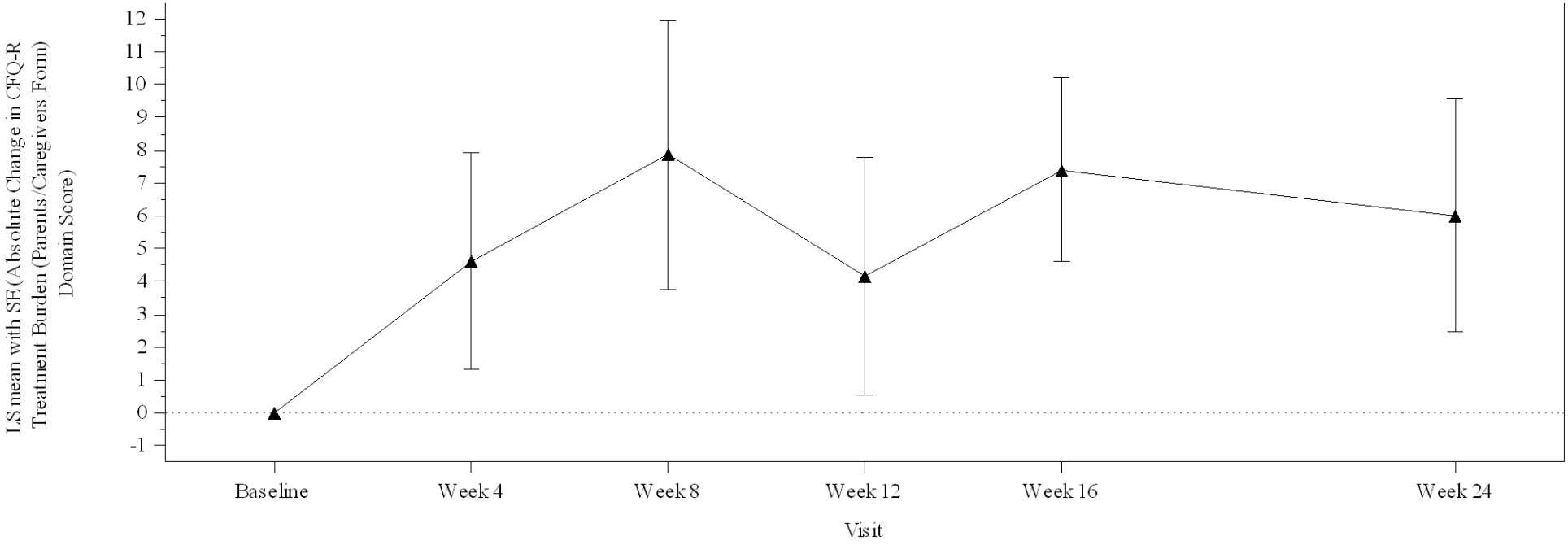
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)



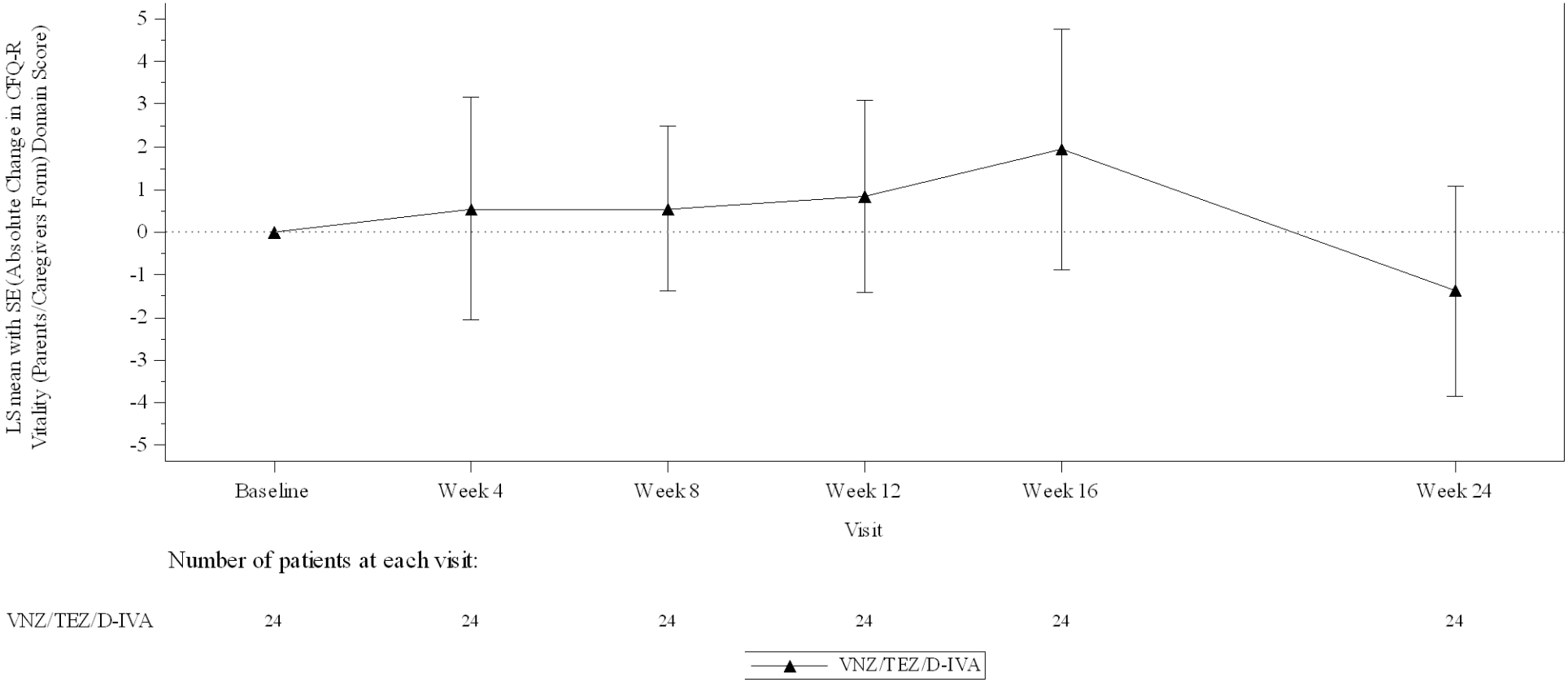
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)



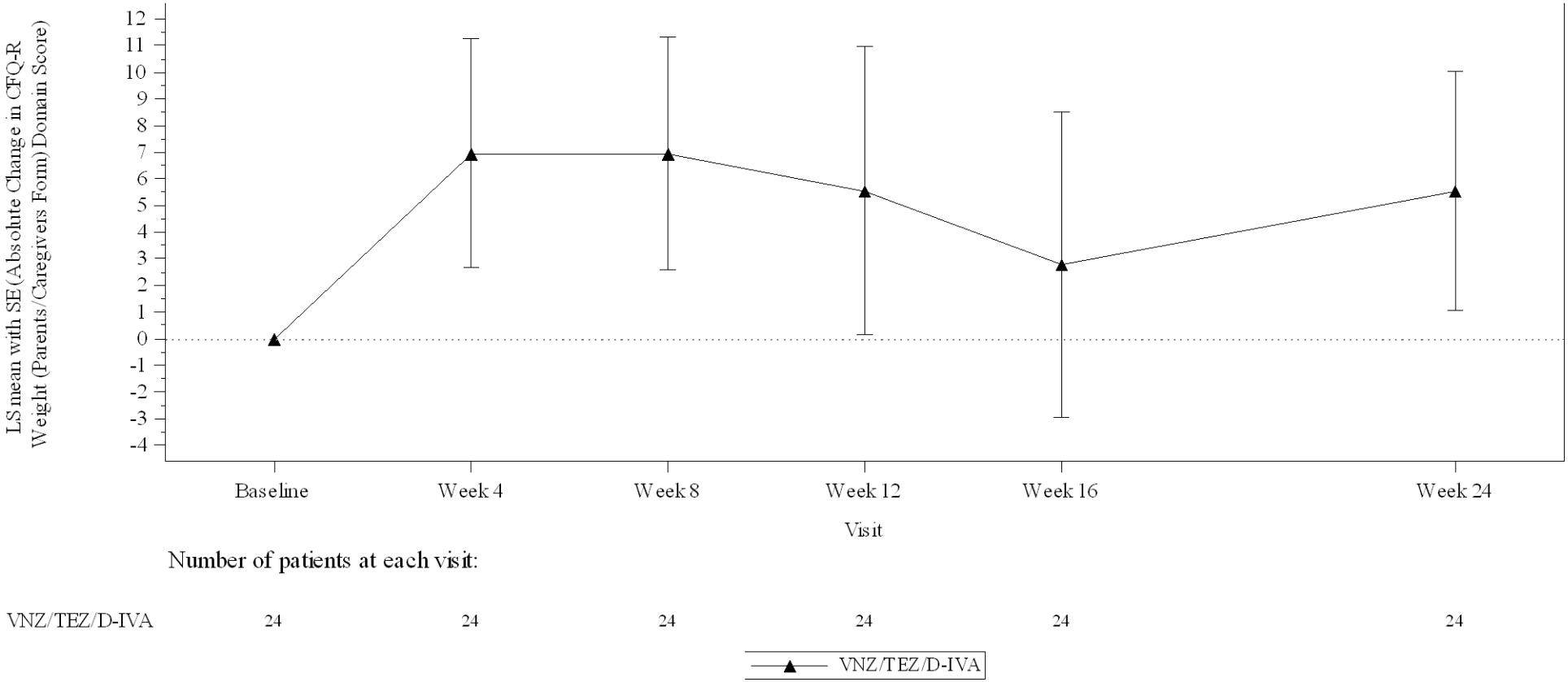
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)



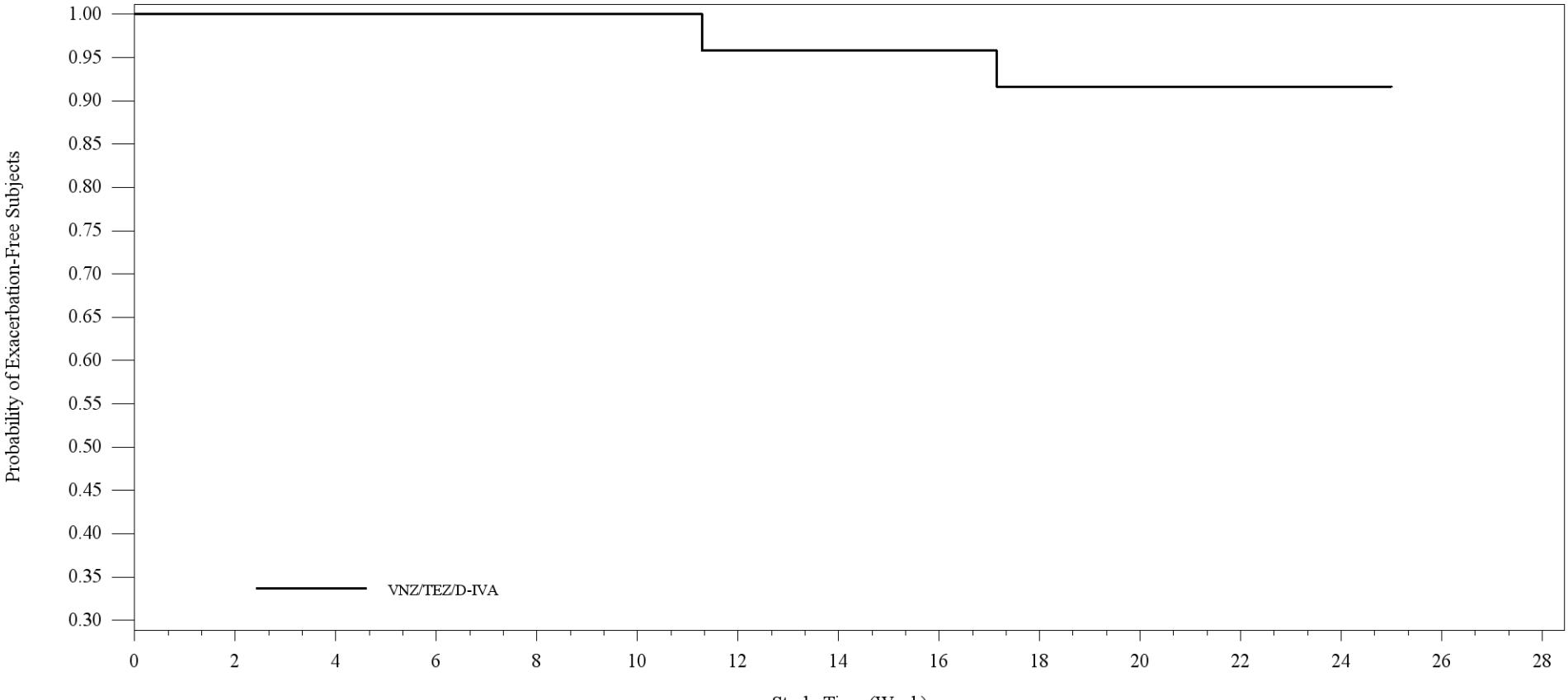
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)



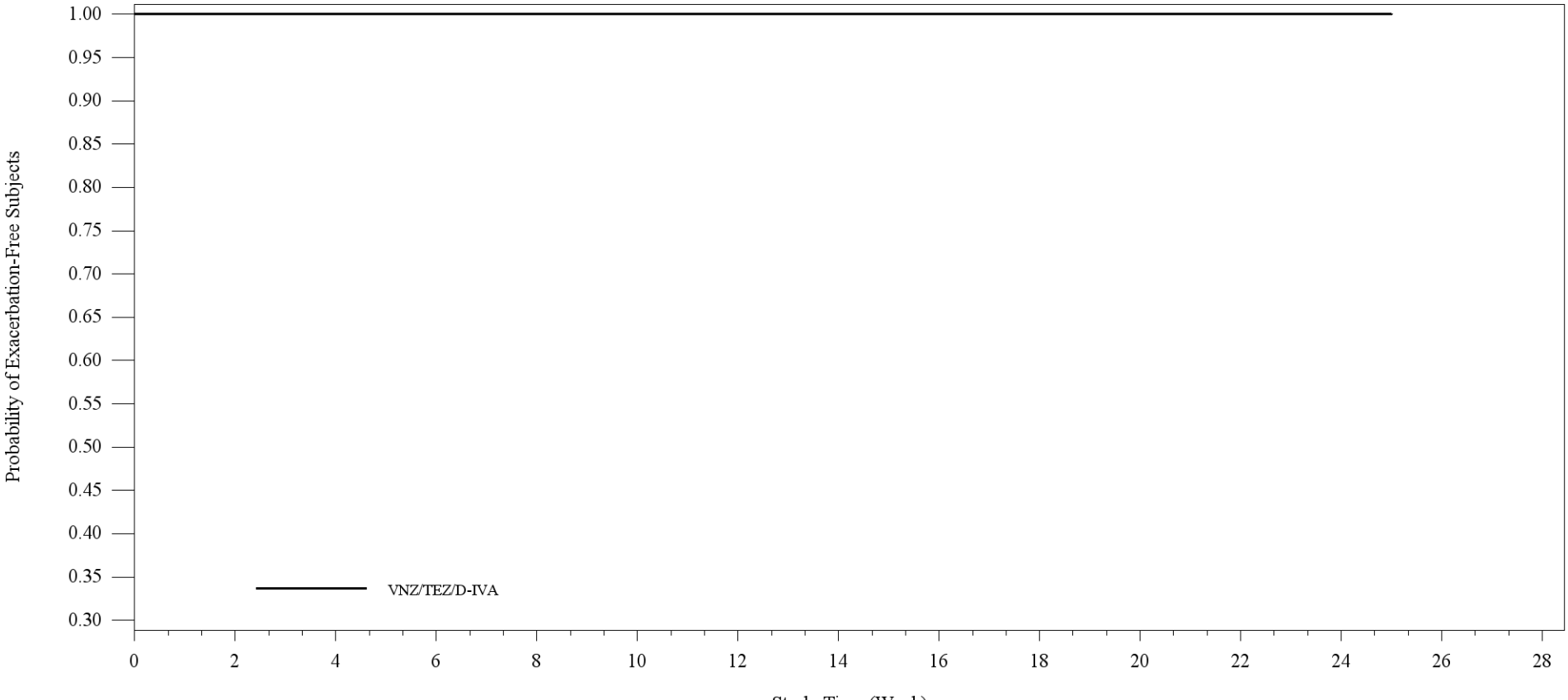
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.1.14.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 24 for F/MF
Full Analysis Set



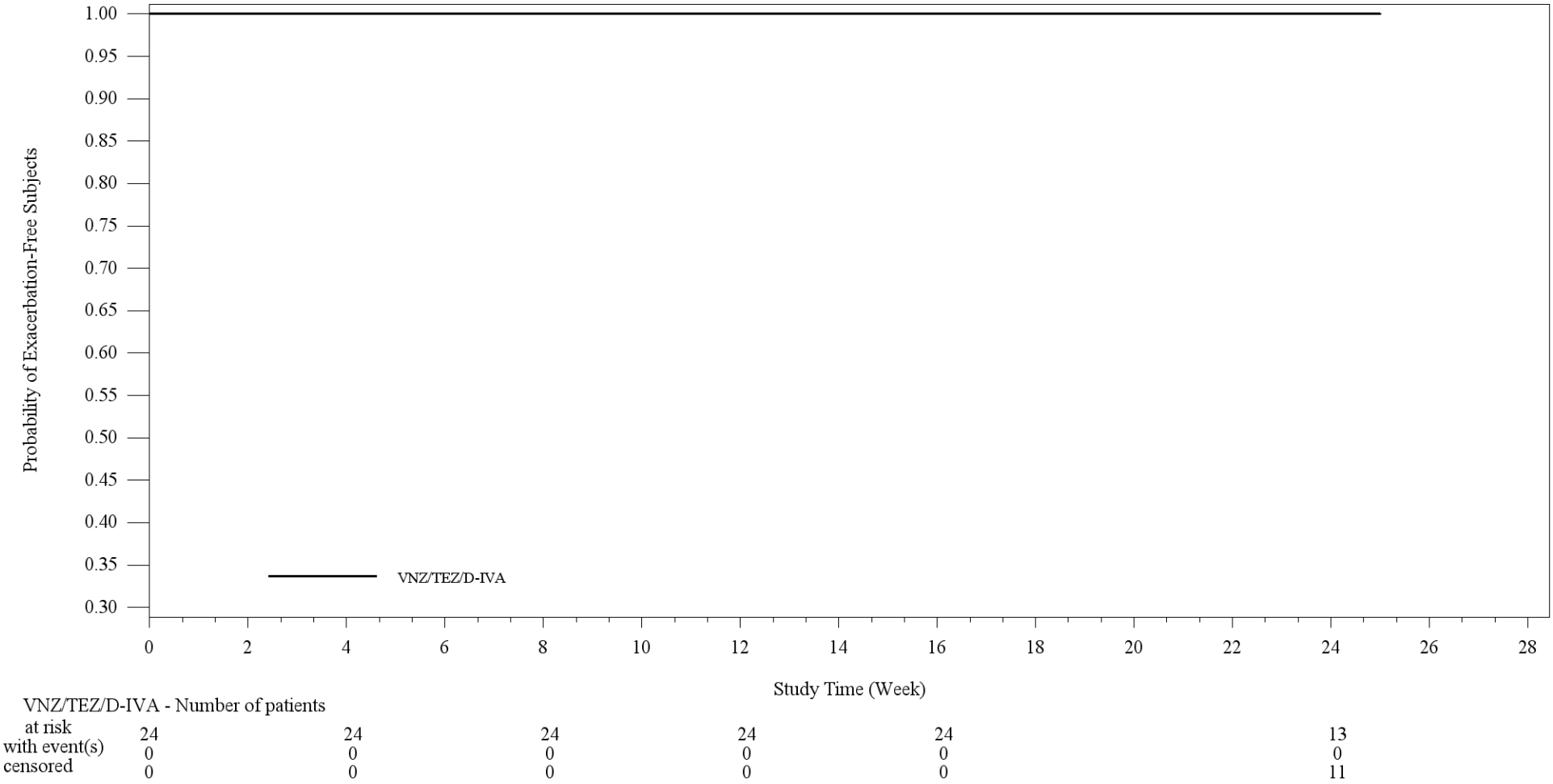
VNZ/TEZ/D-IVA - Number of patients						
at risk	24	24	24	23	23	13
with event(s)	0	0	0	1	1	2
censored	0	0	0	0	0	9

Figure 1.2.1.15.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24 for F/MF
Full Analysis Set



VNZ/TEZ/D-IVA - Number of patients						
at risk	24	24	24	24	24	13
with event(s)	0	0	0	0	0	0
censored	0	0	0	0	0	11

Figure 1.2.1.16.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24 for F/MF
Full Analysis Set



- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration
Sex = Male

Subgroup criteria are not met for this subgroup factor.

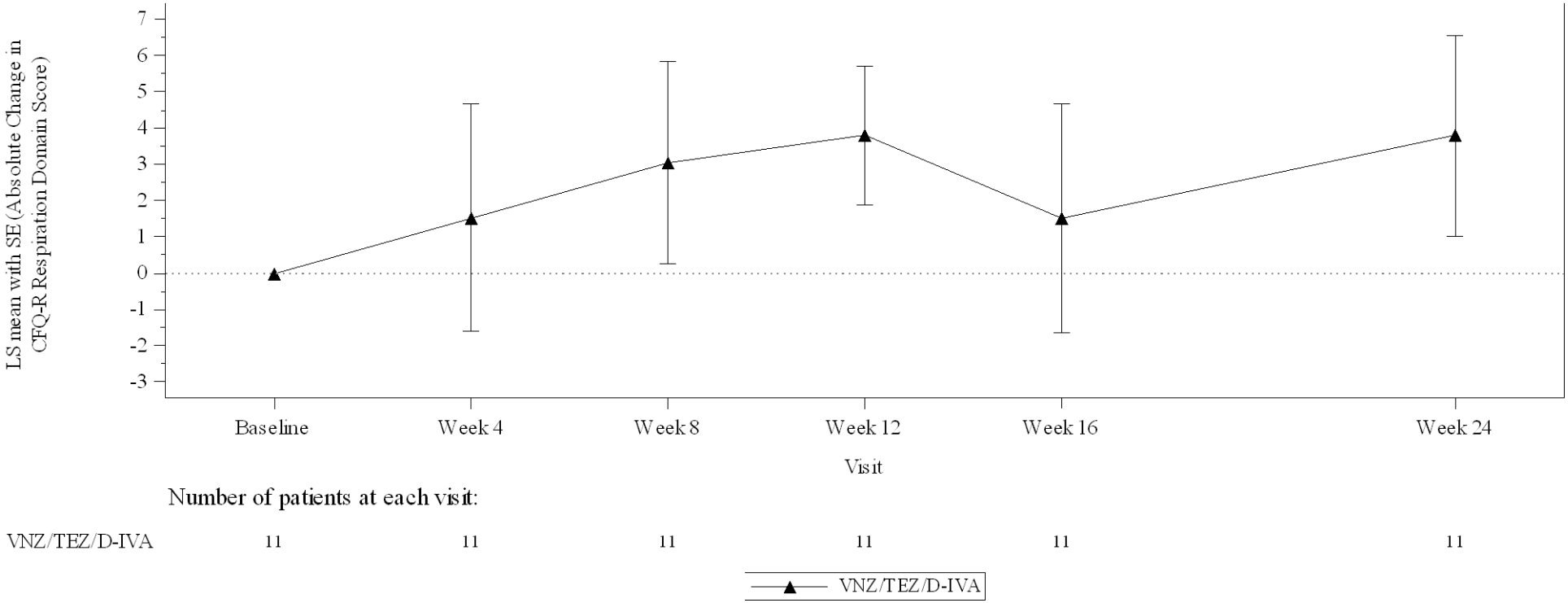
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration
Sex = Female

Subgroup criteria are not met for this subgroup factor.

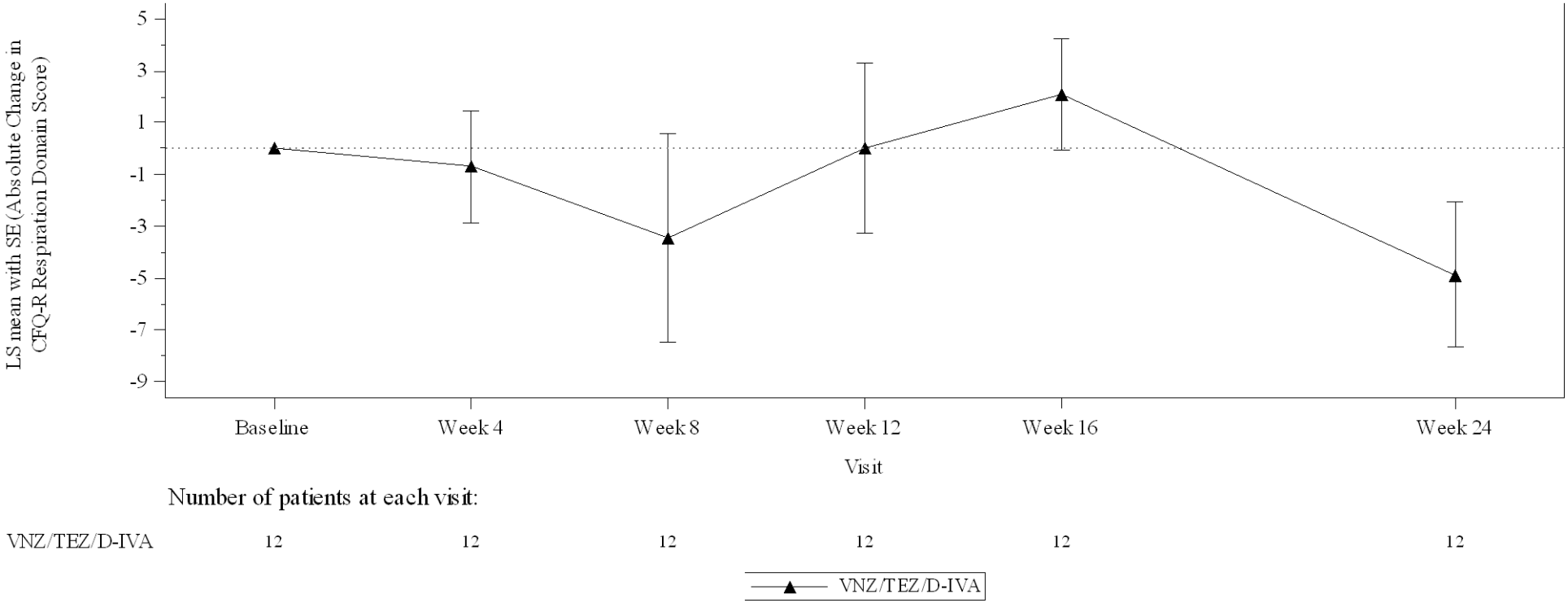
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body
Sex = Male

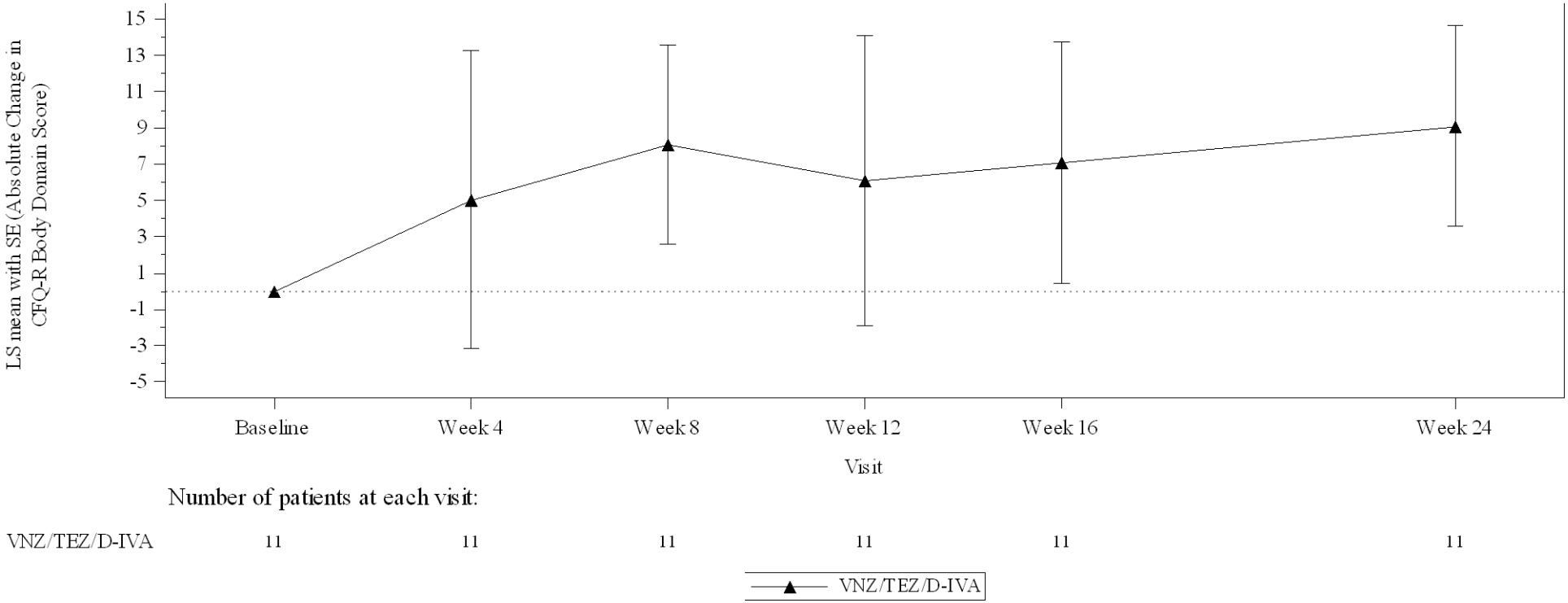
Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body
Sex = Female

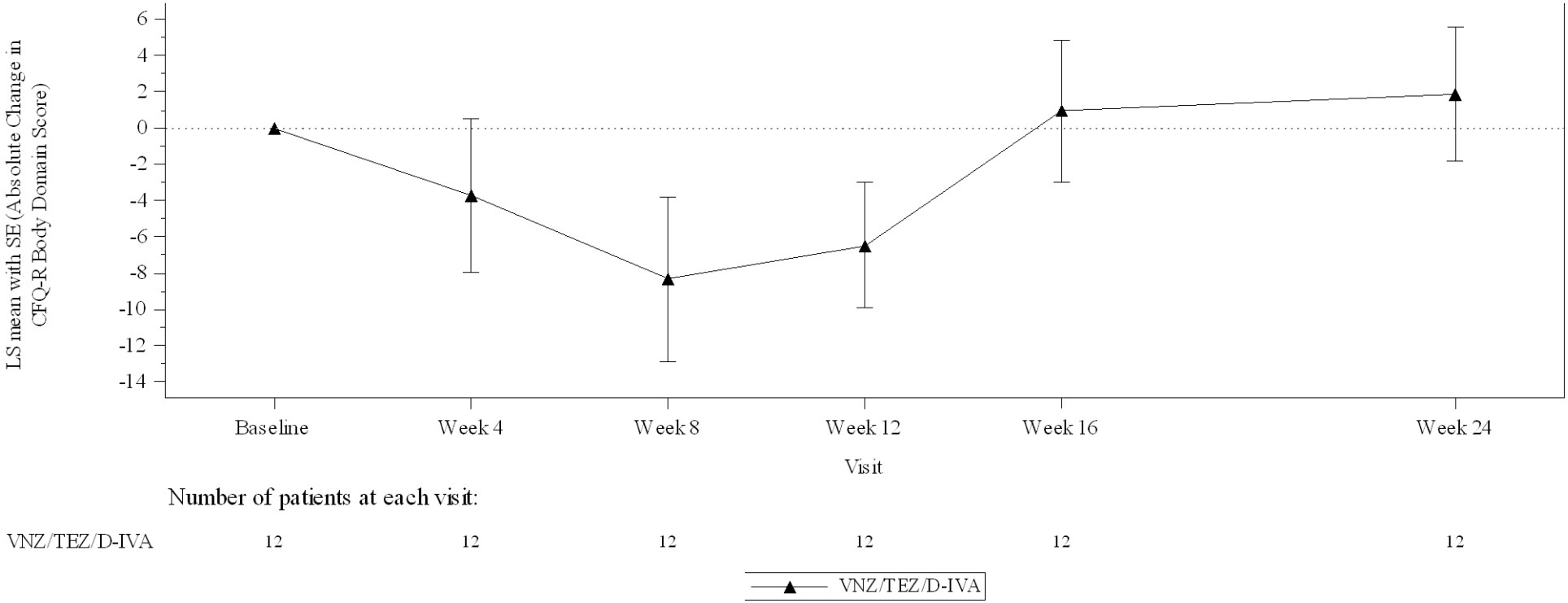
Subgroup criteria are not met for this subgroup factor.

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion
Sex = Male

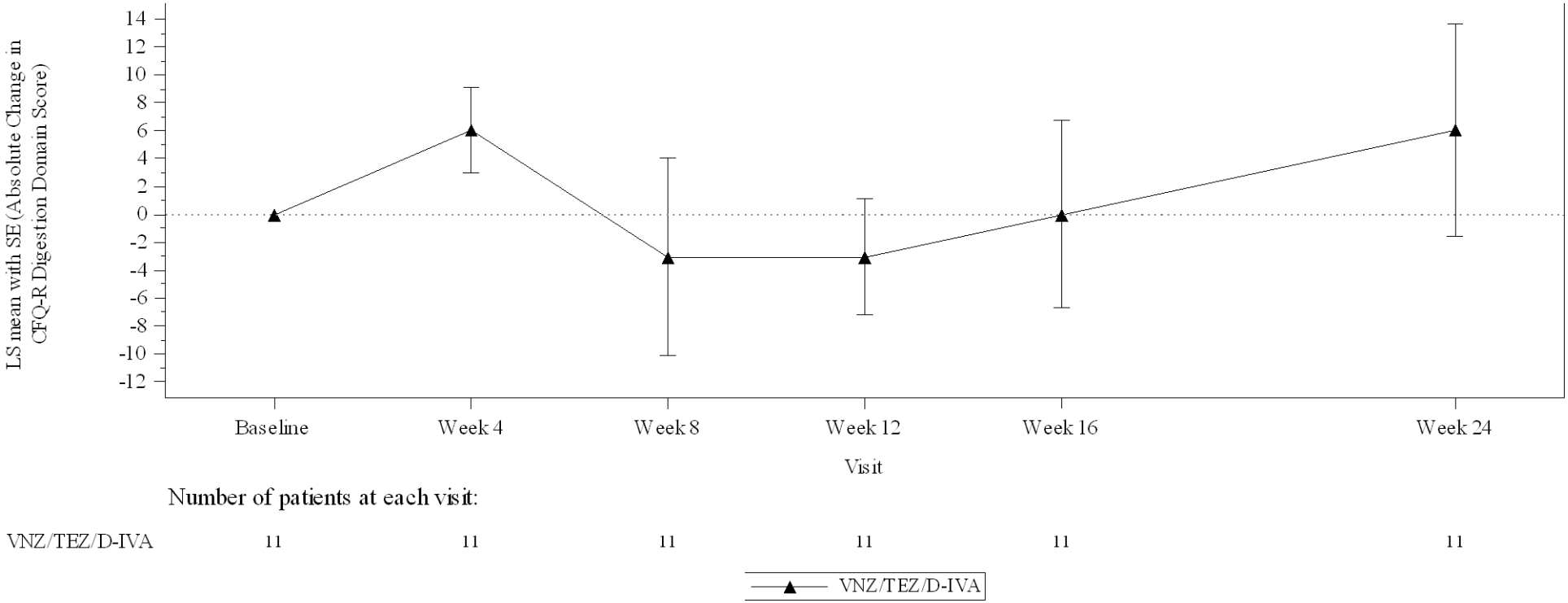
Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion
Sex = Female

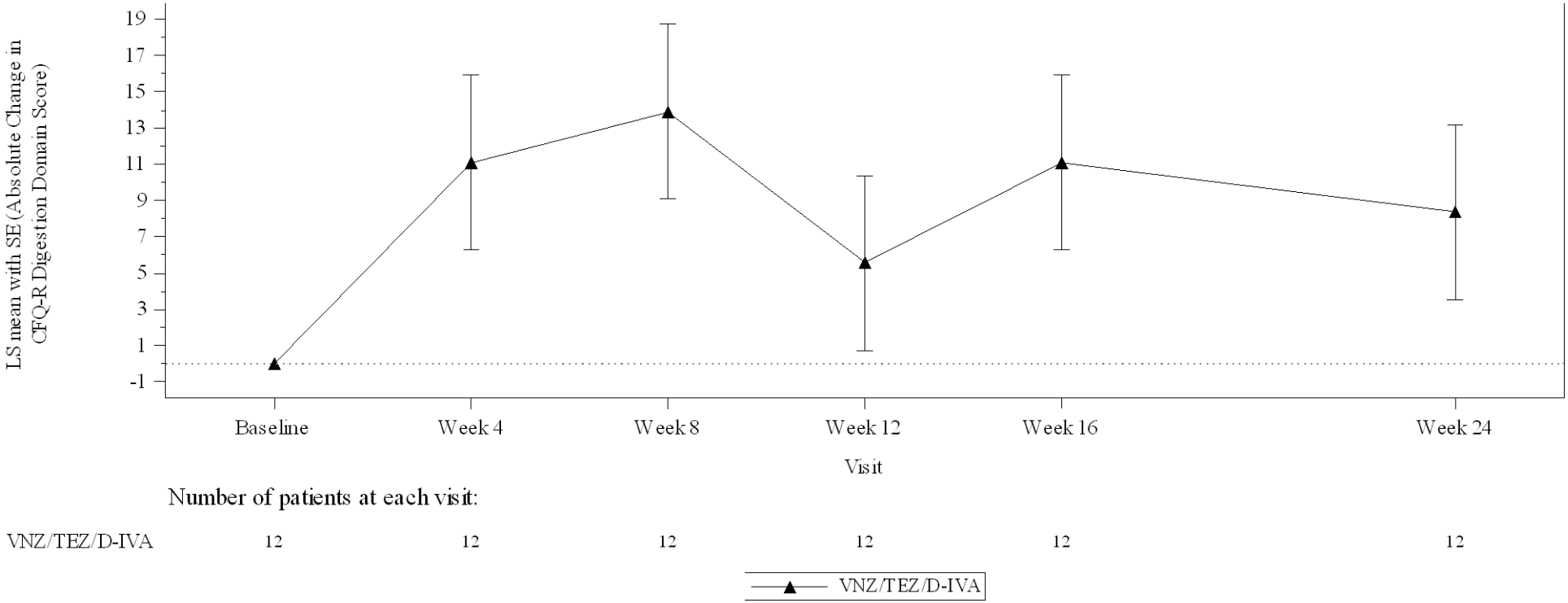
Subgroup criteria are not met for this subgroup factor.

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

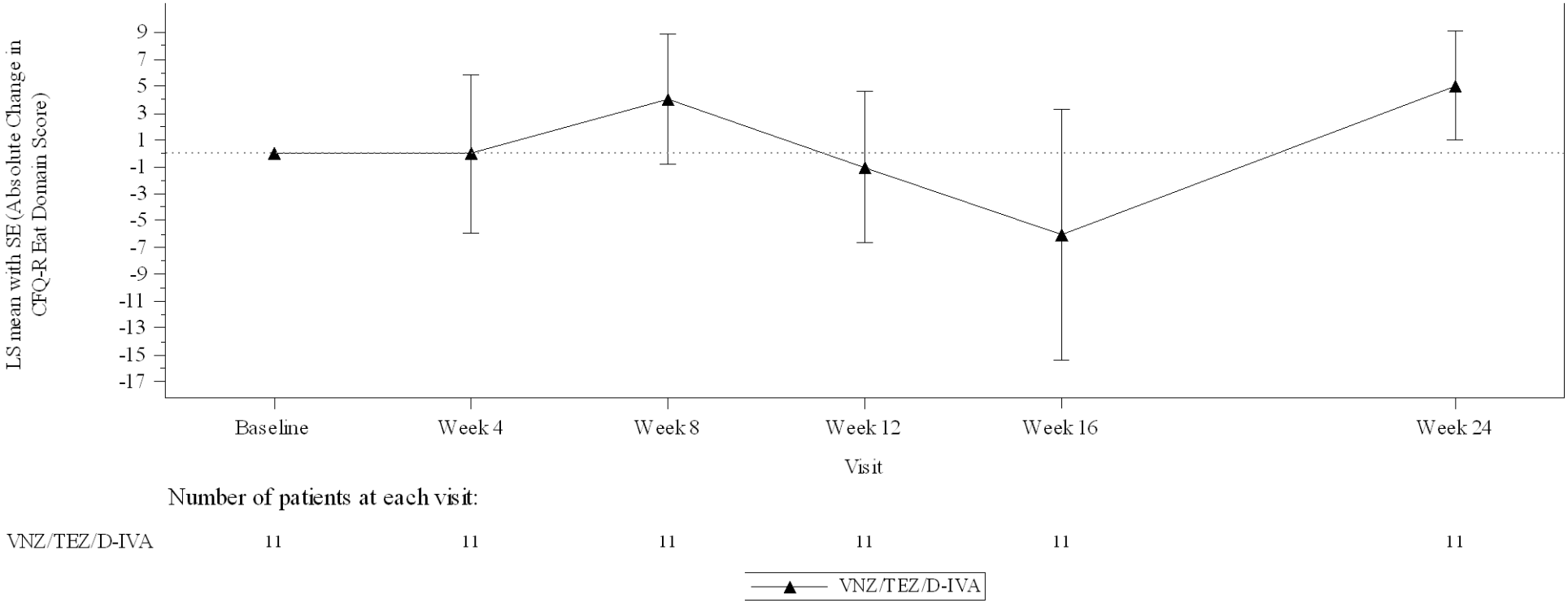
Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat
Sex = Male

Subgroup criteria are not met for this subgroup factor.

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat
Sex = Female

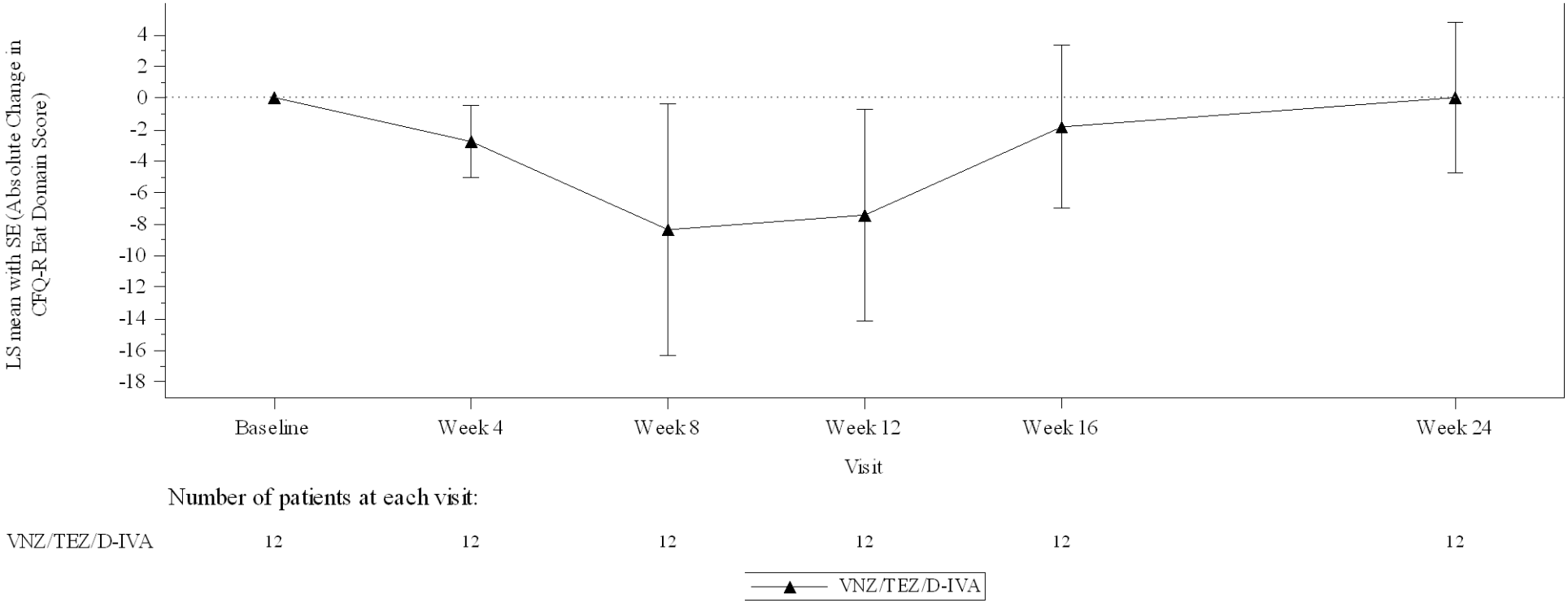
Subgroup criteria are not met for this subgroup factor.

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion
Sex = Male

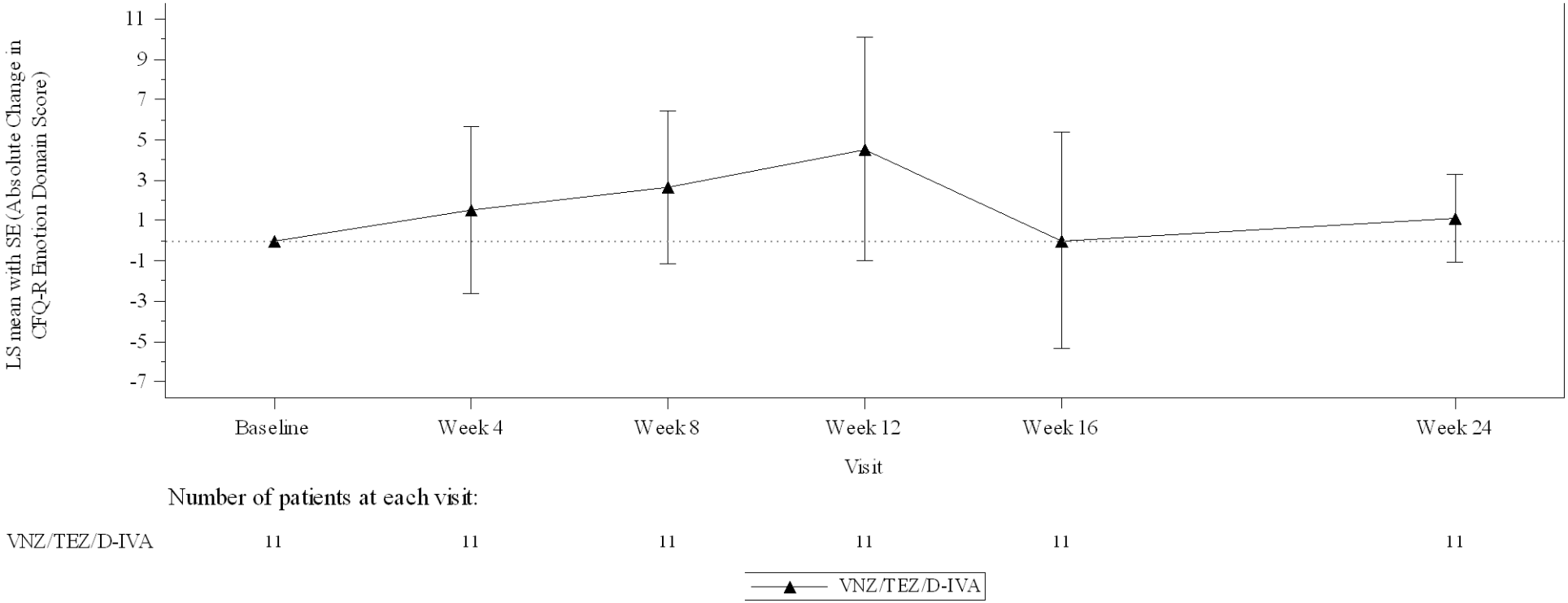
Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion
Sex = Female

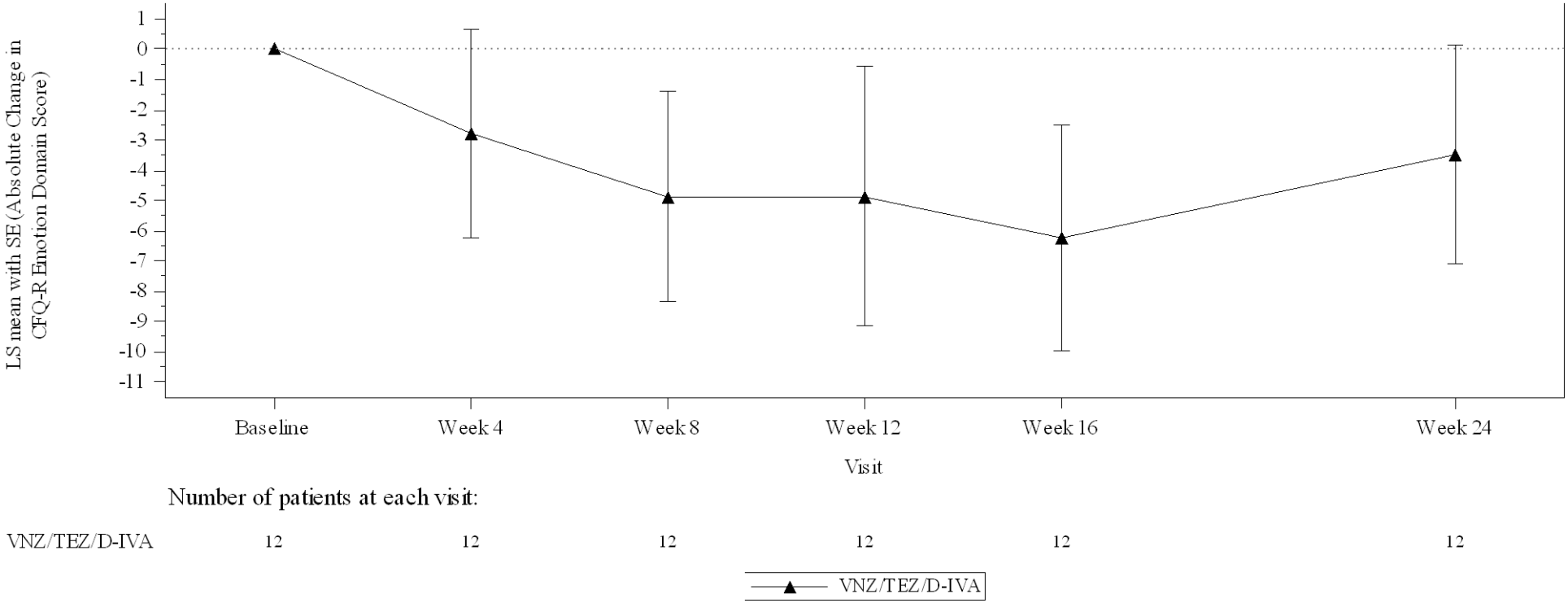
Subgroup criteria are not met for this subgroup factor.

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

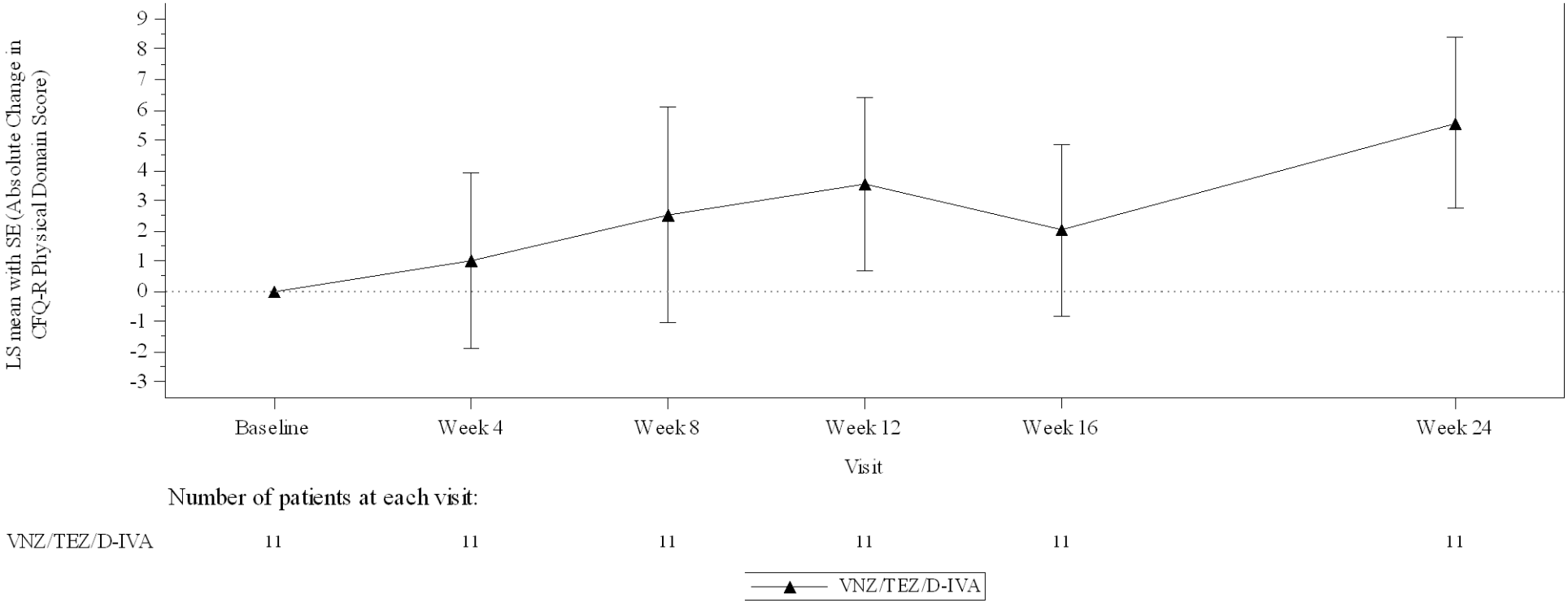
Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical
Sex = Male

Subgroup criteria are not met for this subgroup factor.

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical
Sex = Female

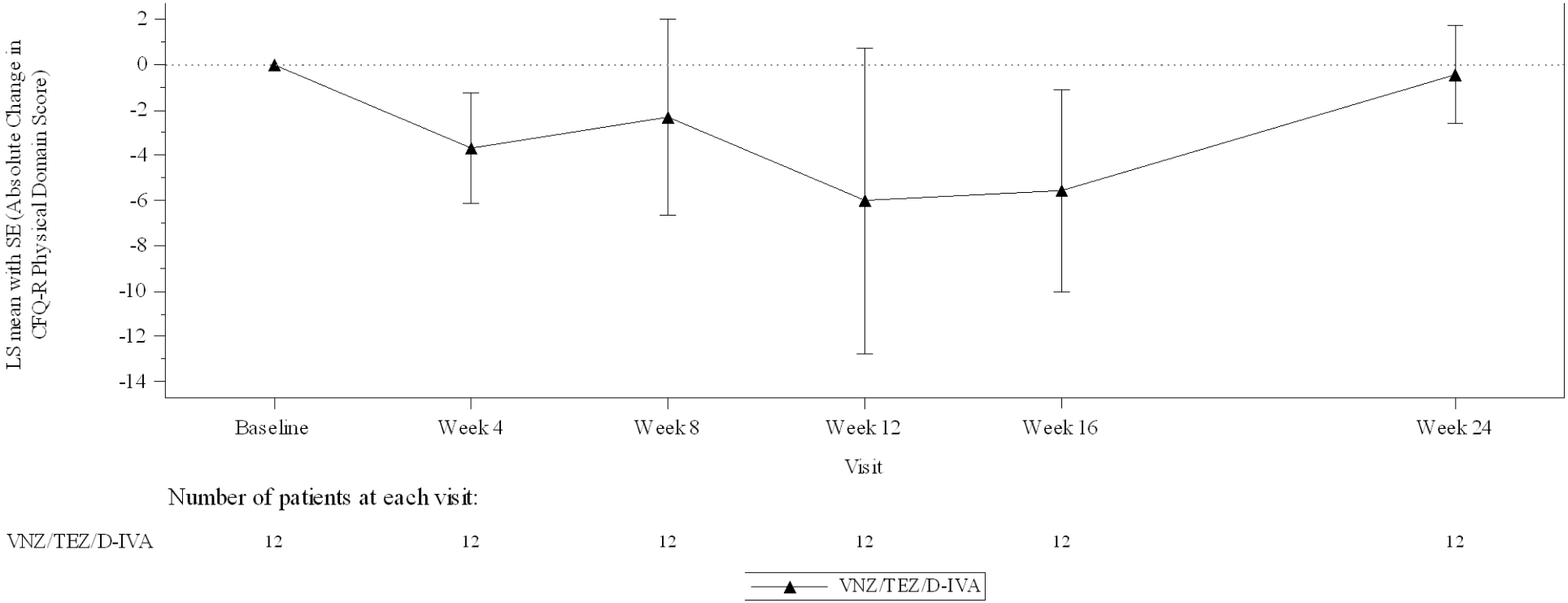
Subgroup criteria are not met for this subgroup factor.

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Social
Sex = Male

Subgroup criteria are not met for this subgroup factor.

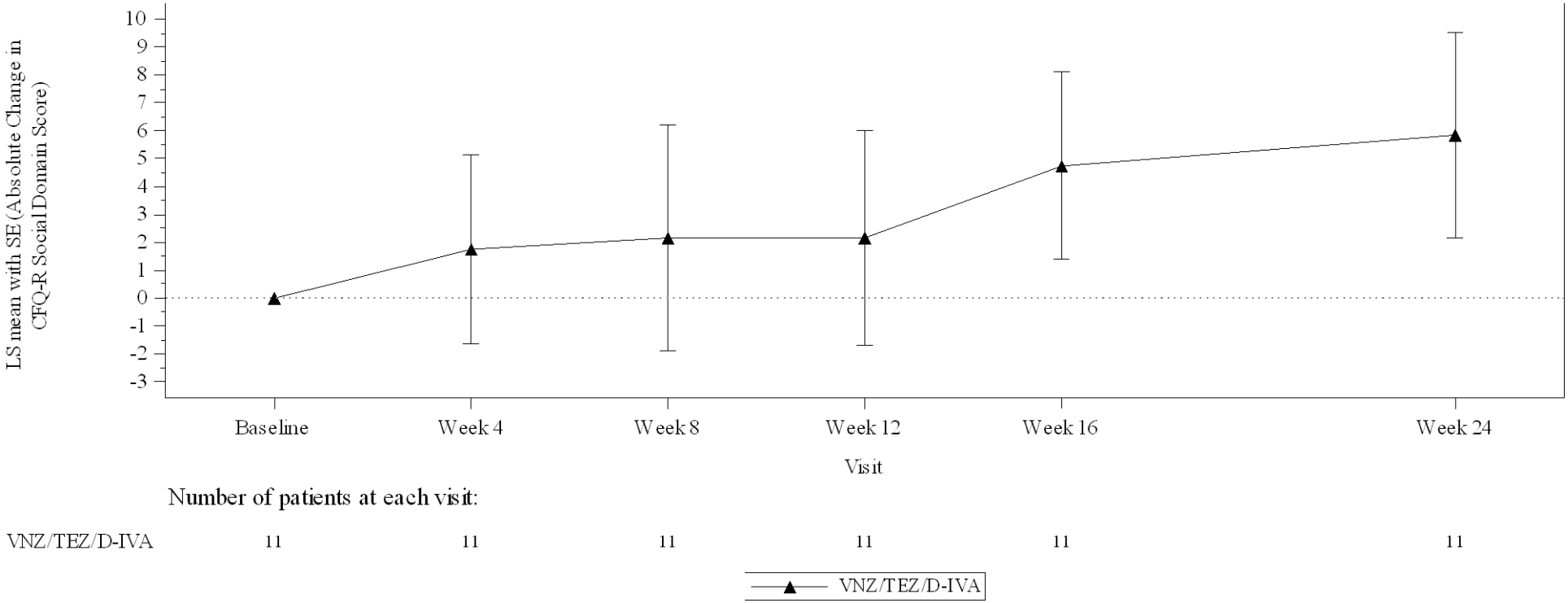
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Social
Sex = Female

Subgroup criteria are not met for this subgroup factor.

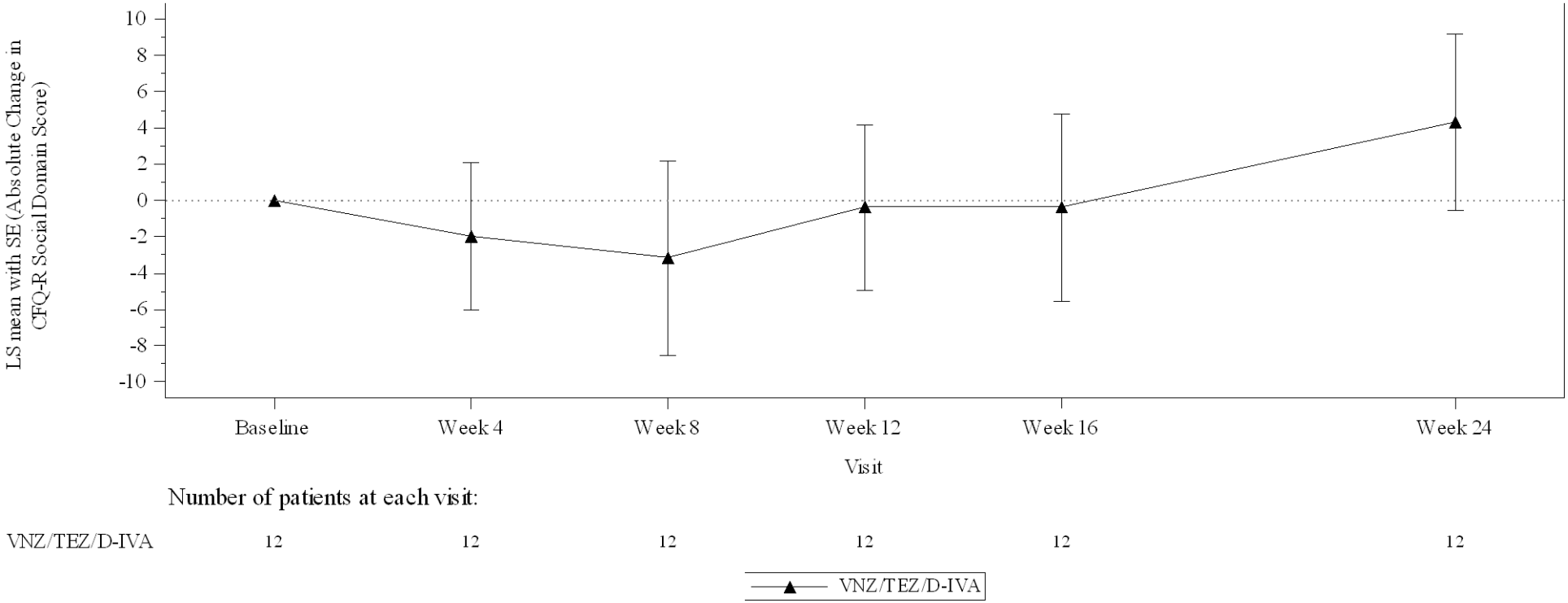
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Social
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Social
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Social
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden
Sex = Male

Subgroup criteria are not met for this subgroup factor.

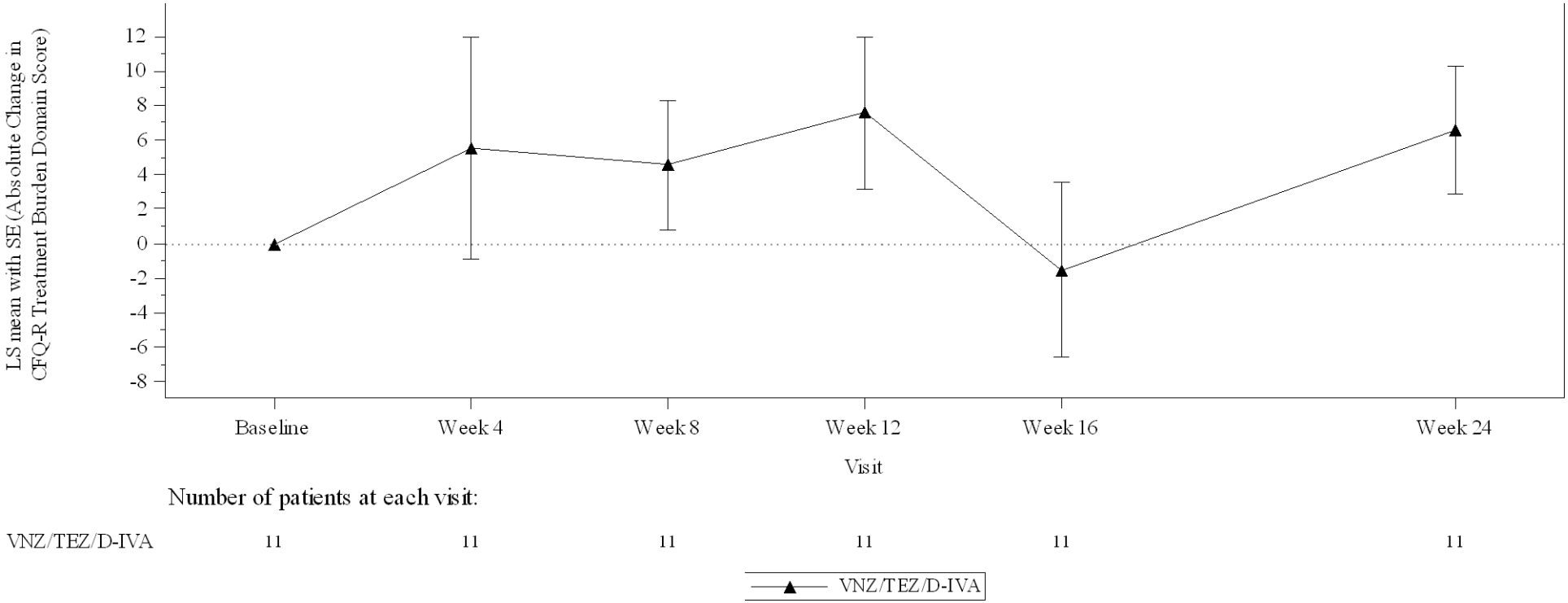
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden
Sex = Female

Subgroup criteria are not met for this subgroup factor.

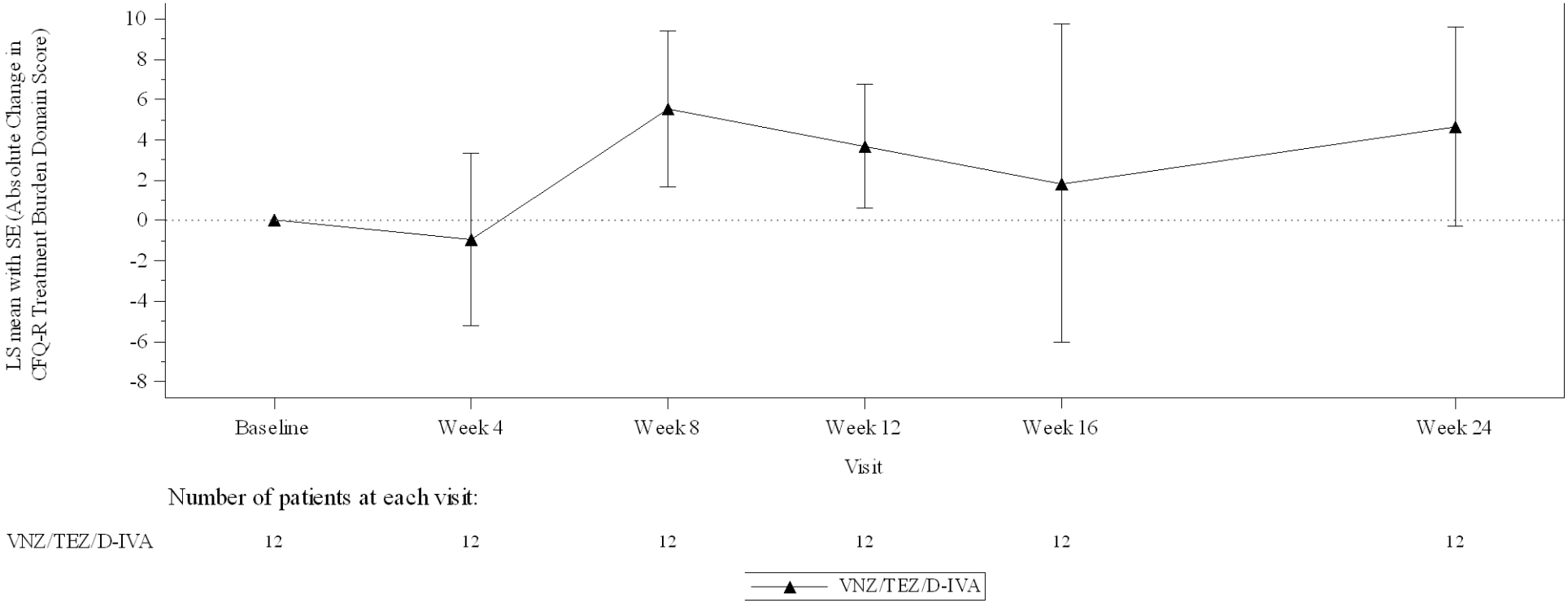
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

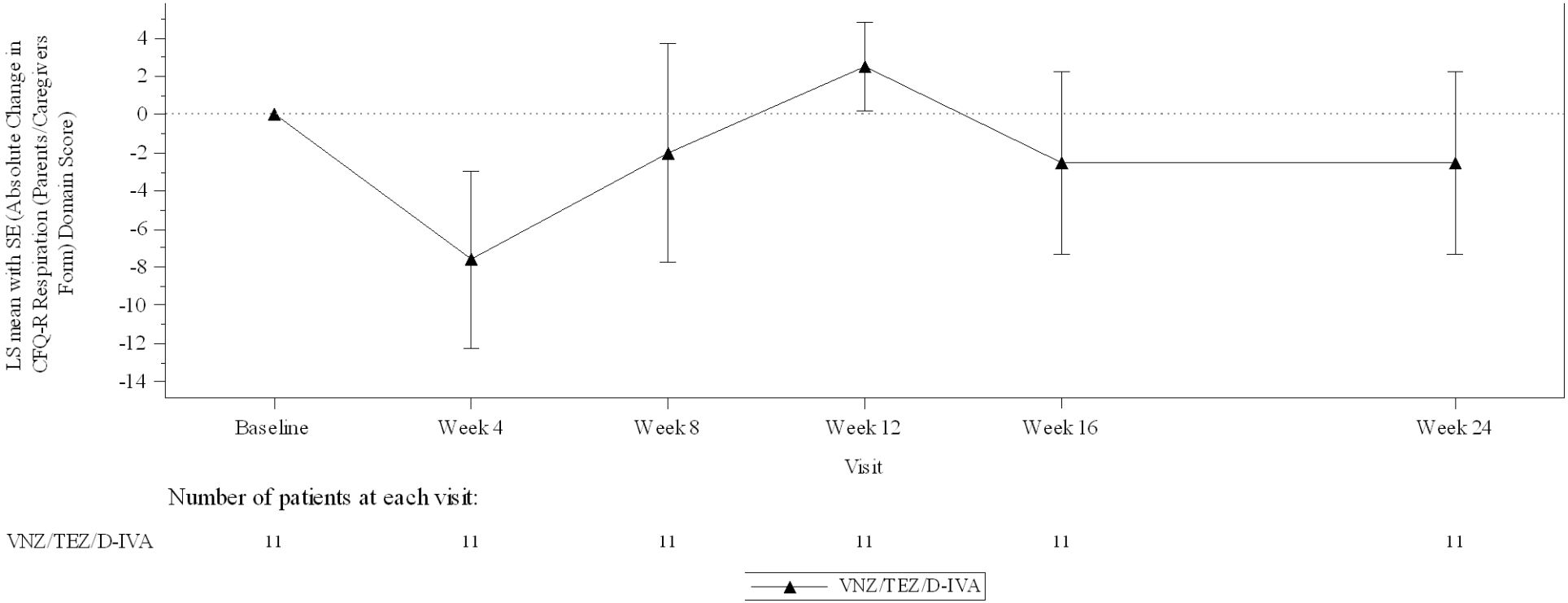
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

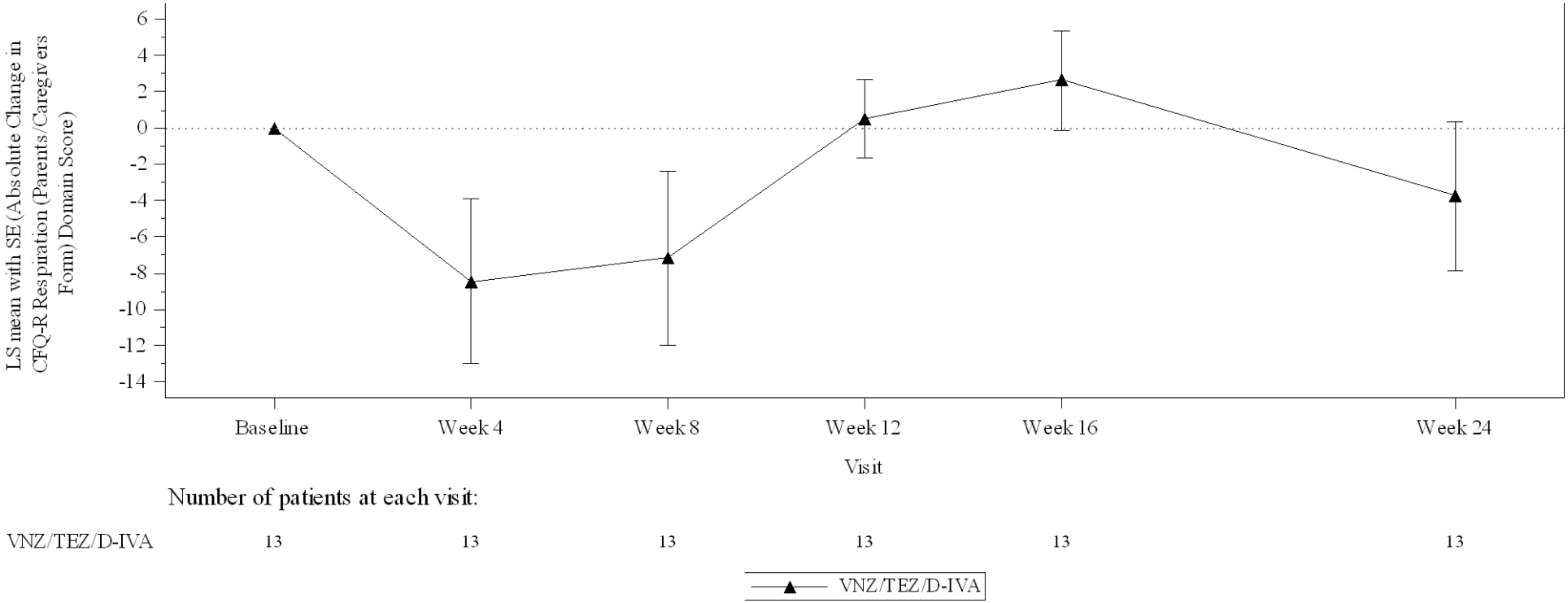
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

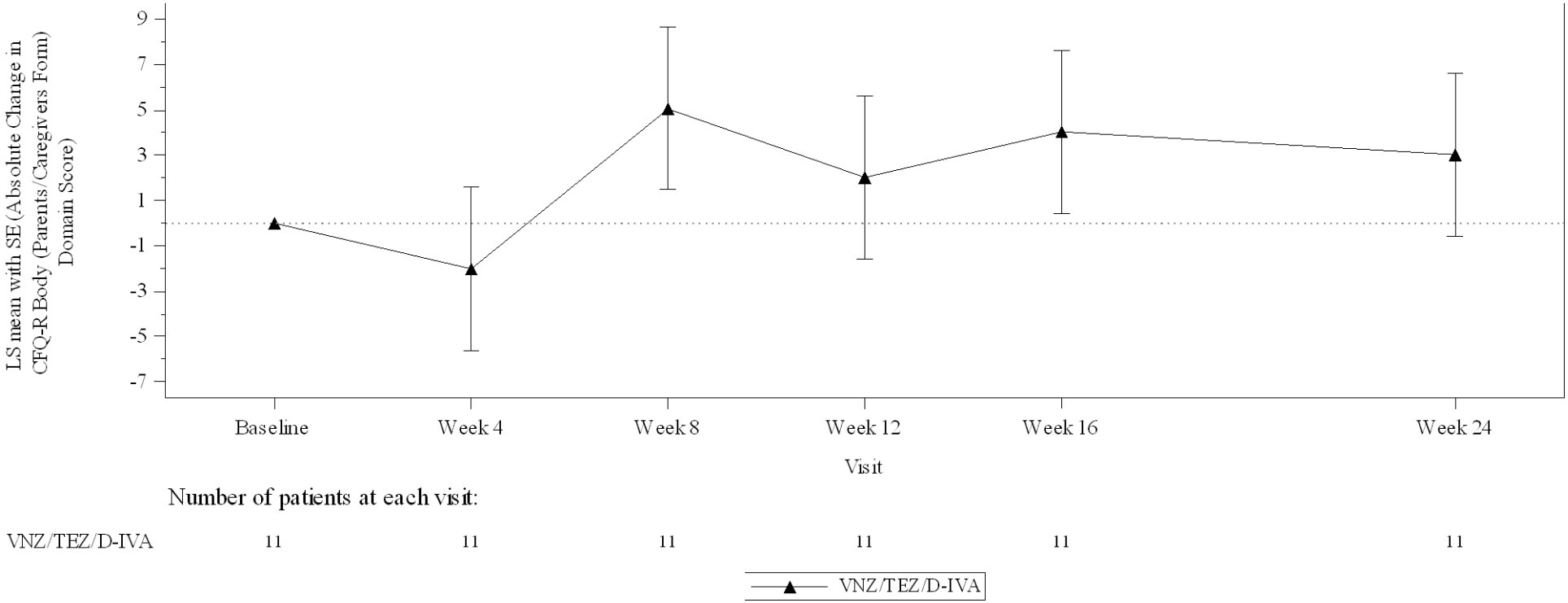
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

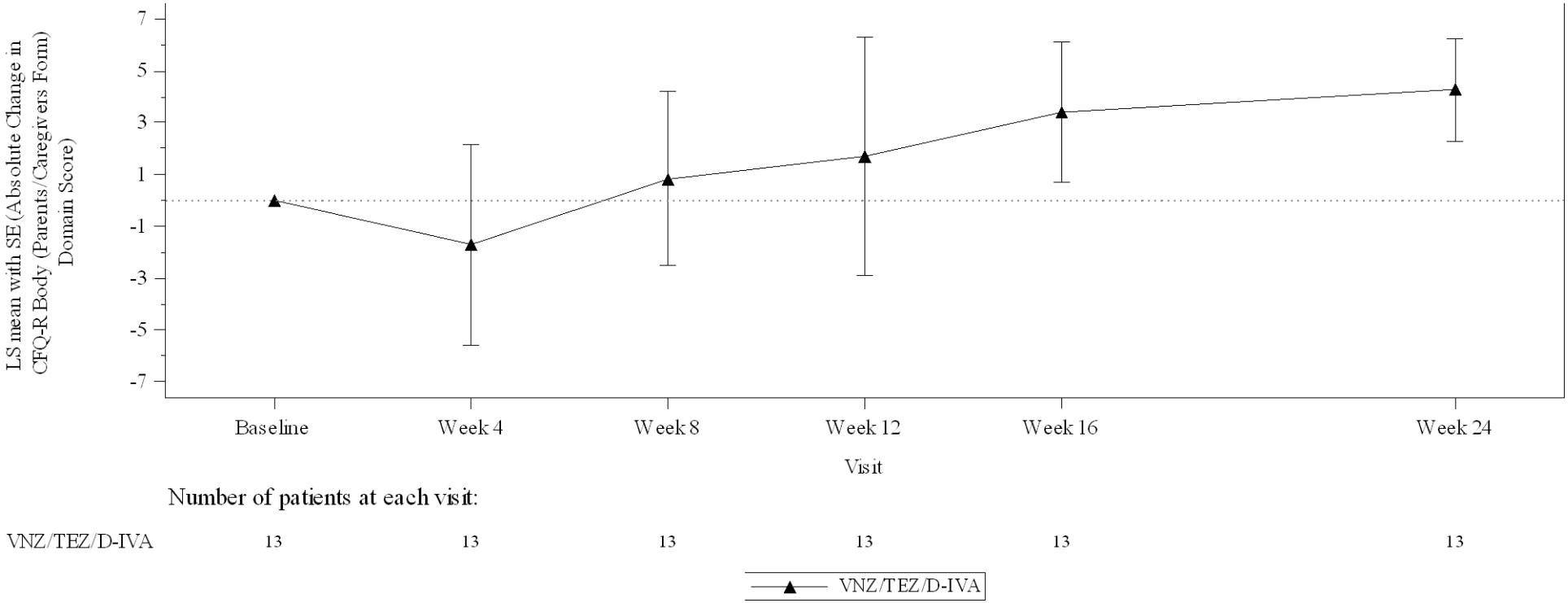
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

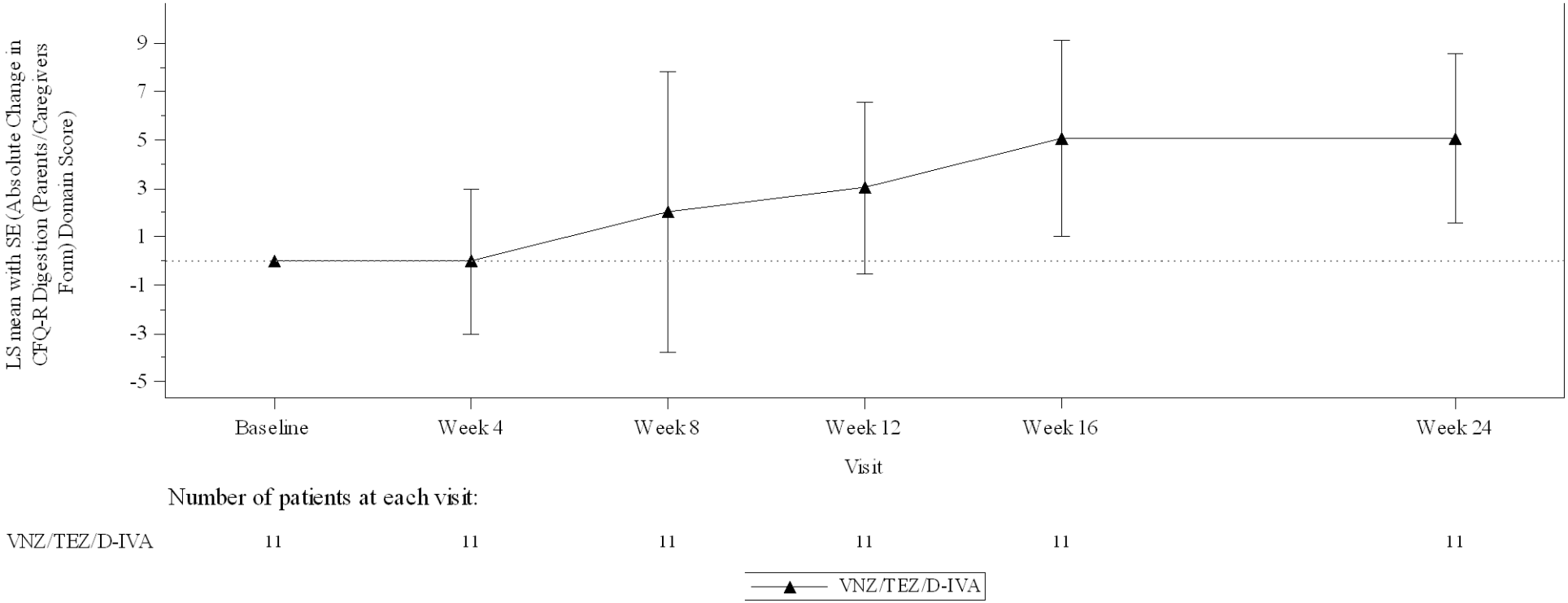
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

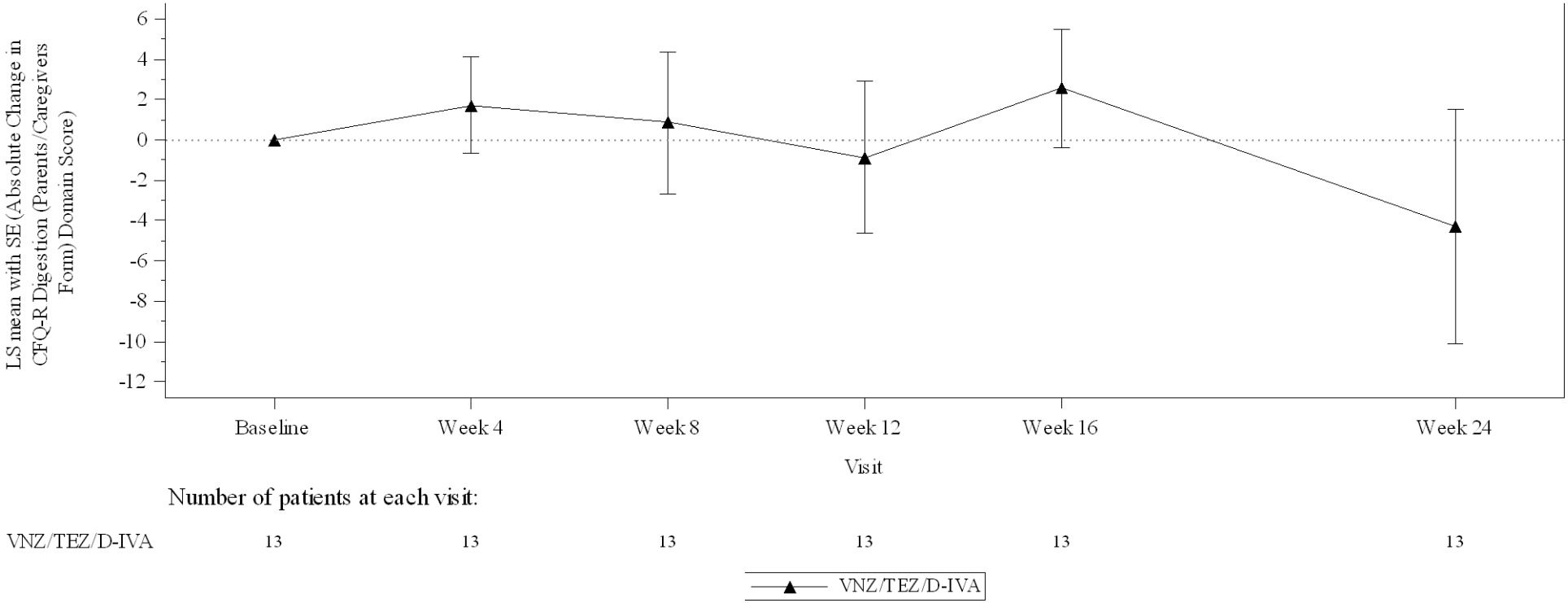
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

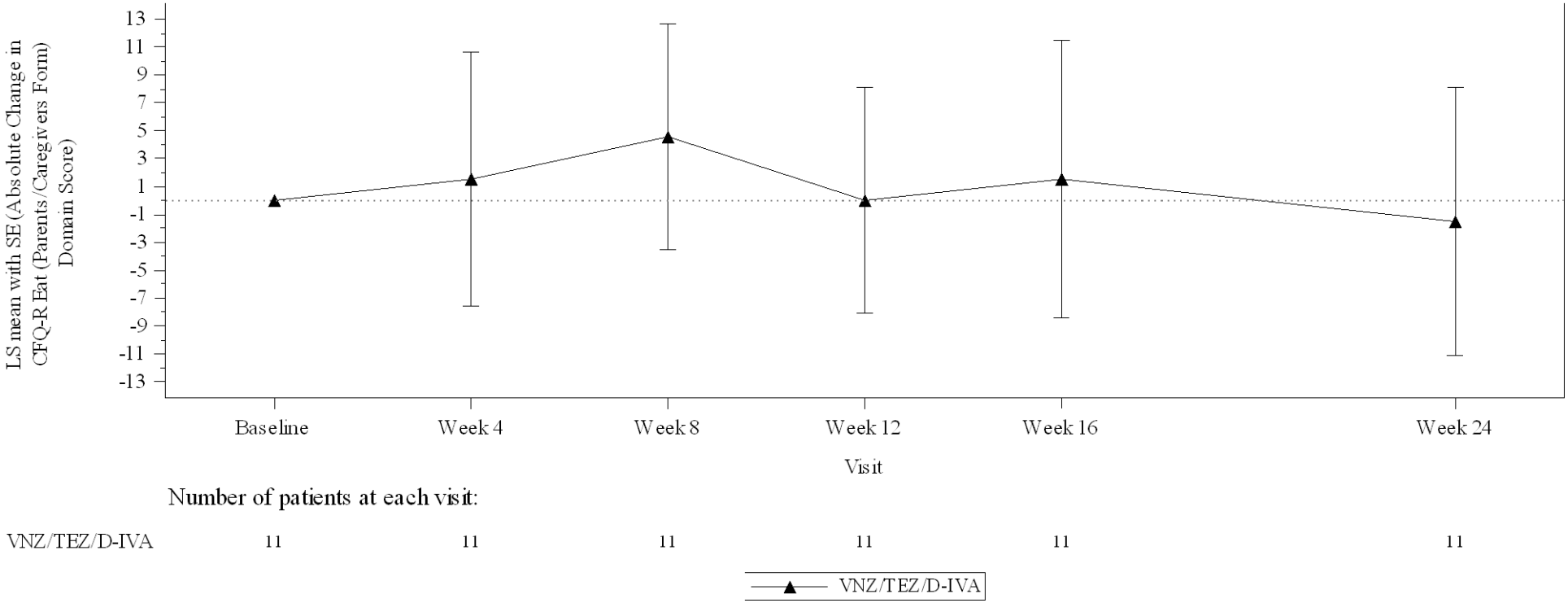
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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

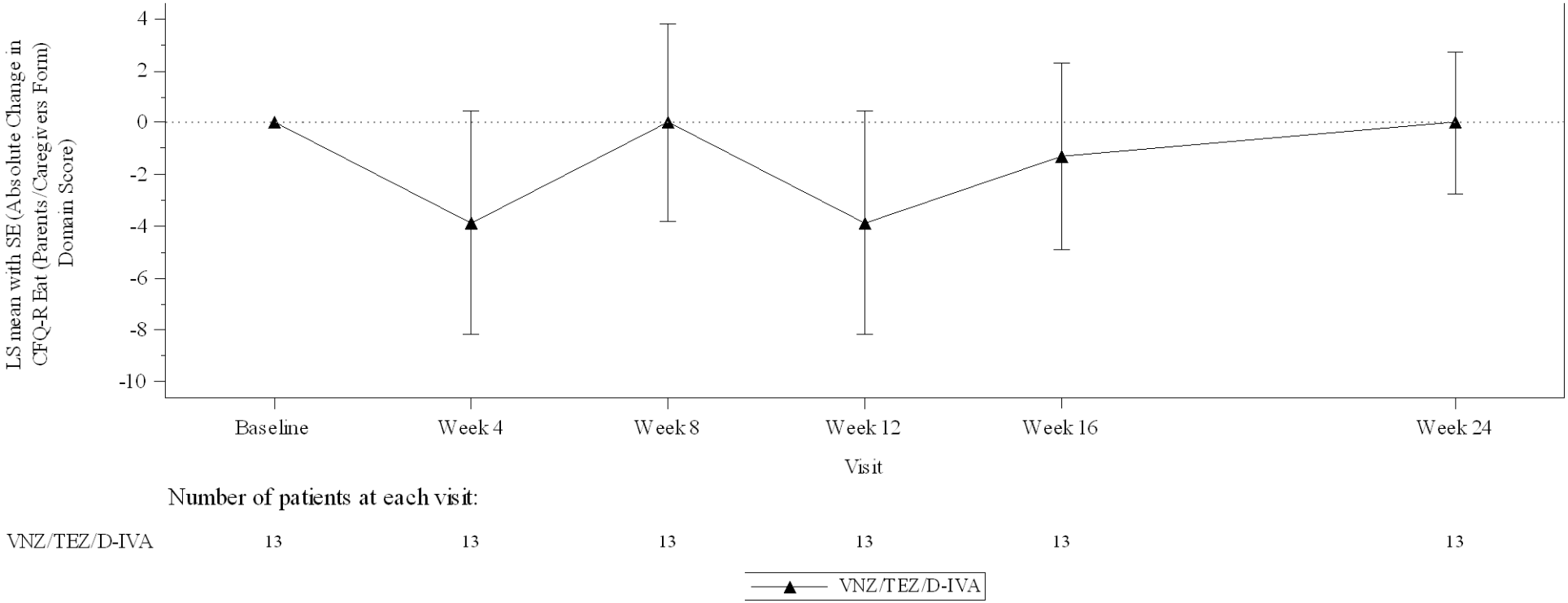
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

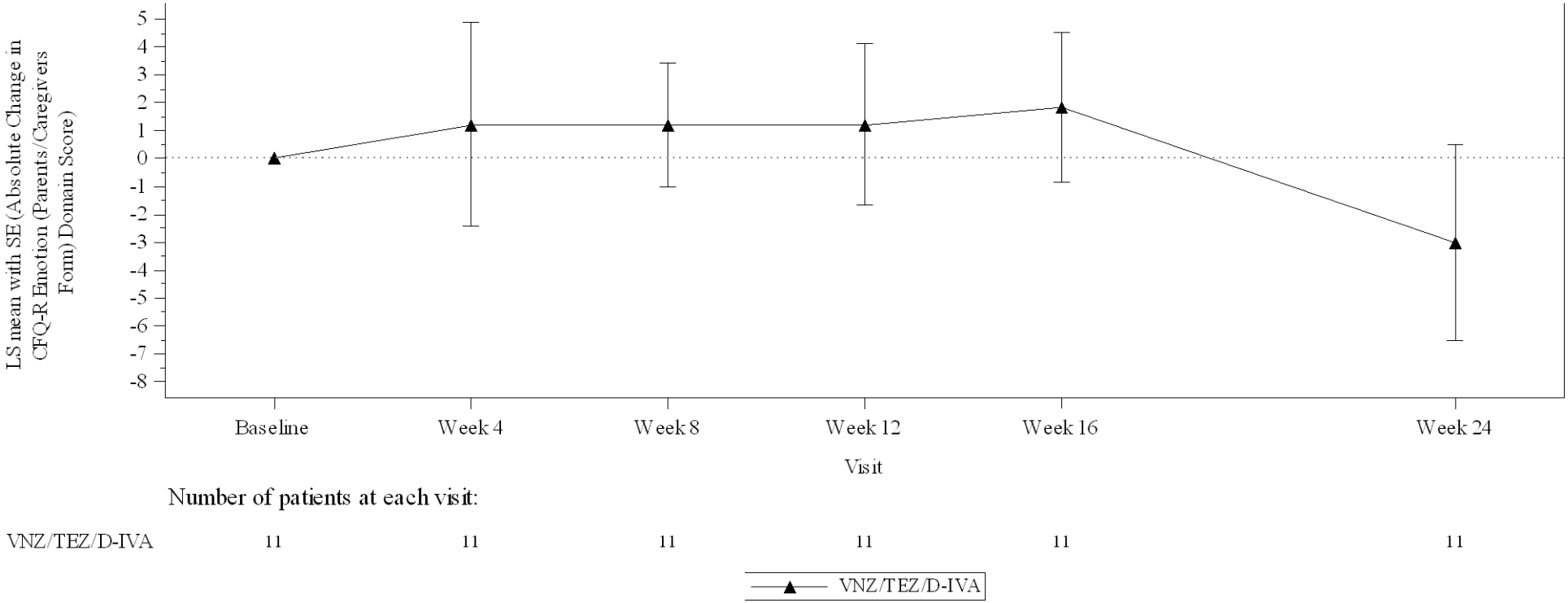
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

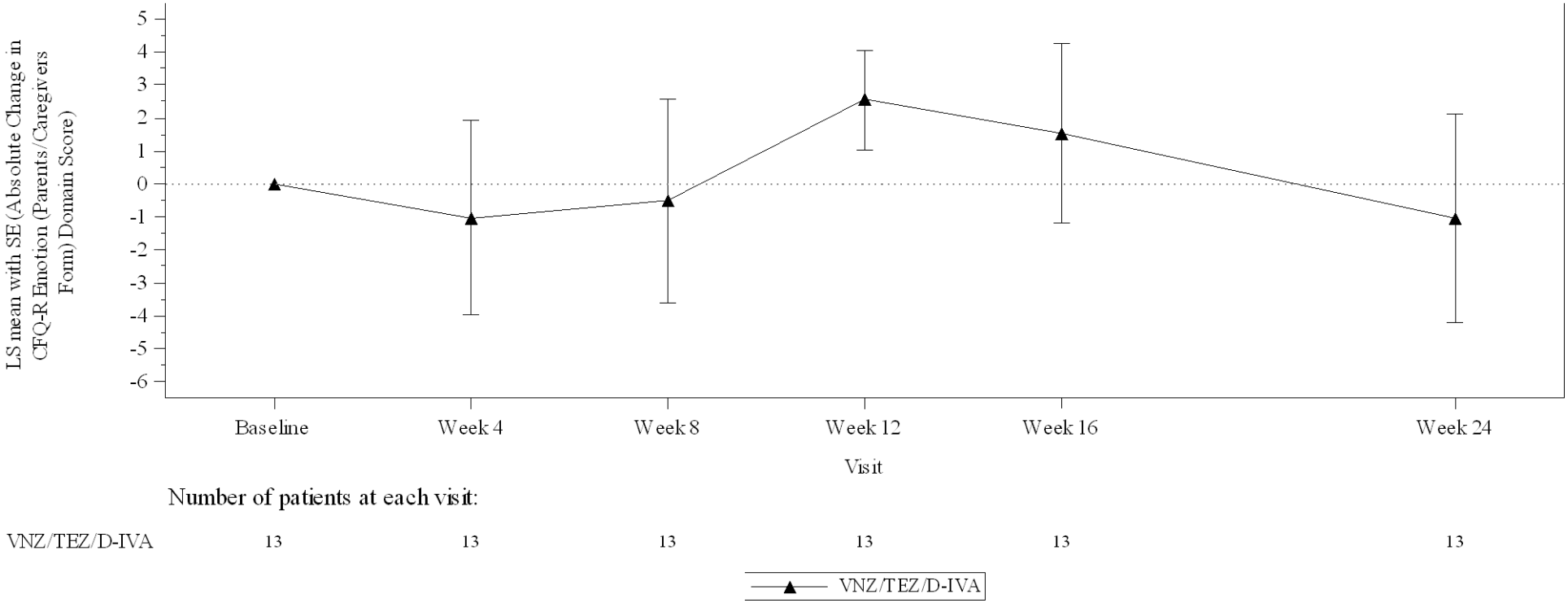
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

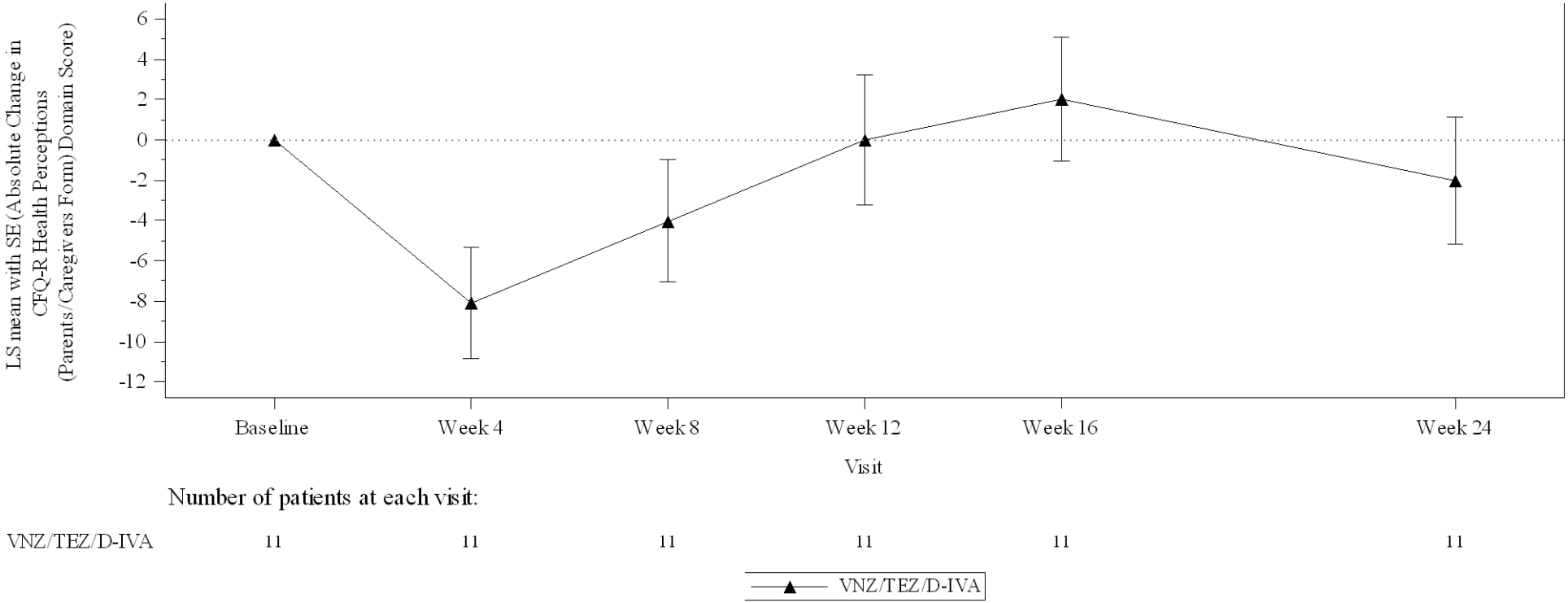
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

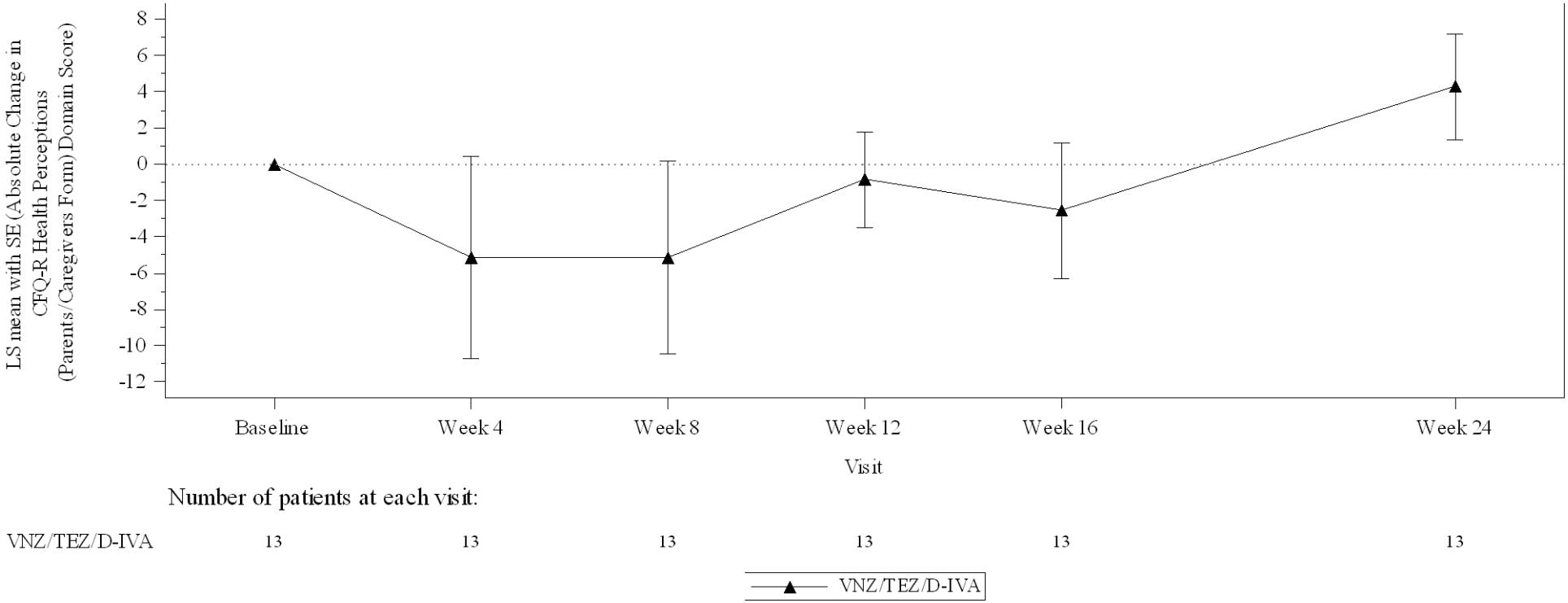
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

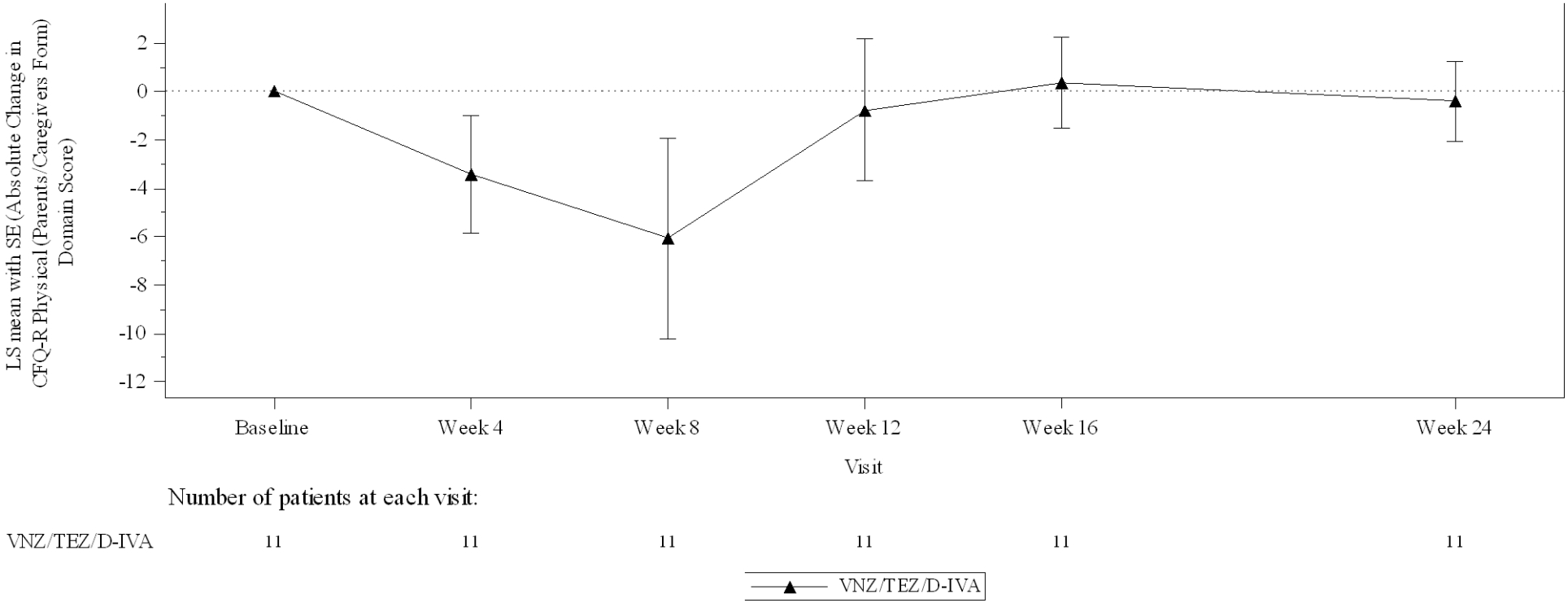
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

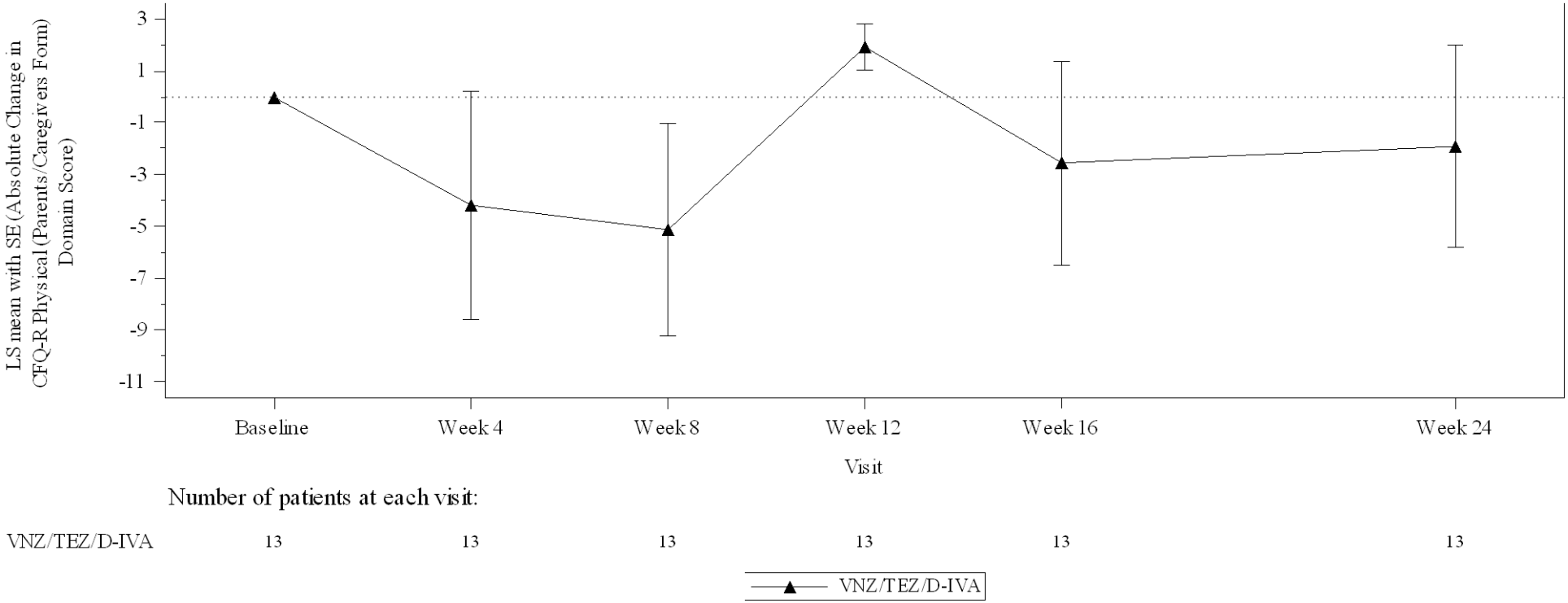
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

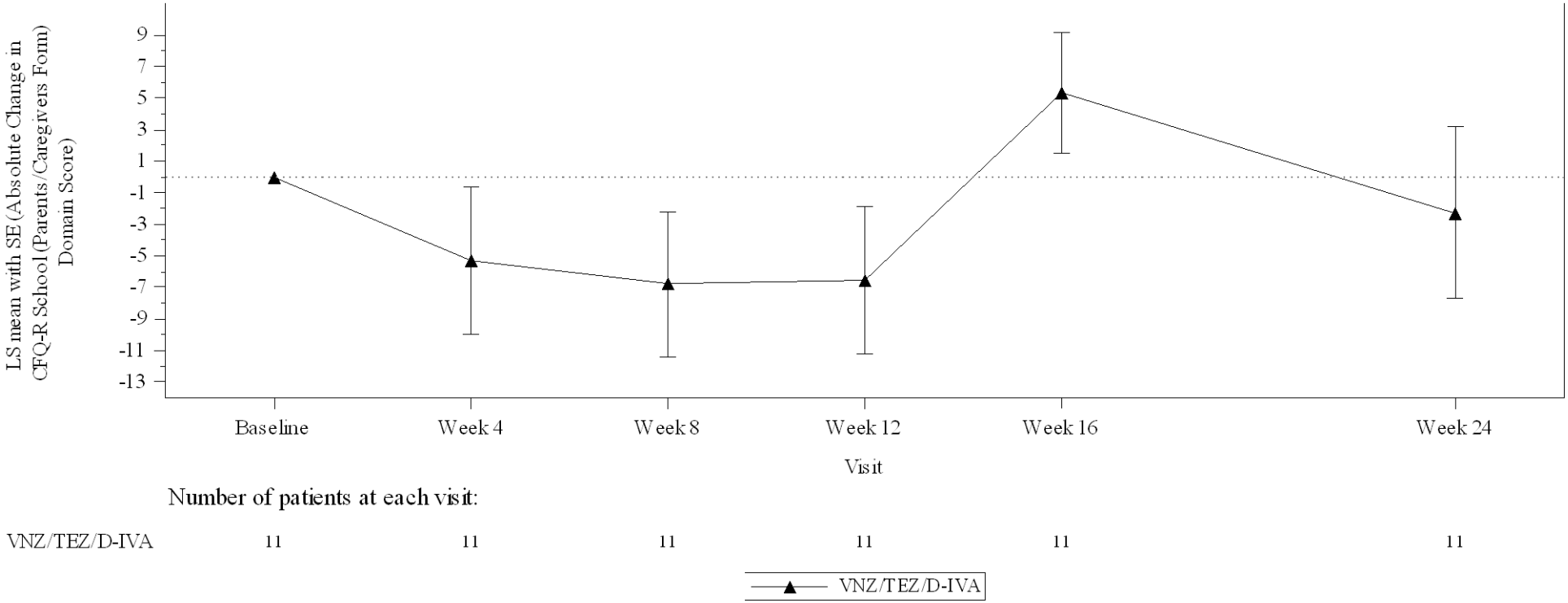
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

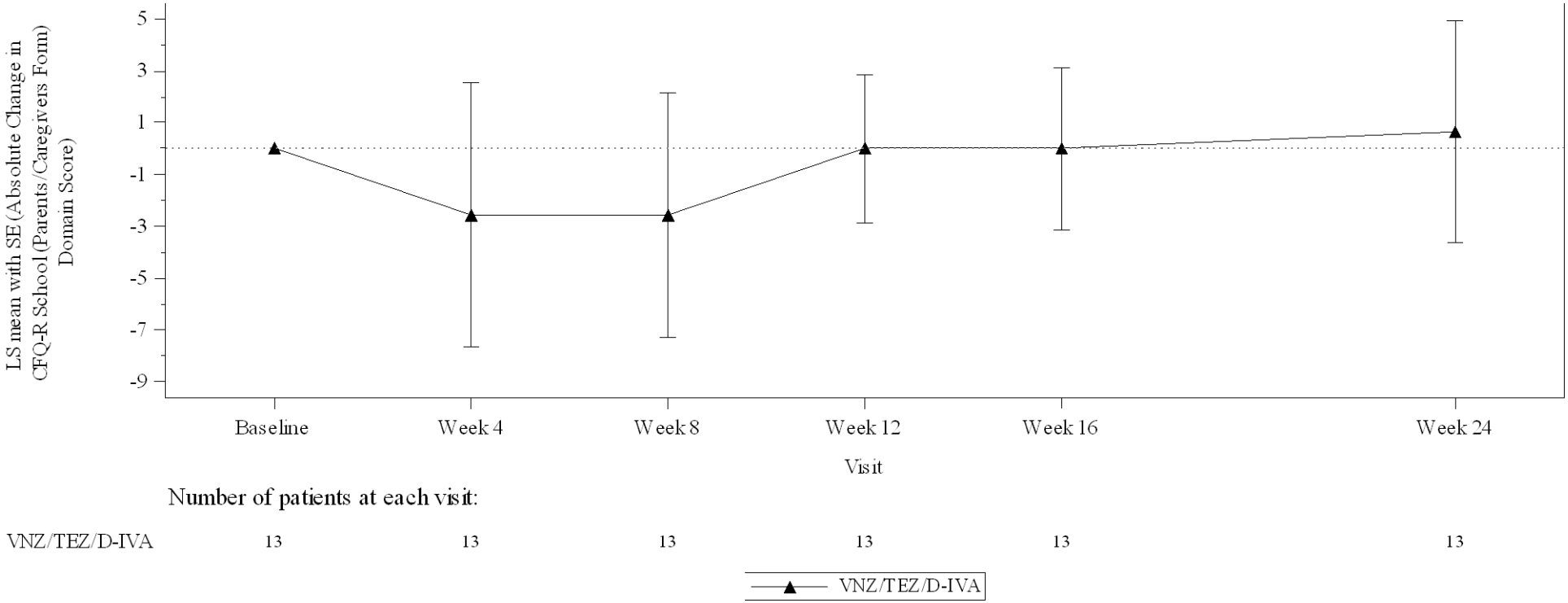
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

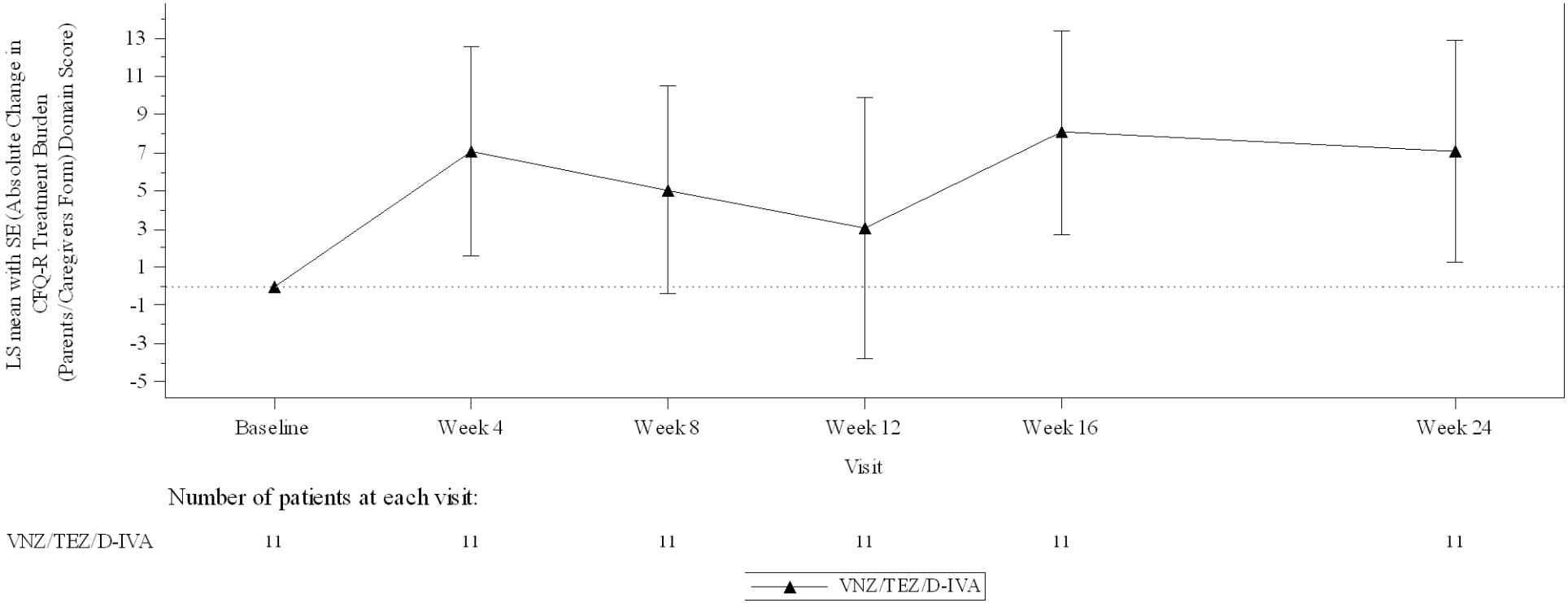
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

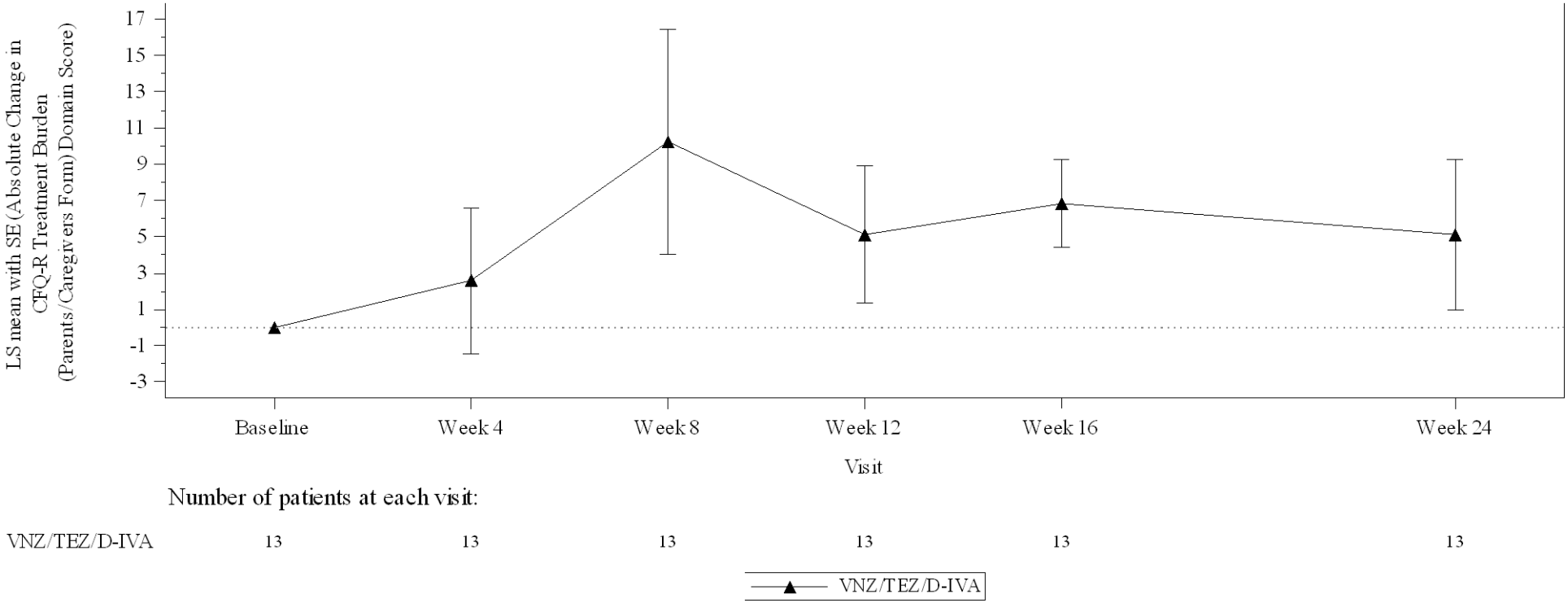
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

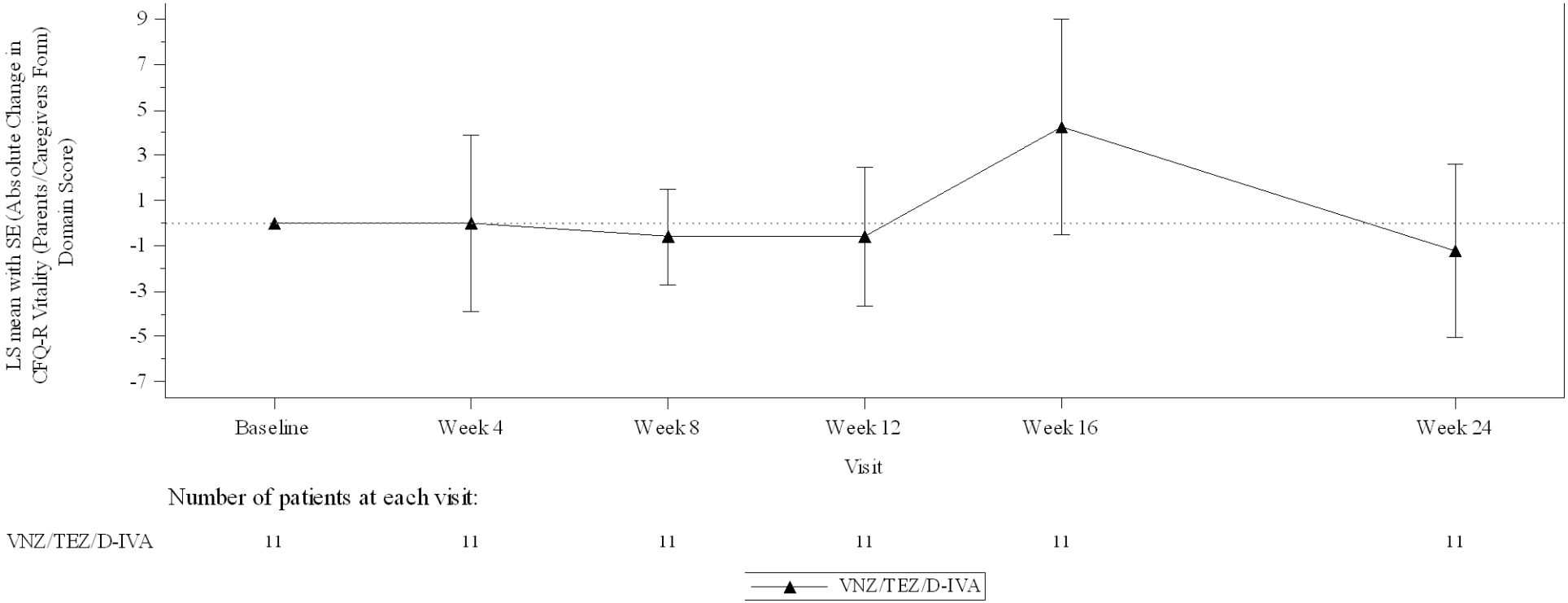
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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

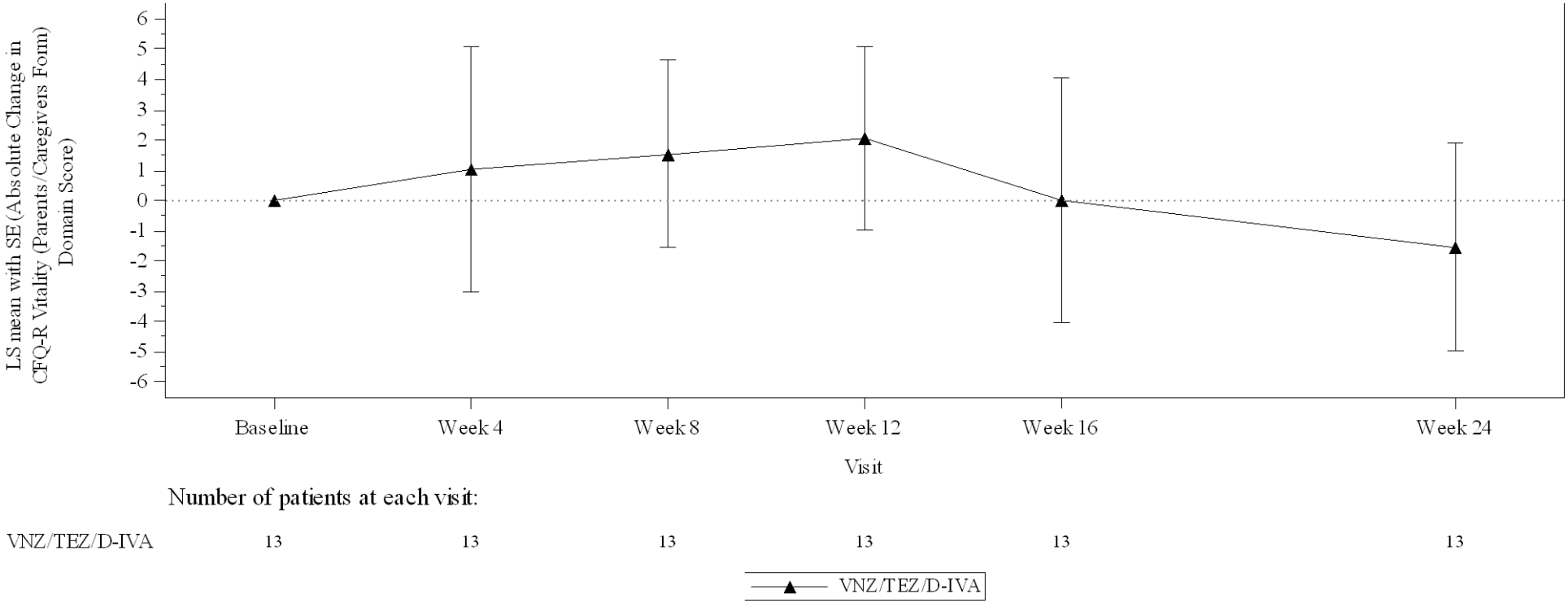
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Sex = Male

Subgroup criteria are not met for this subgroup factor.

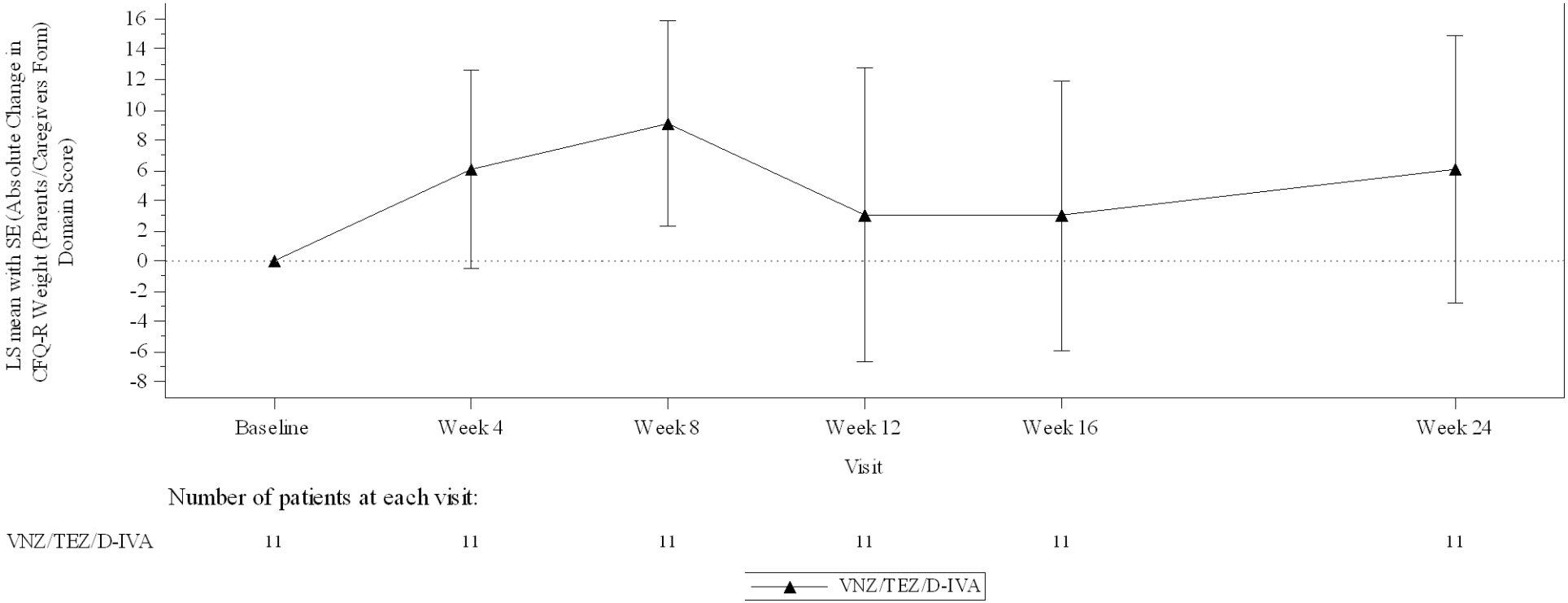
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Sex = Female

Subgroup criteria are not met for this subgroup factor.

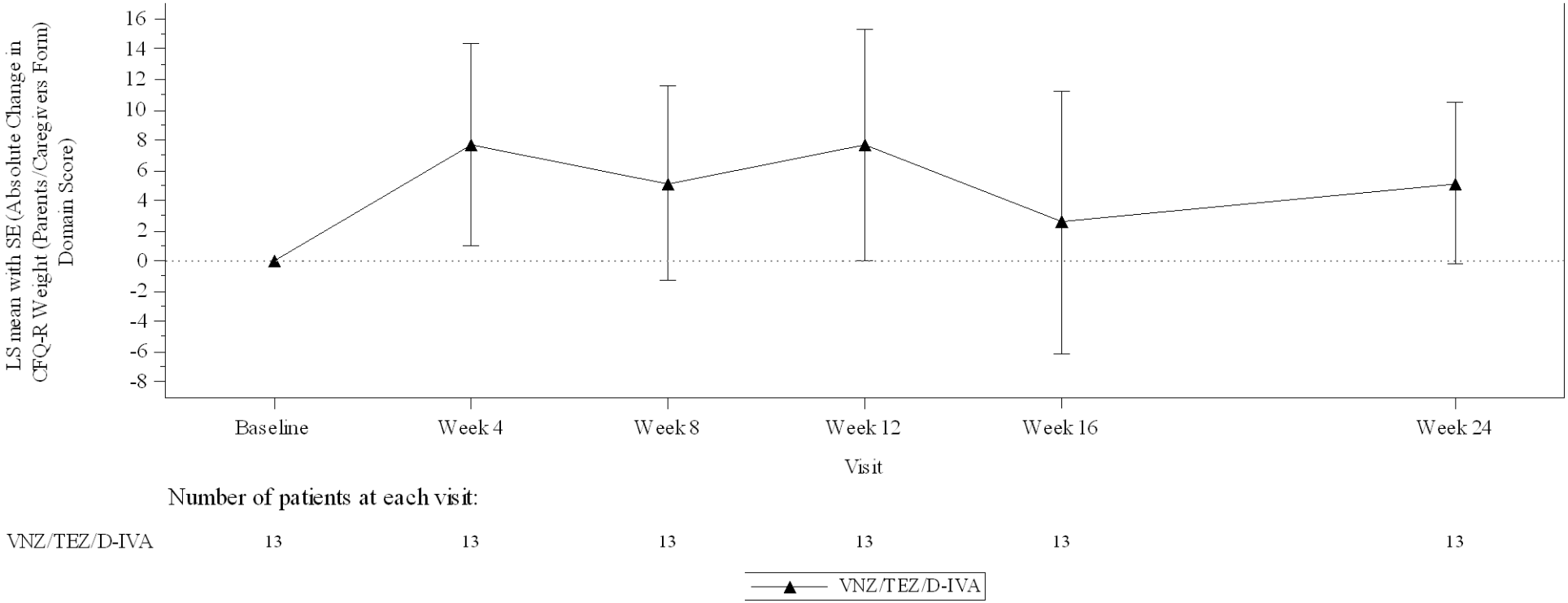
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

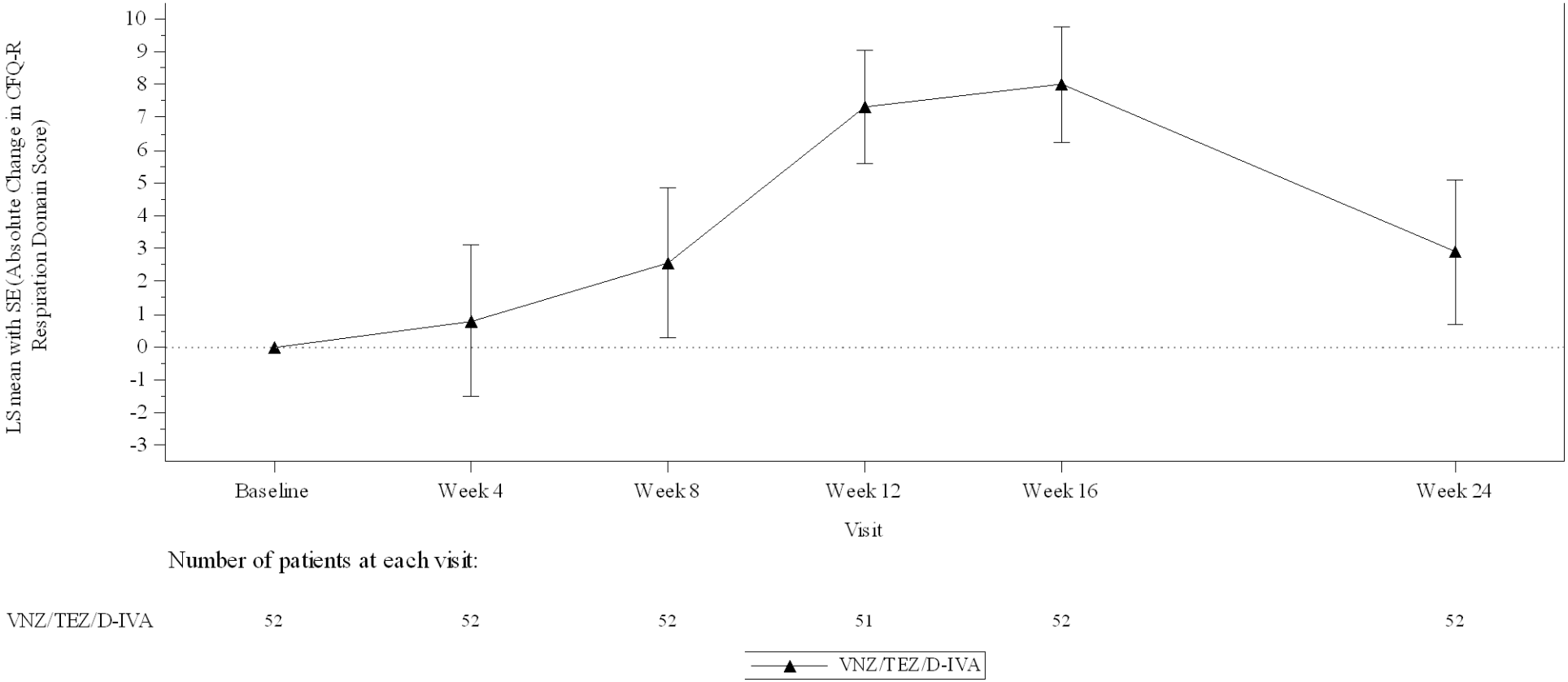
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 1.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups for F/MF
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

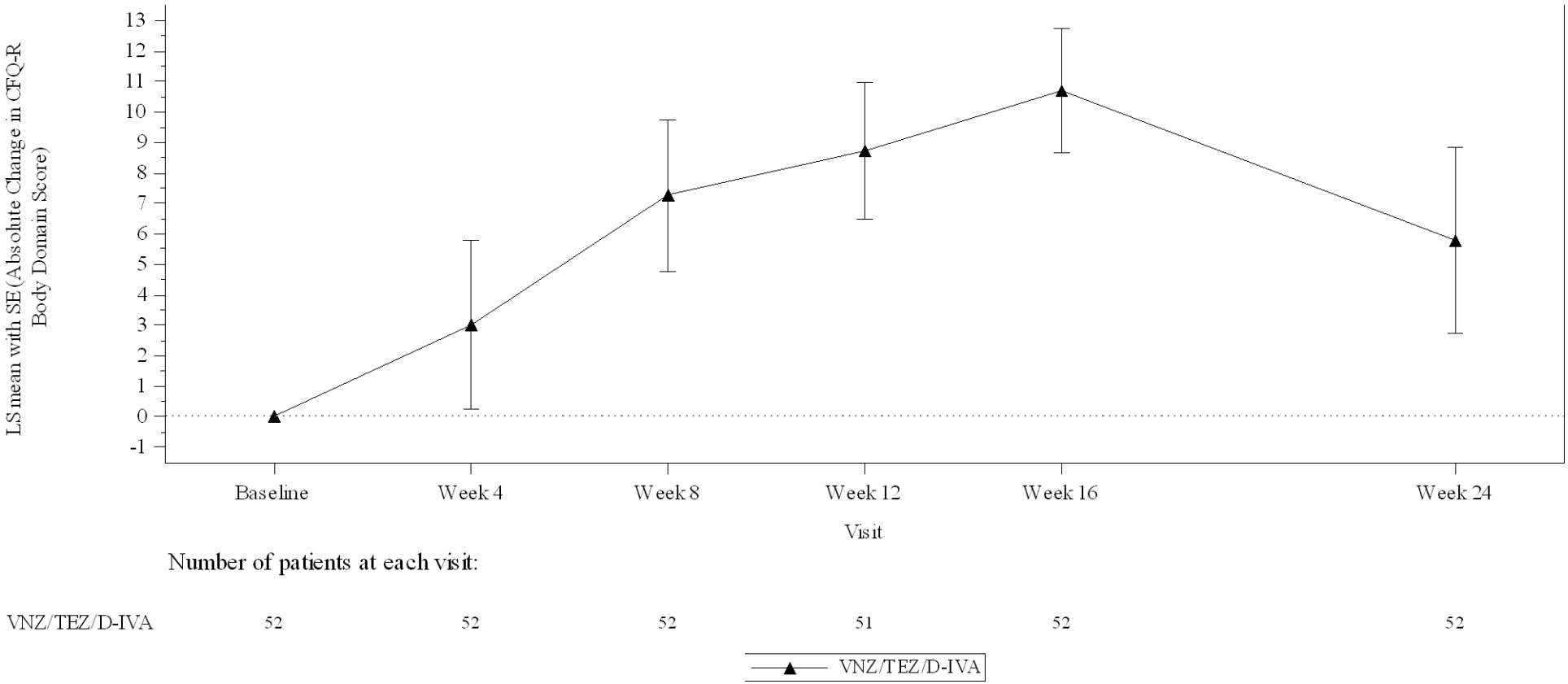
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Respiration



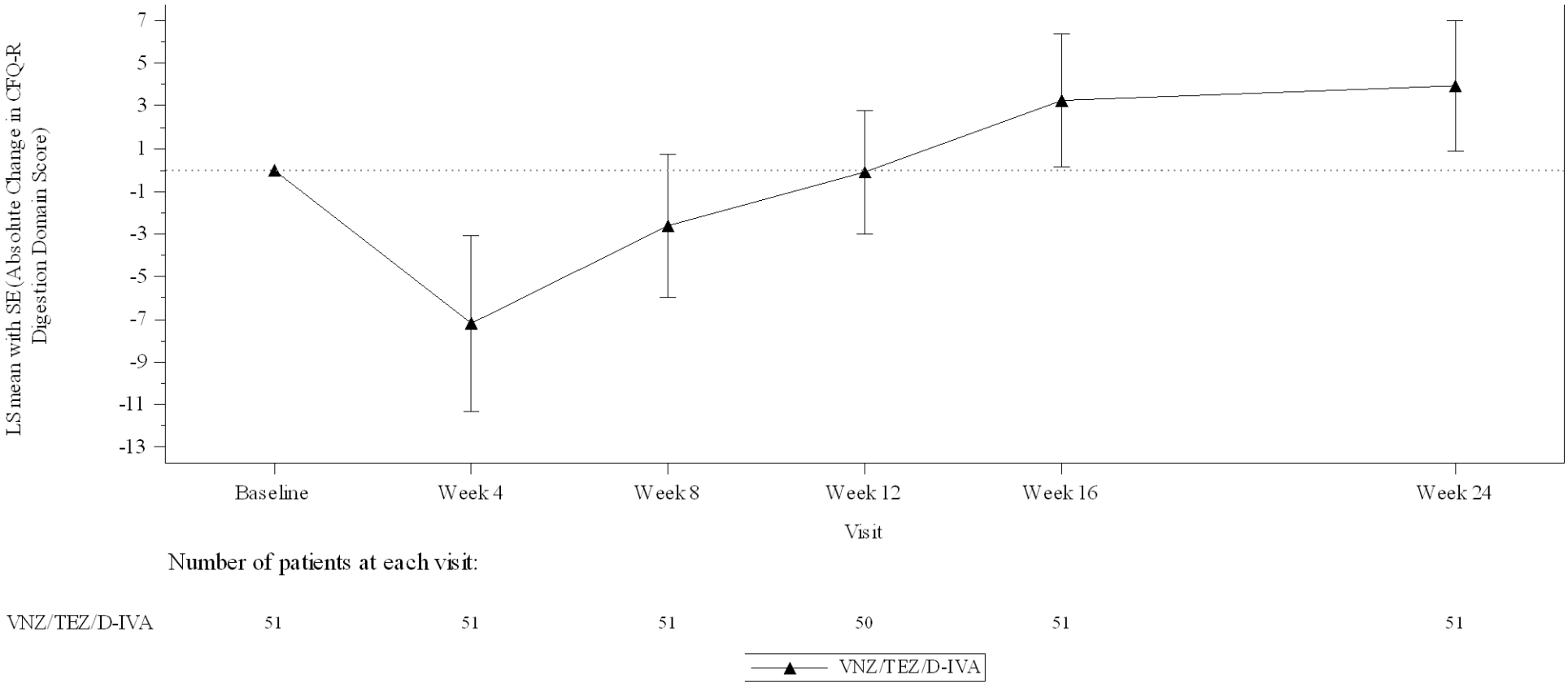
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Body



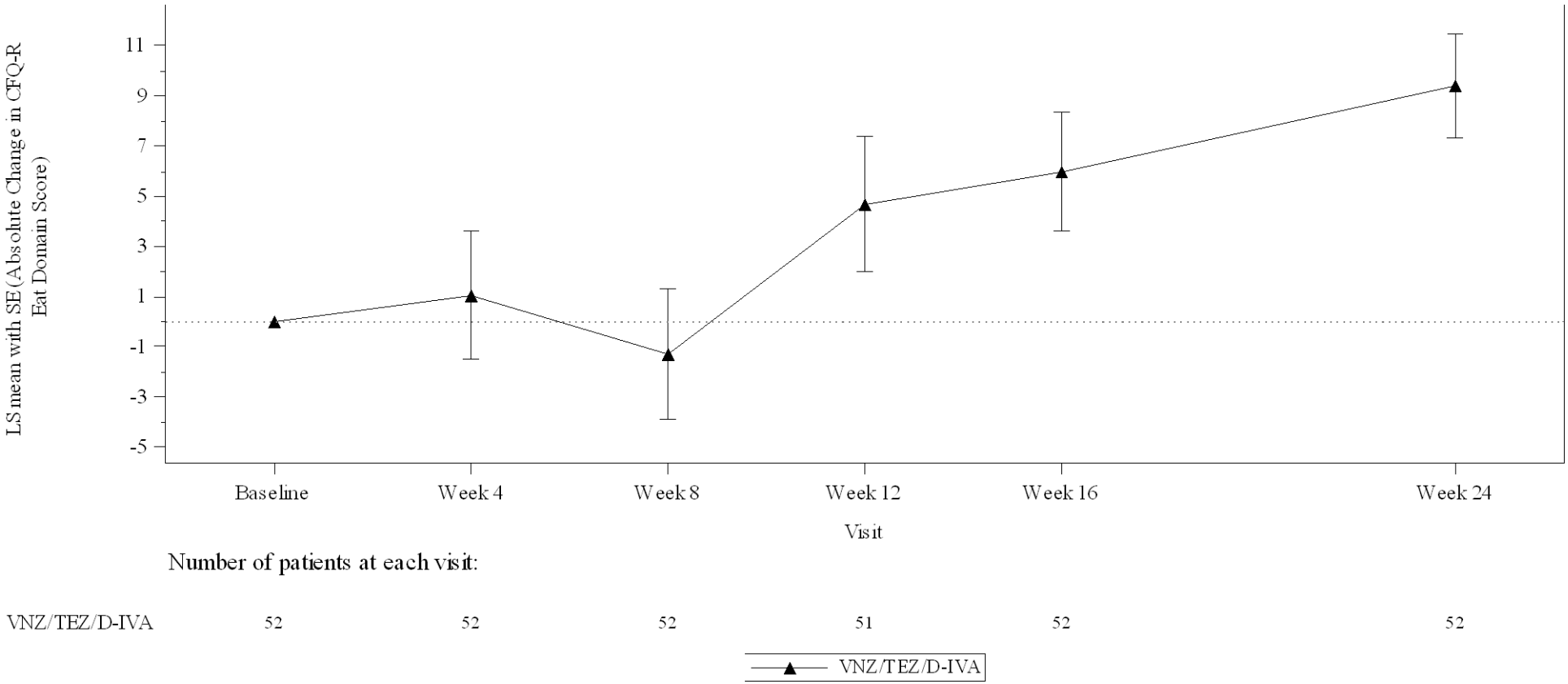
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Digestion



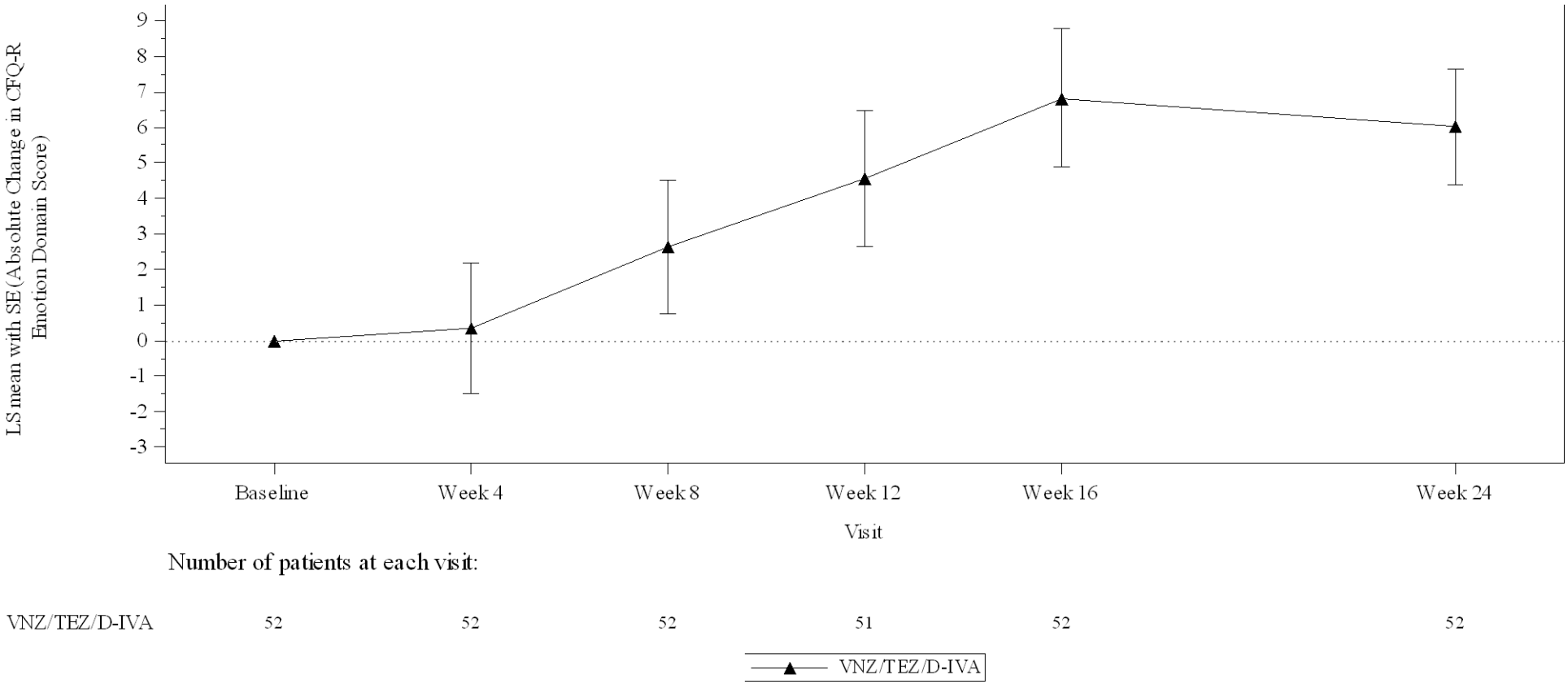
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Eat



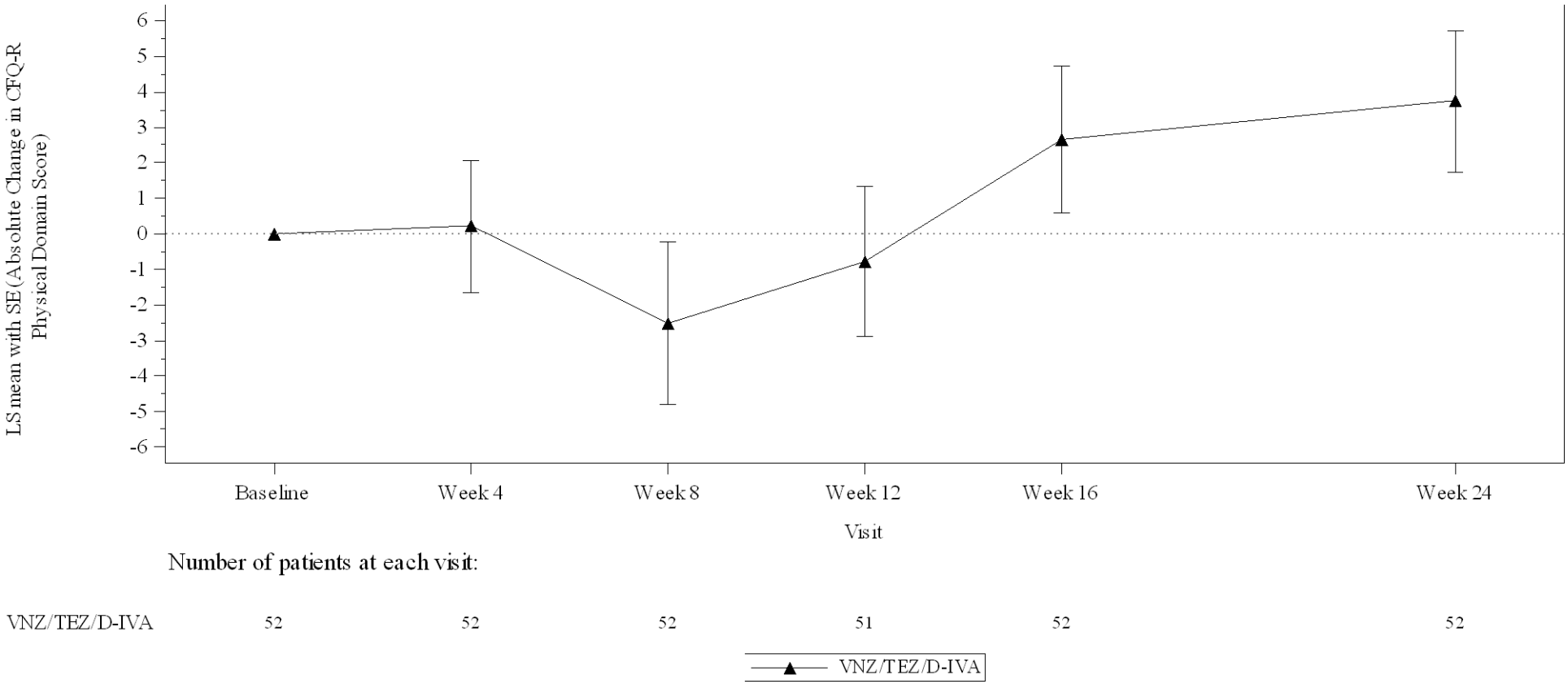
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Emotion



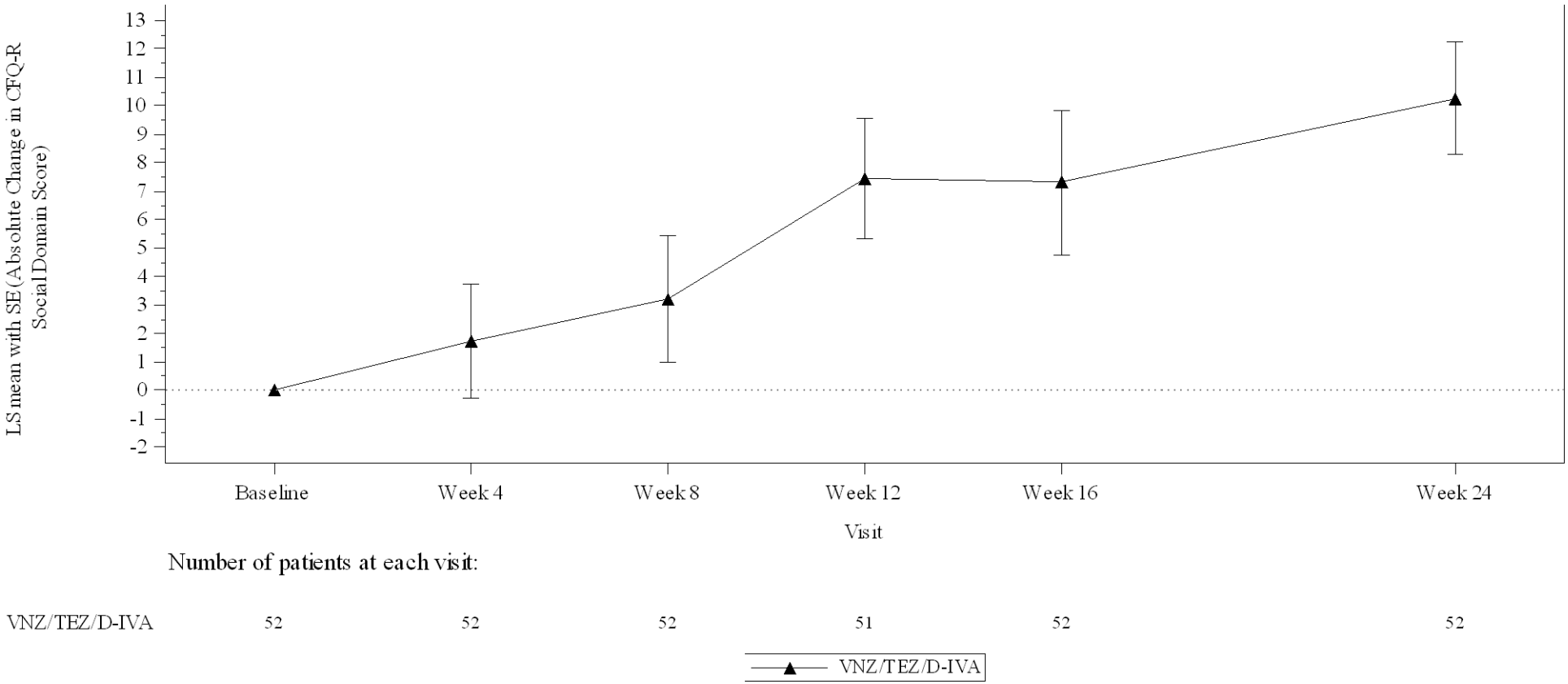
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Physical



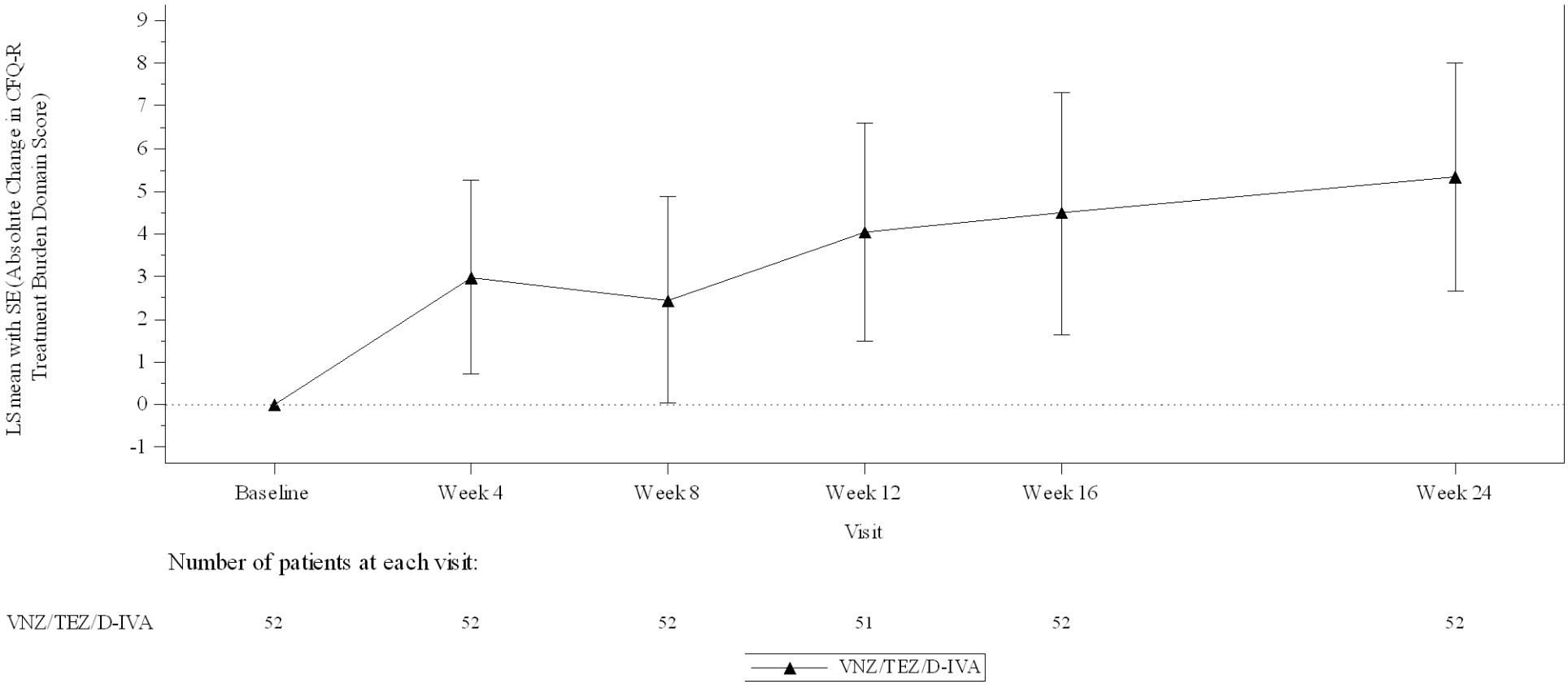
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Social



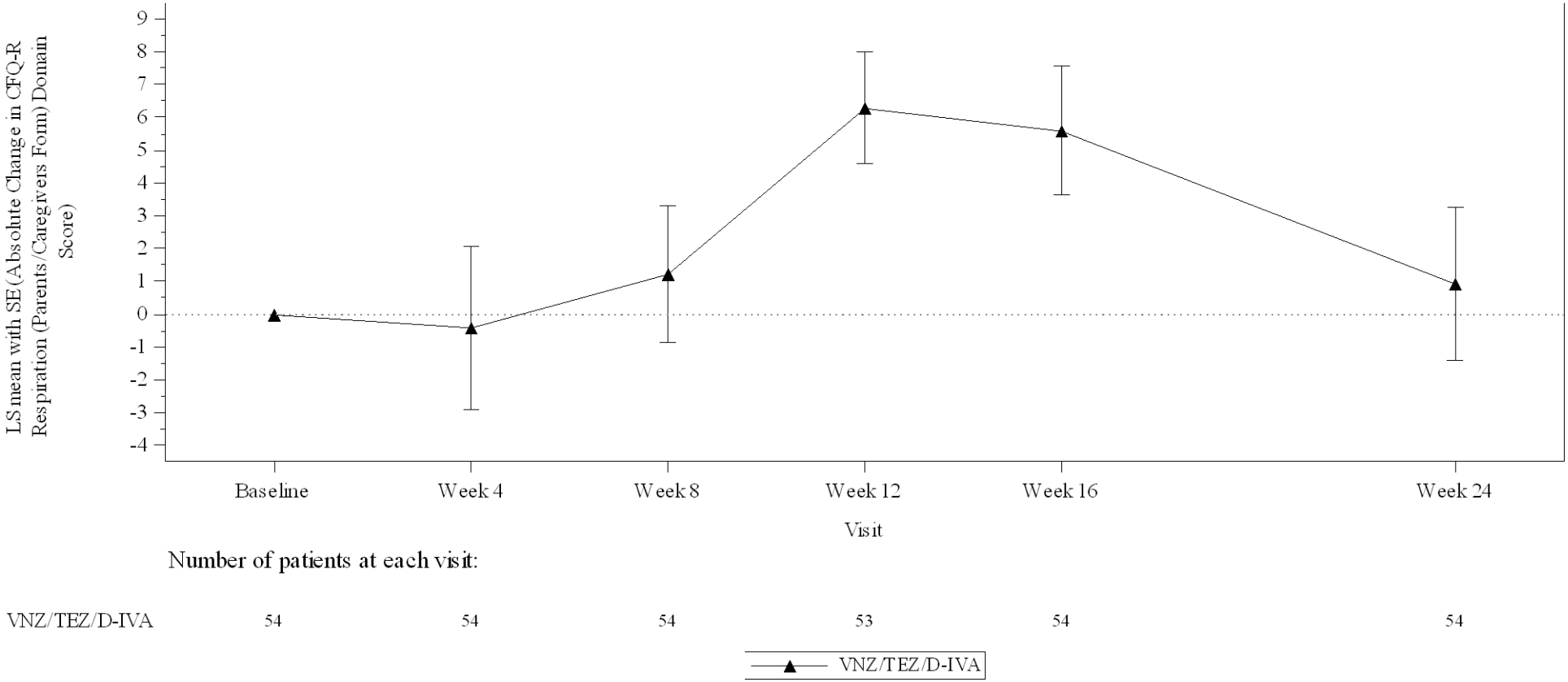
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Treatment Burden



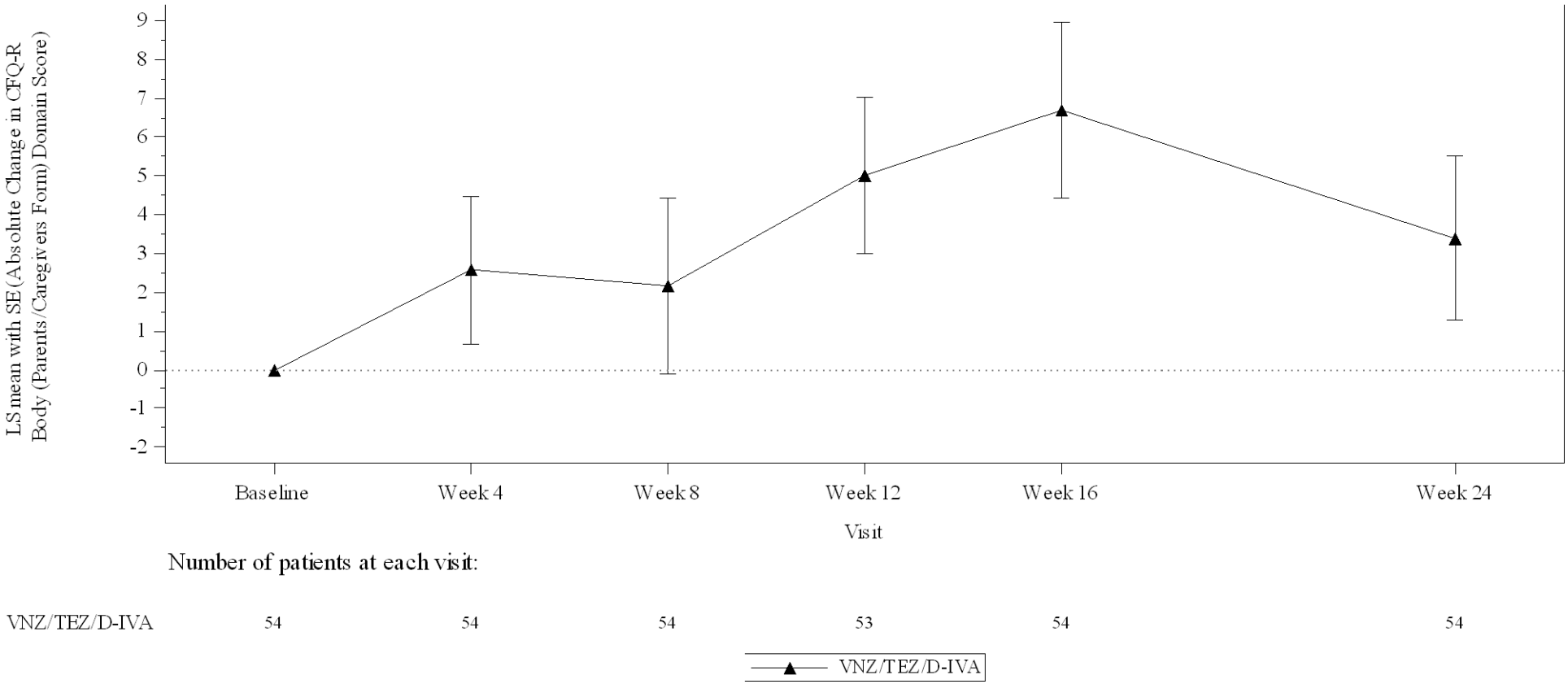
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)



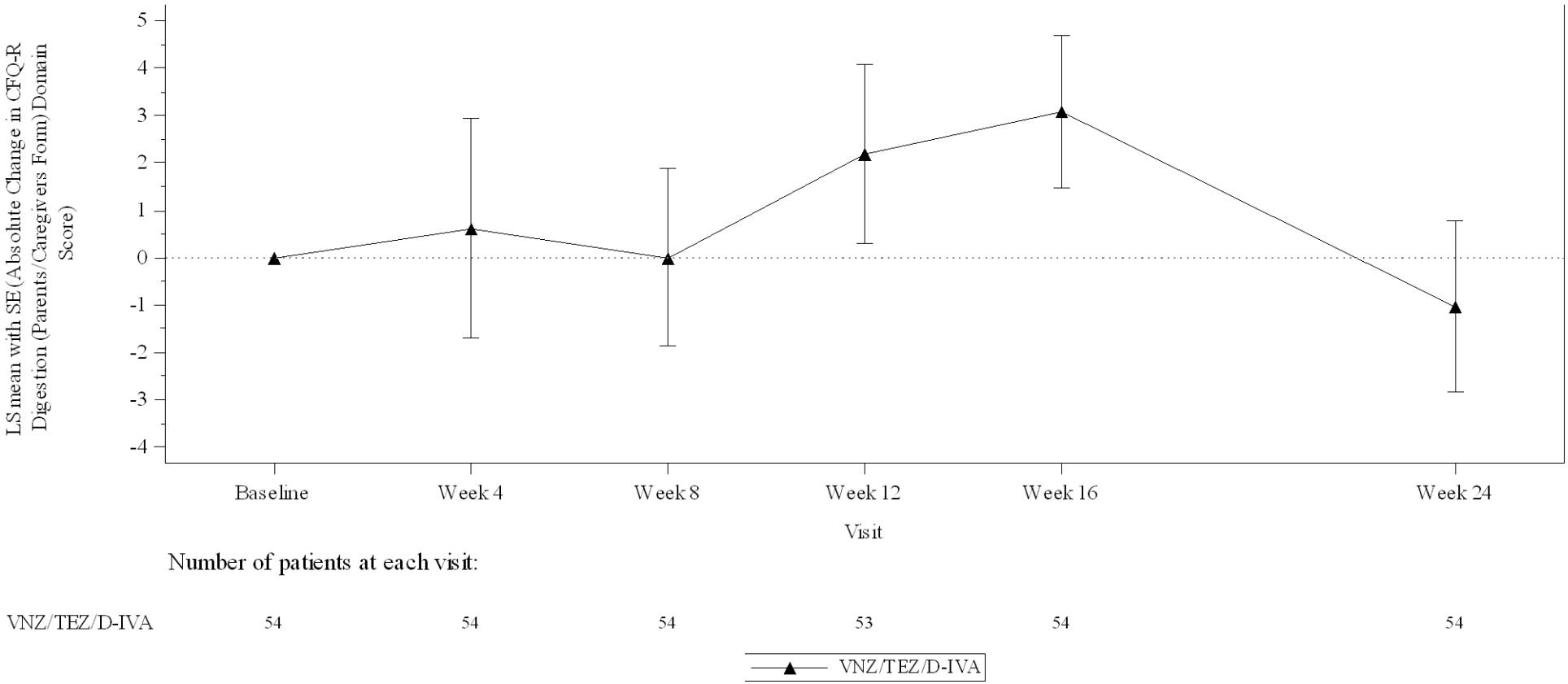
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)



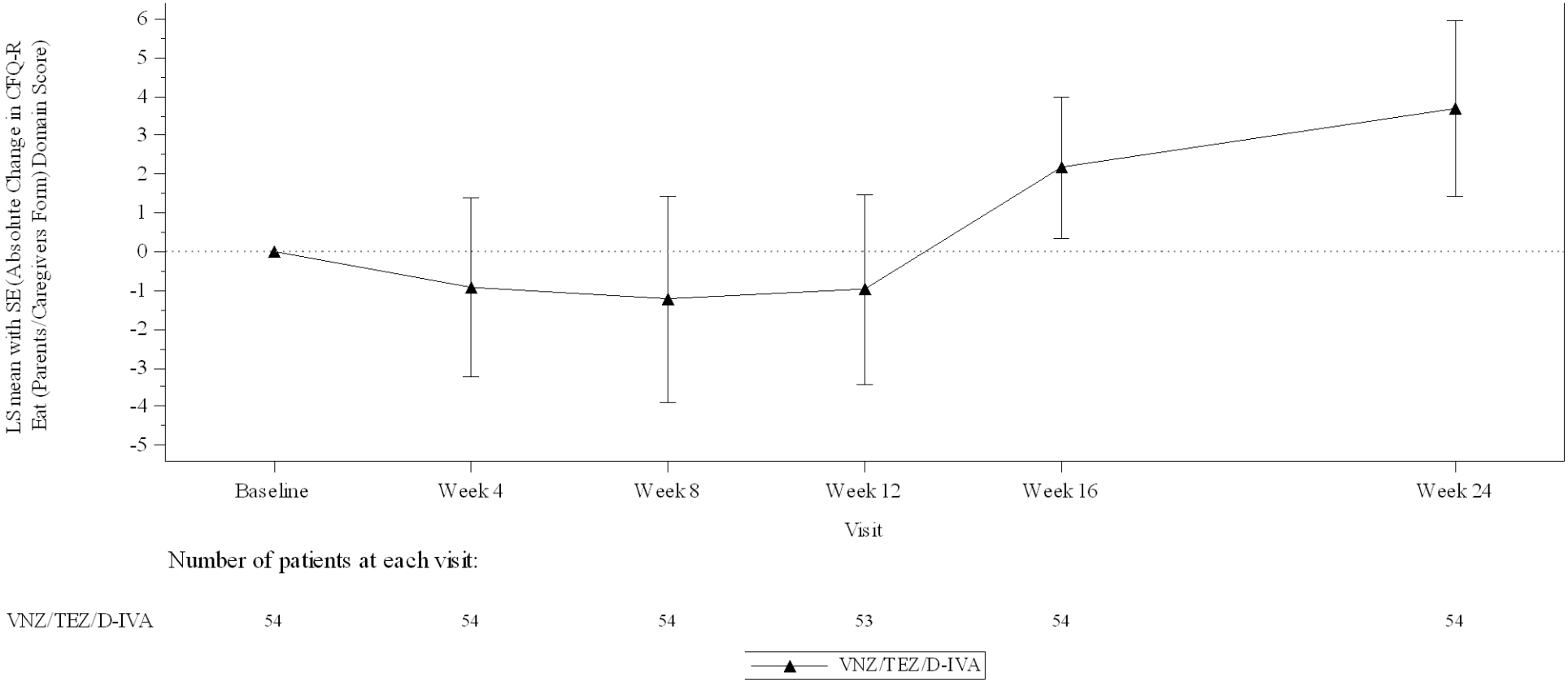
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)



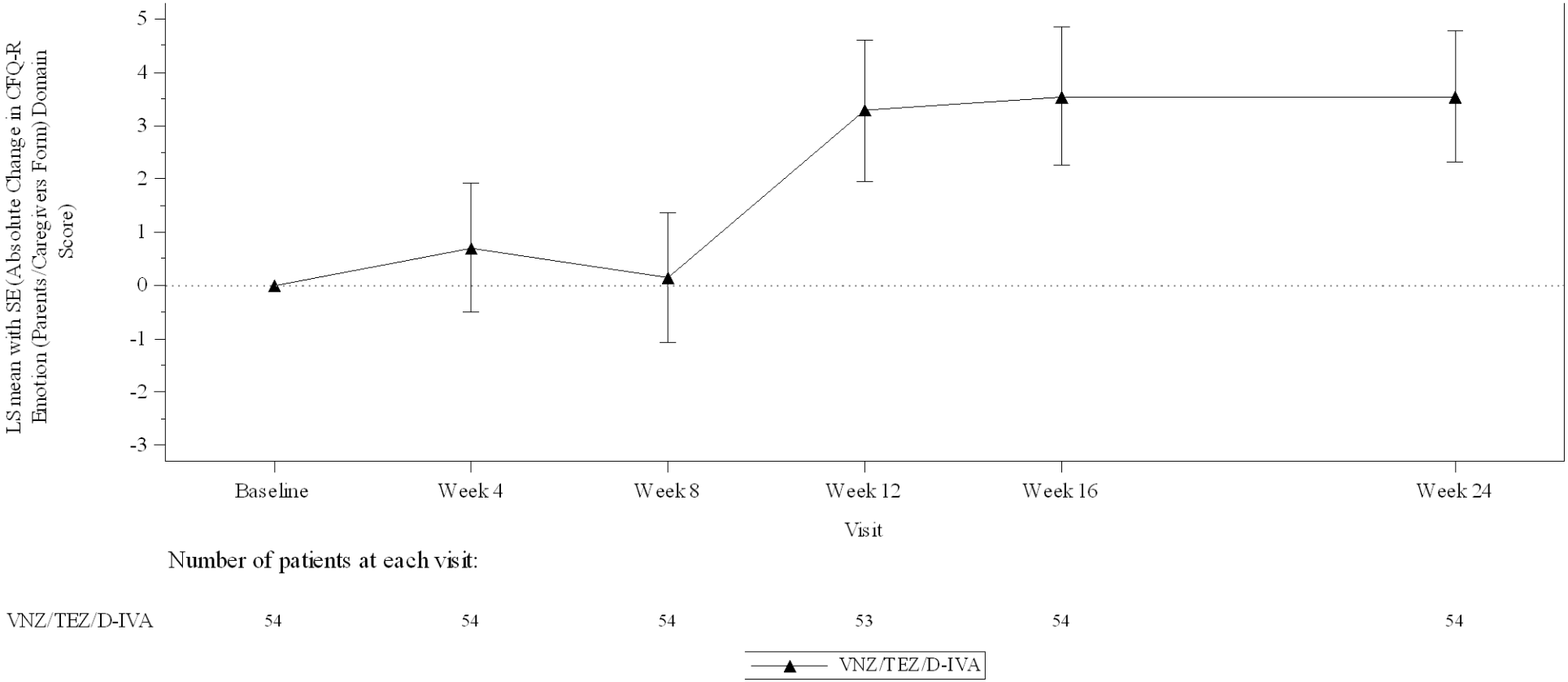
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)



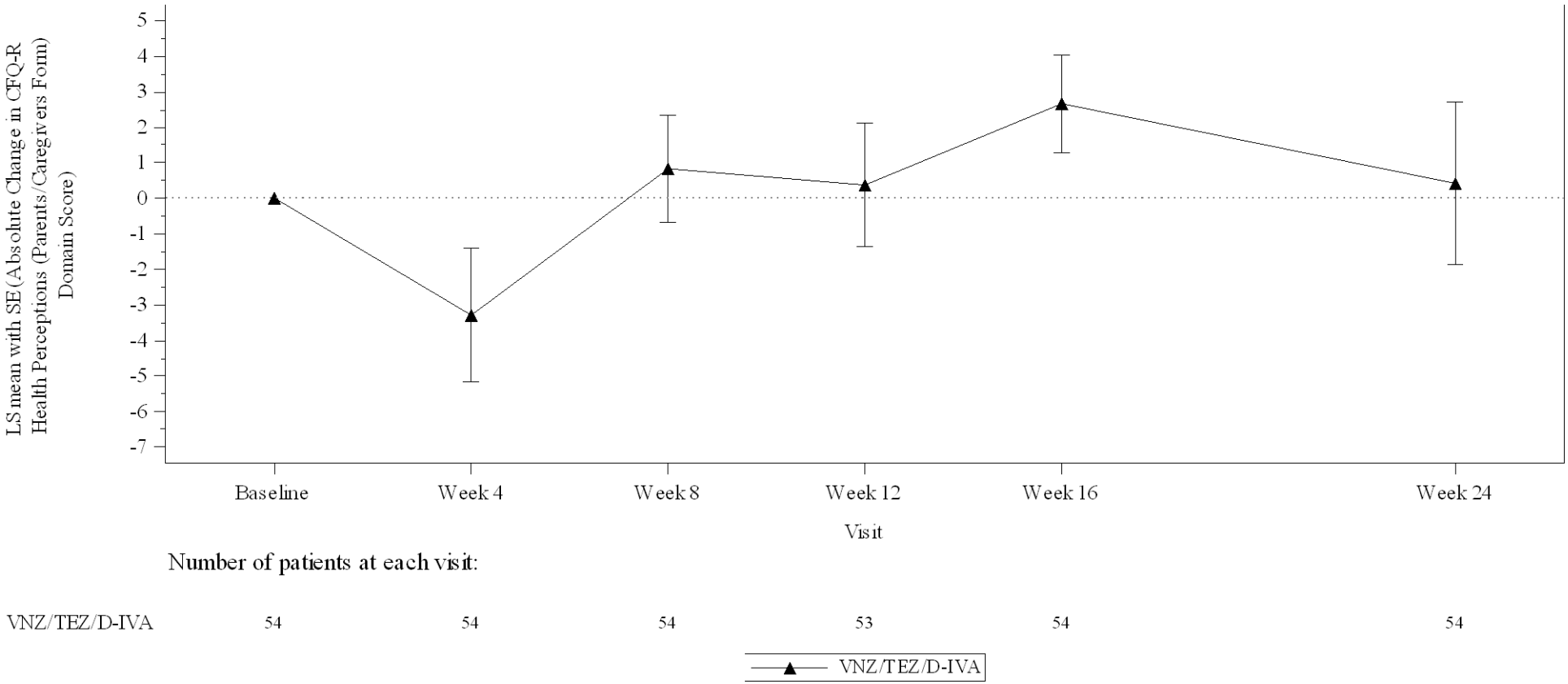
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)



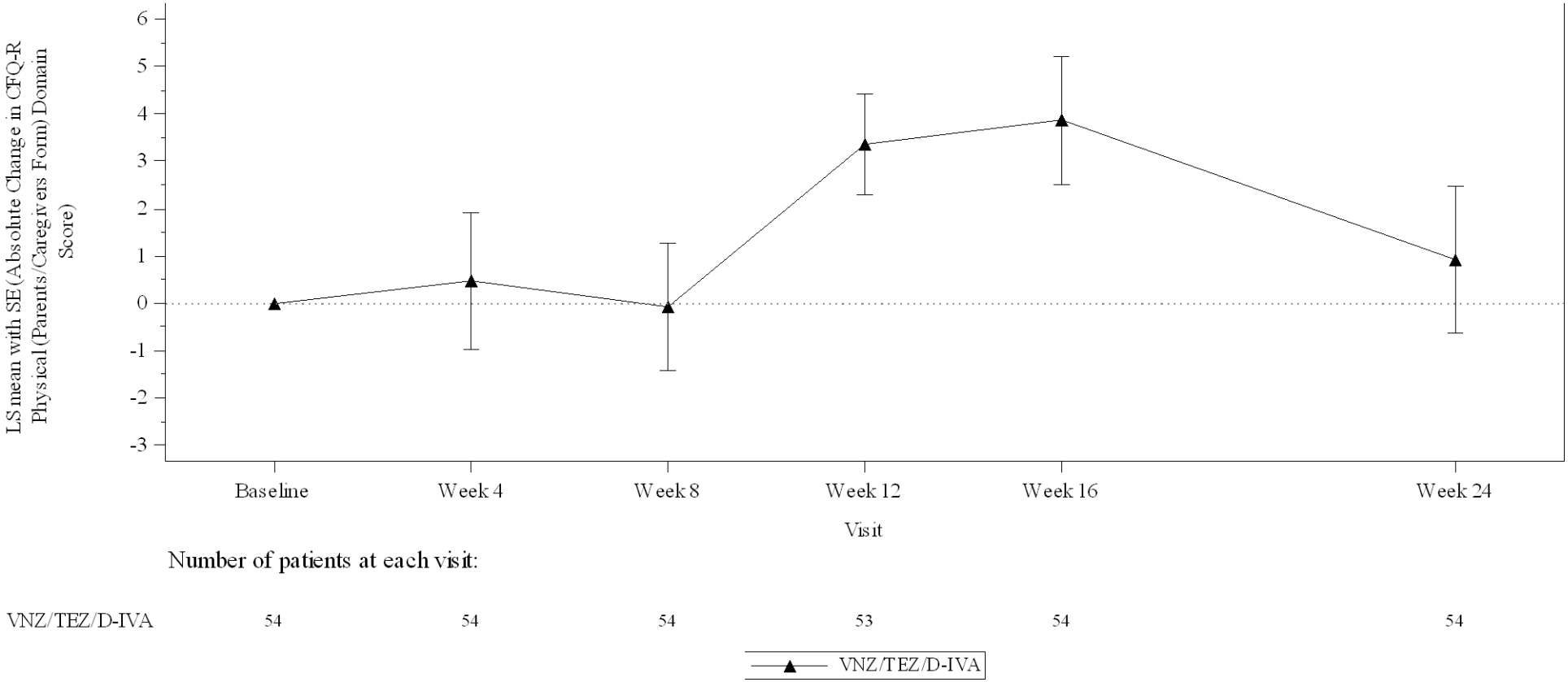
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)



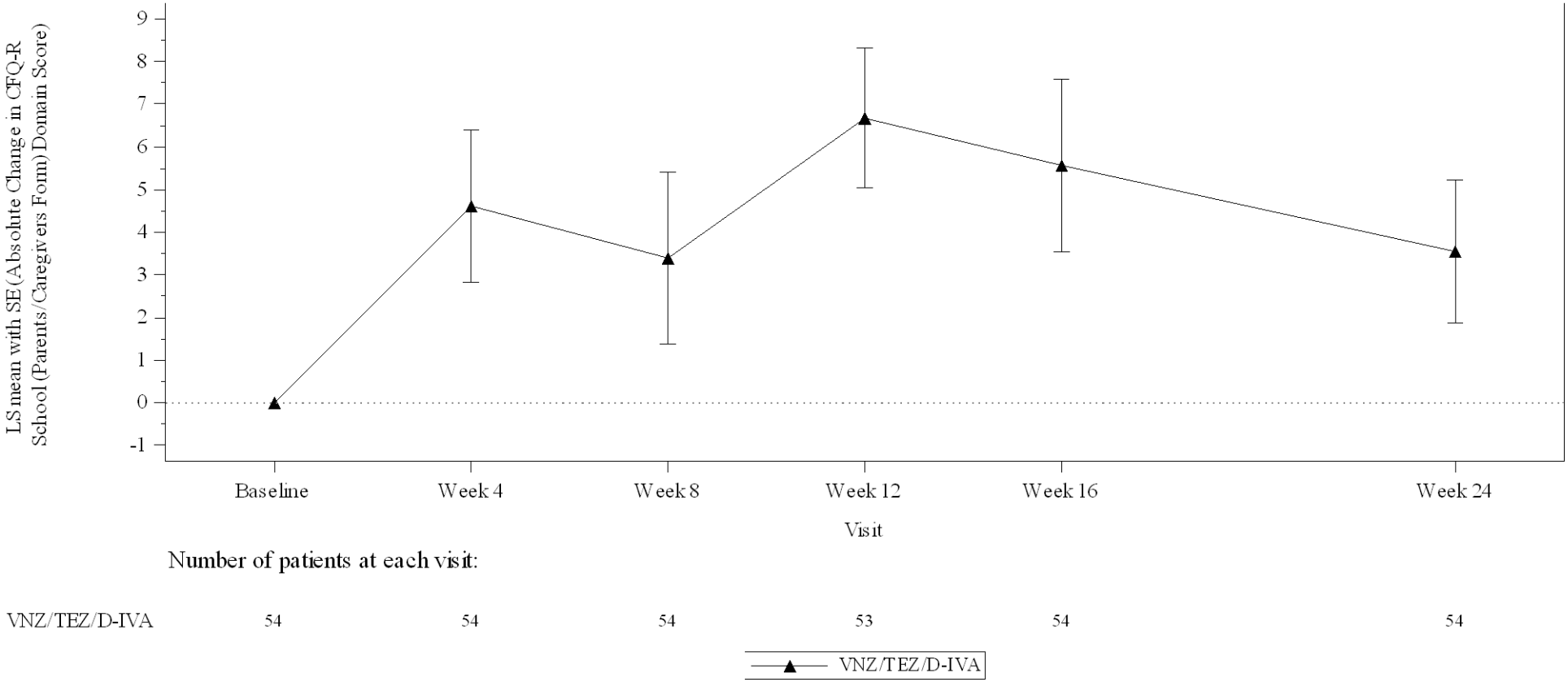
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)



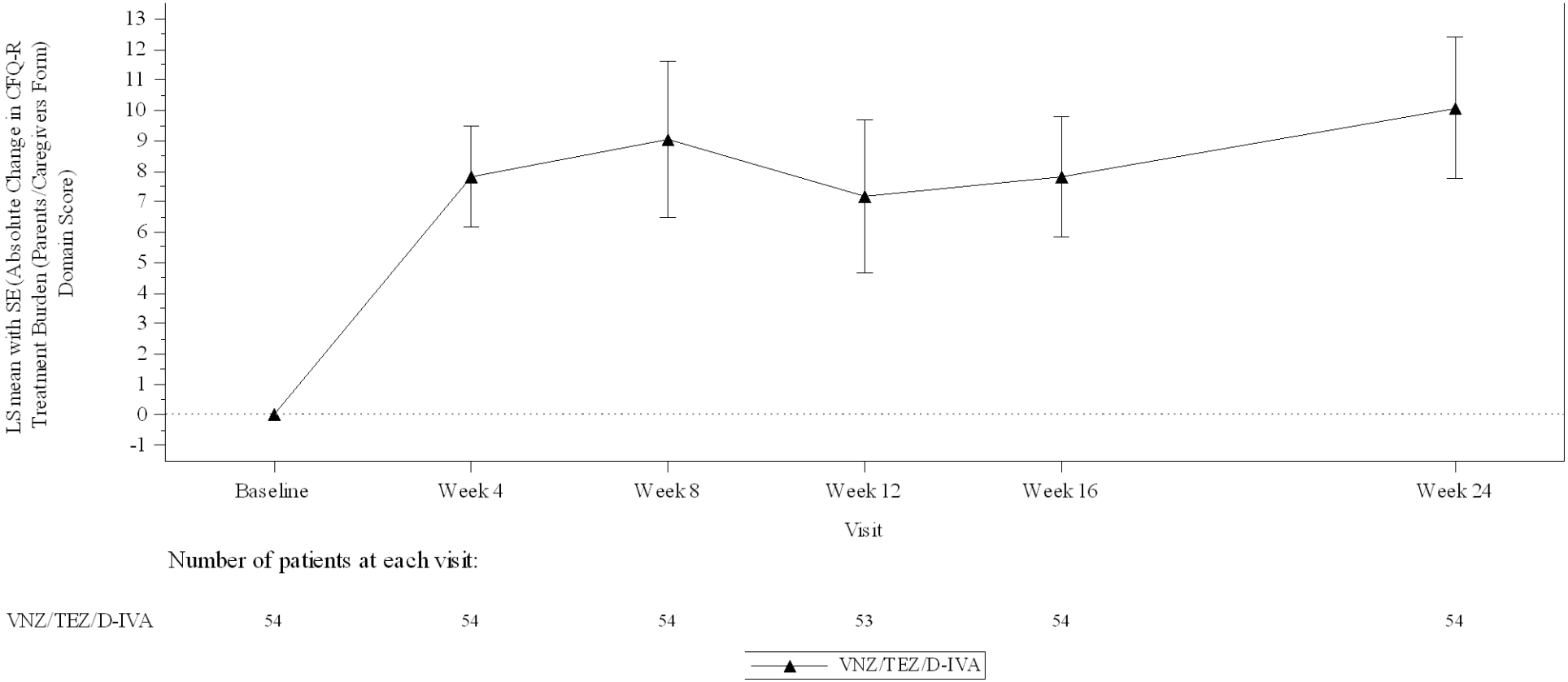
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)



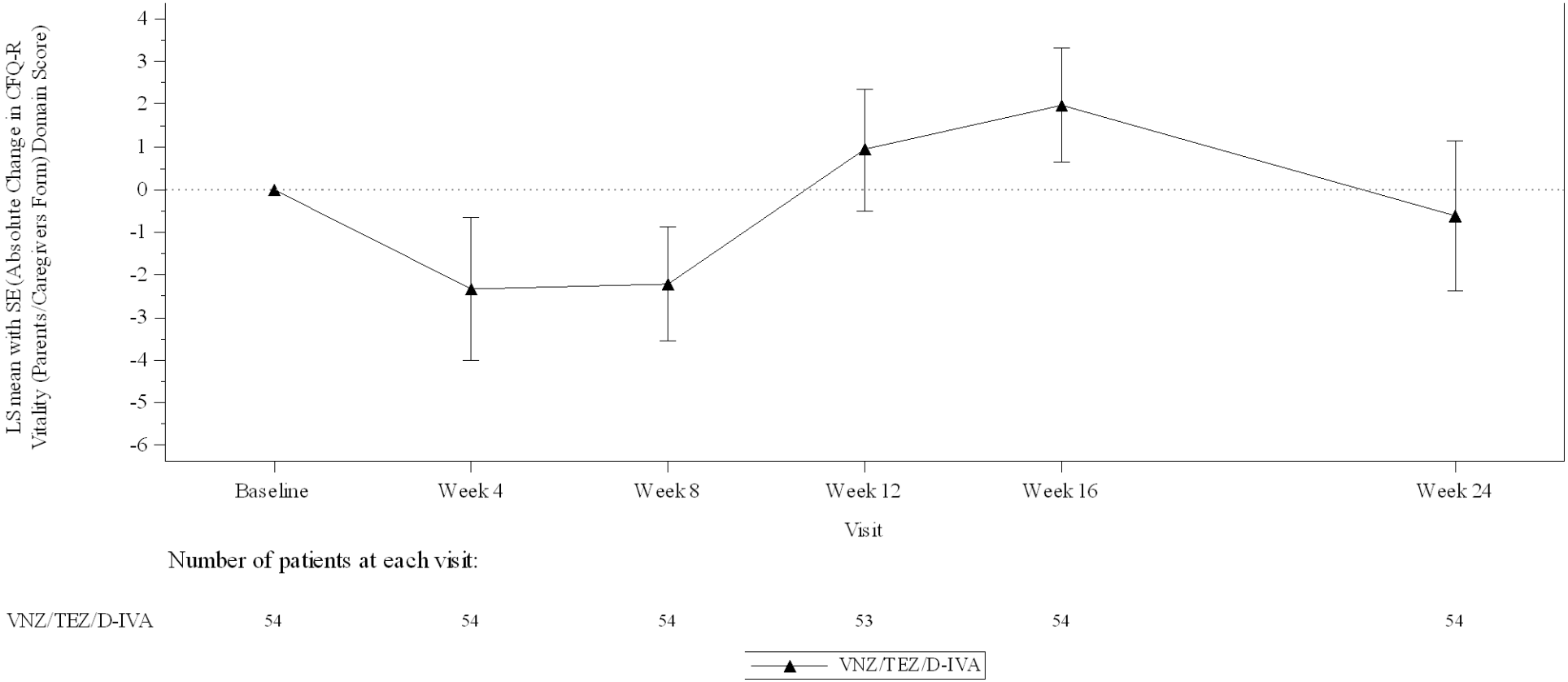
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)



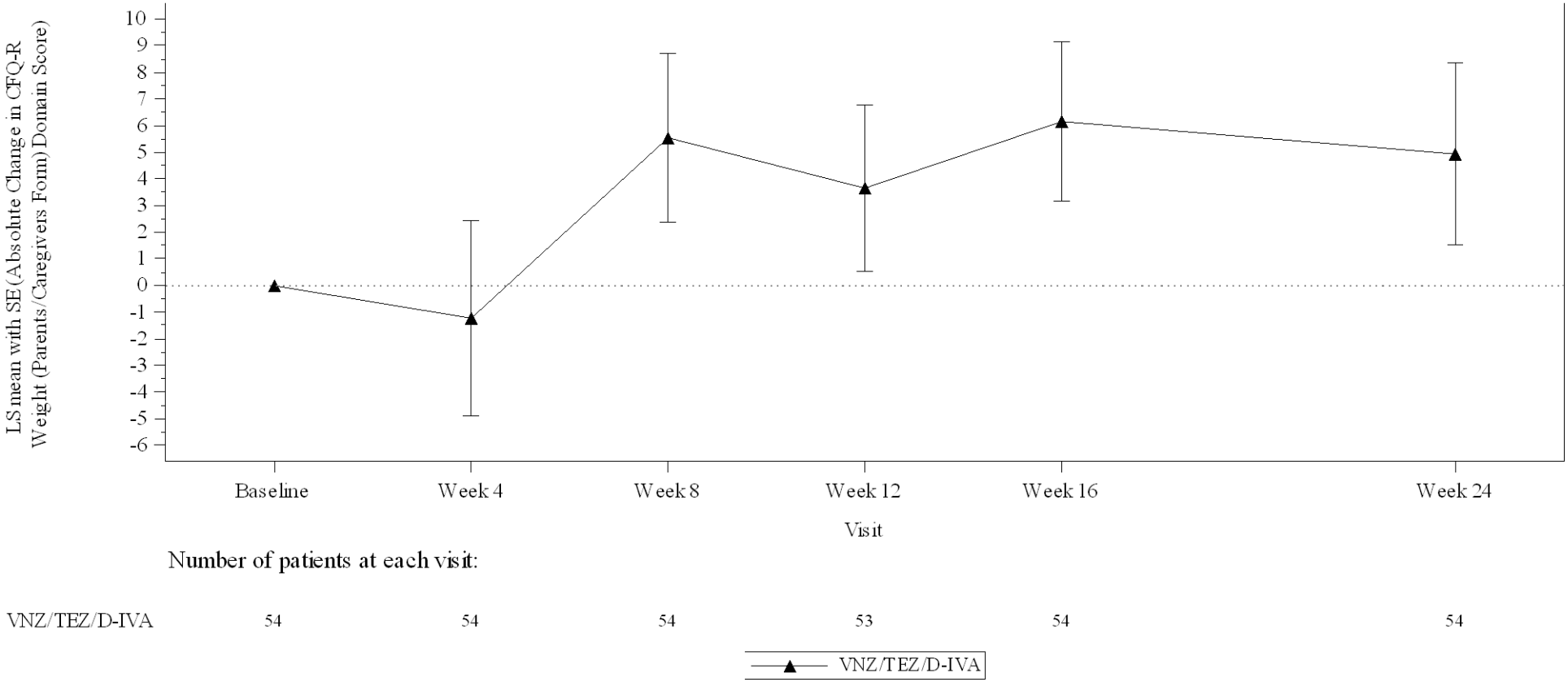
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)



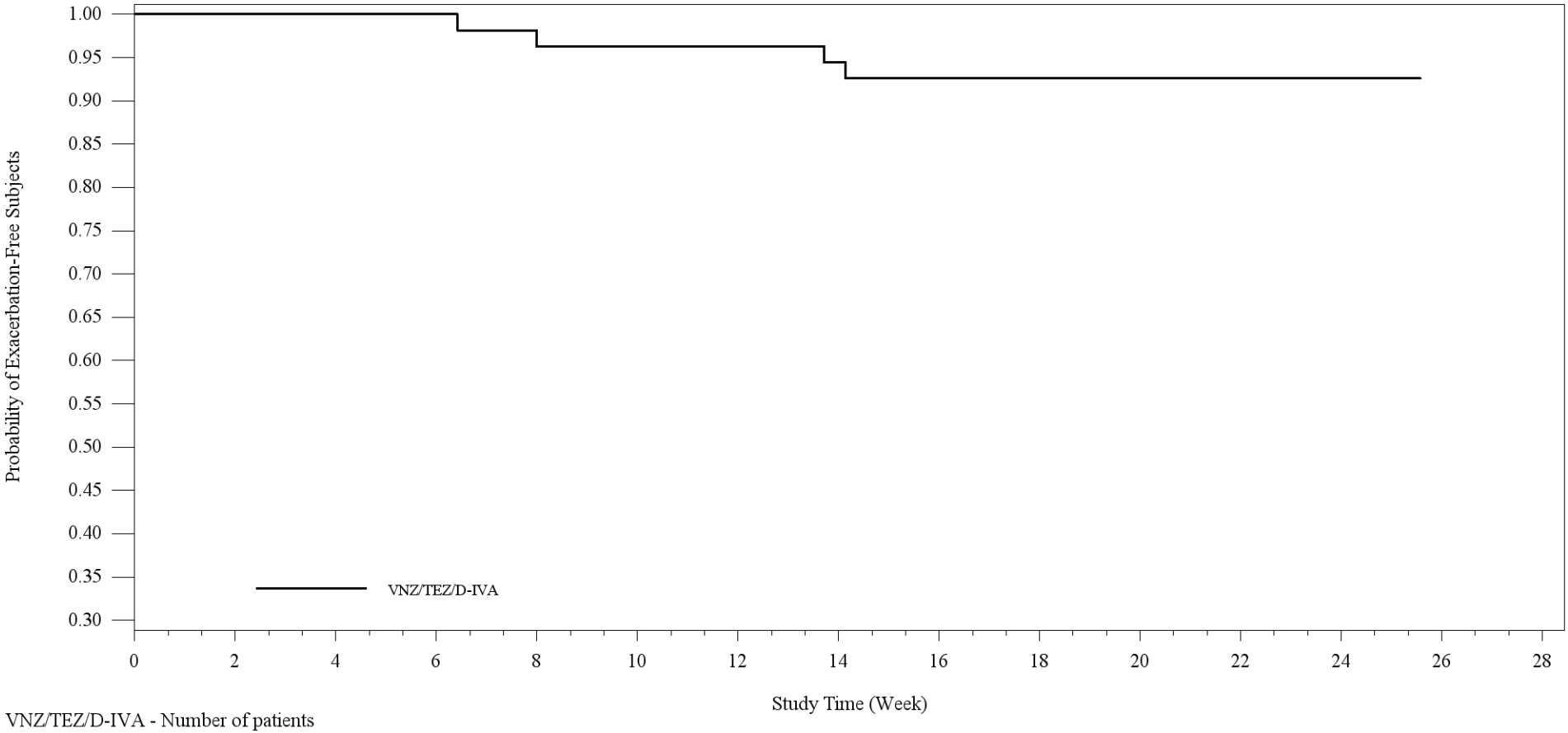
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

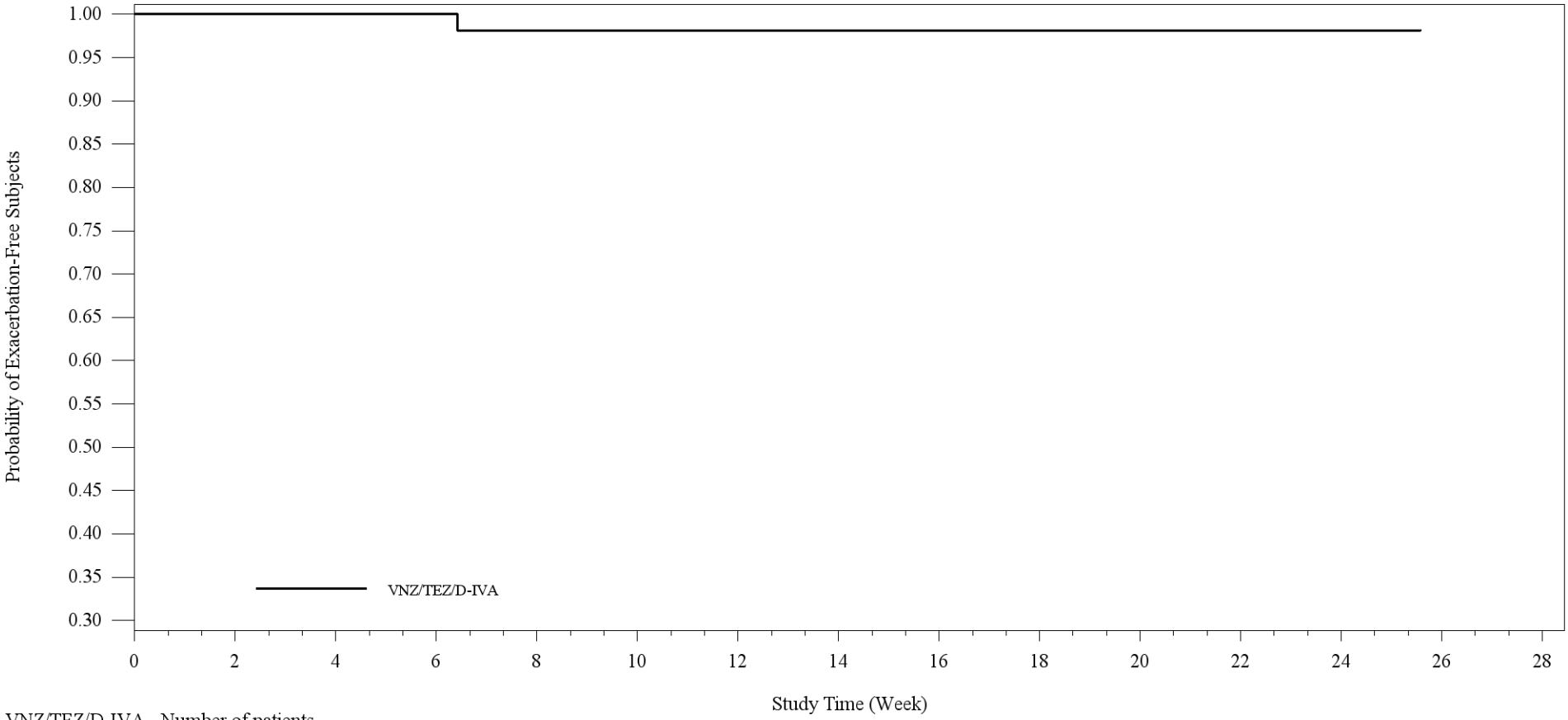
Figure 2.2.1.14.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 24 non-(F/MF)
Full Analysis Set



VNZ/TEZ/D-IVA - Number of patients						
at risk	54	54	52	52	50	31
with event(s)	0	0	2	2	4	4
censored	0	0	0	0	0	19

Zusatzanalysen zur Studie VX21-121-105

Figure 2.2.1.15.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24 non-(F/MF)
Full Analysis Set

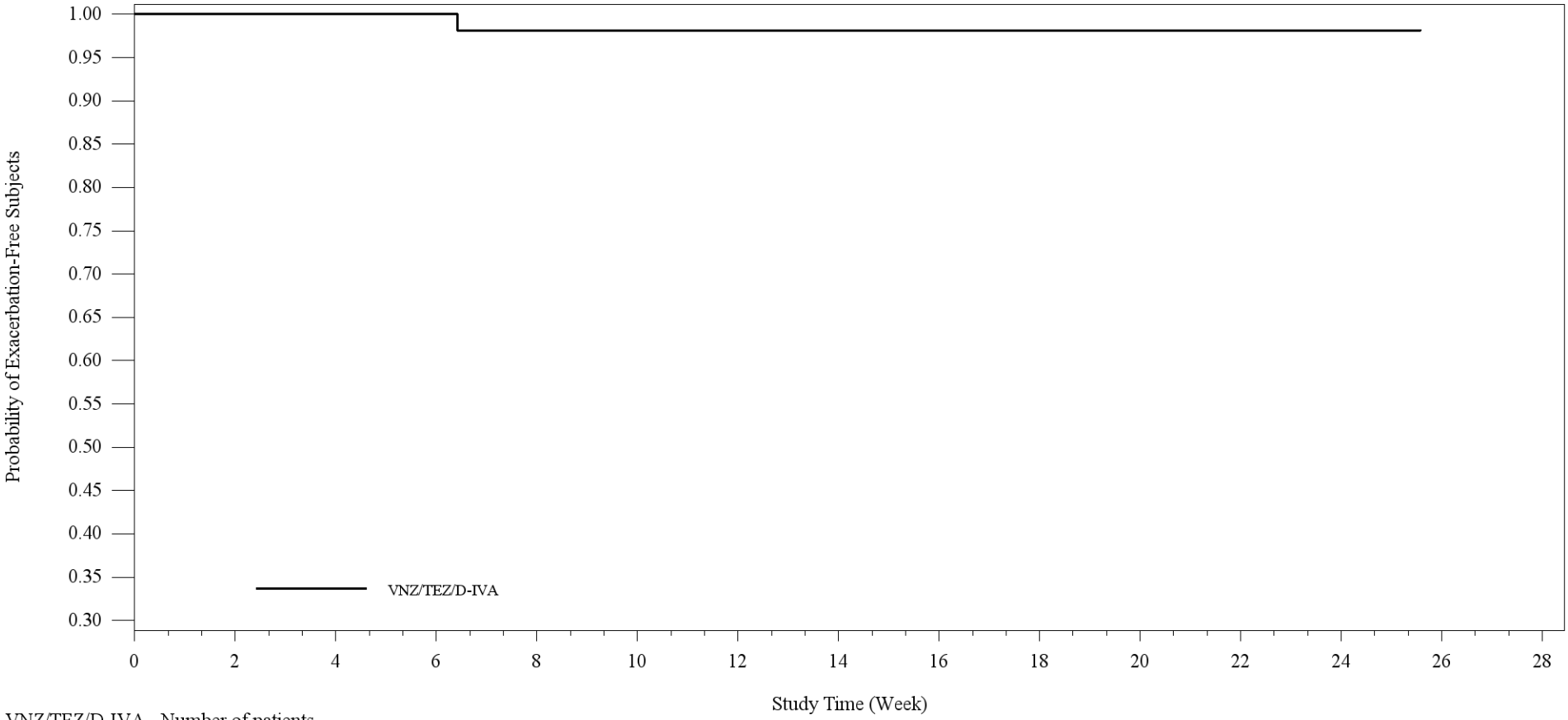


VNZ/TEZ/D-IVA - Number of patients						
at risk	54	54	53	53	53	34
with event(s)	0	0	1	1	1	1
censored	0	0	0	0	0	19

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Zusatzanalysen zur Studie VX21-121-105

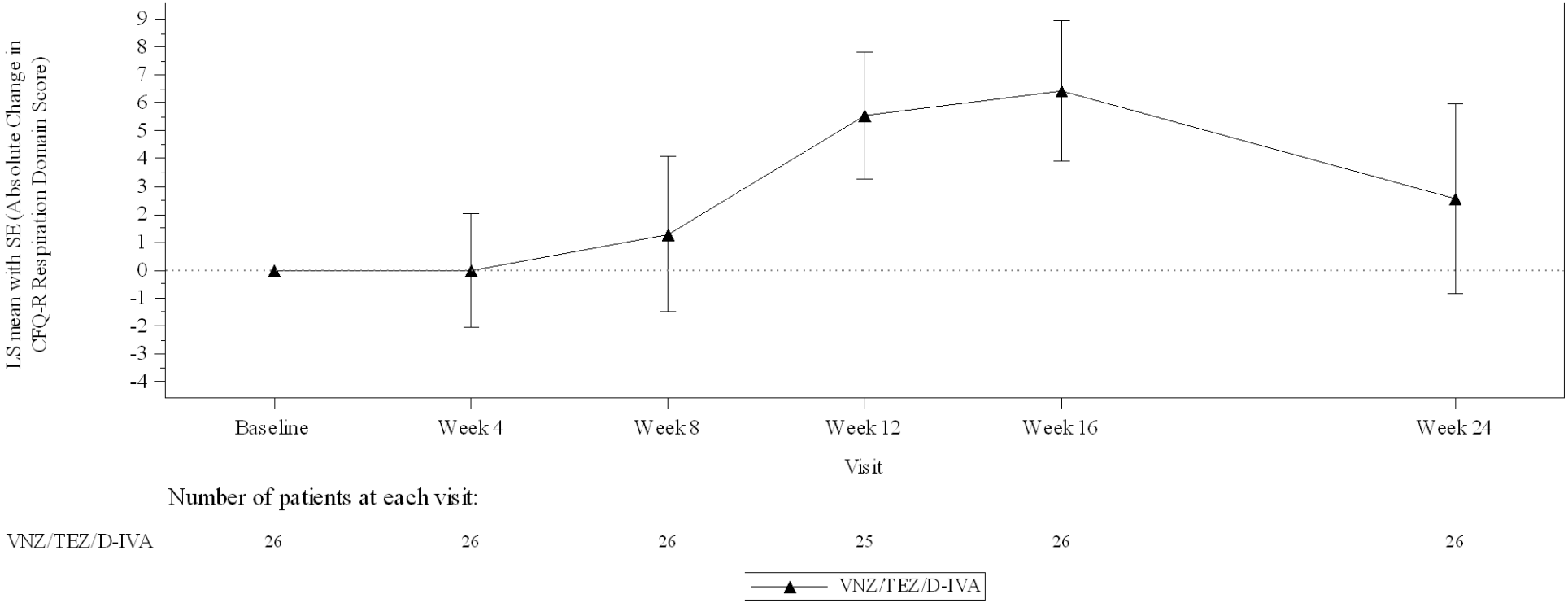
Figure 2.2.1.16.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24 non-(F/MF)
Full Analysis Set



VNZ/TEZ/D-IVA - Number of patients						
at risk	54	54	53	53	53	34
with event(s)	0	0	1	1	1	1
censored	0	0	0	0	0	19

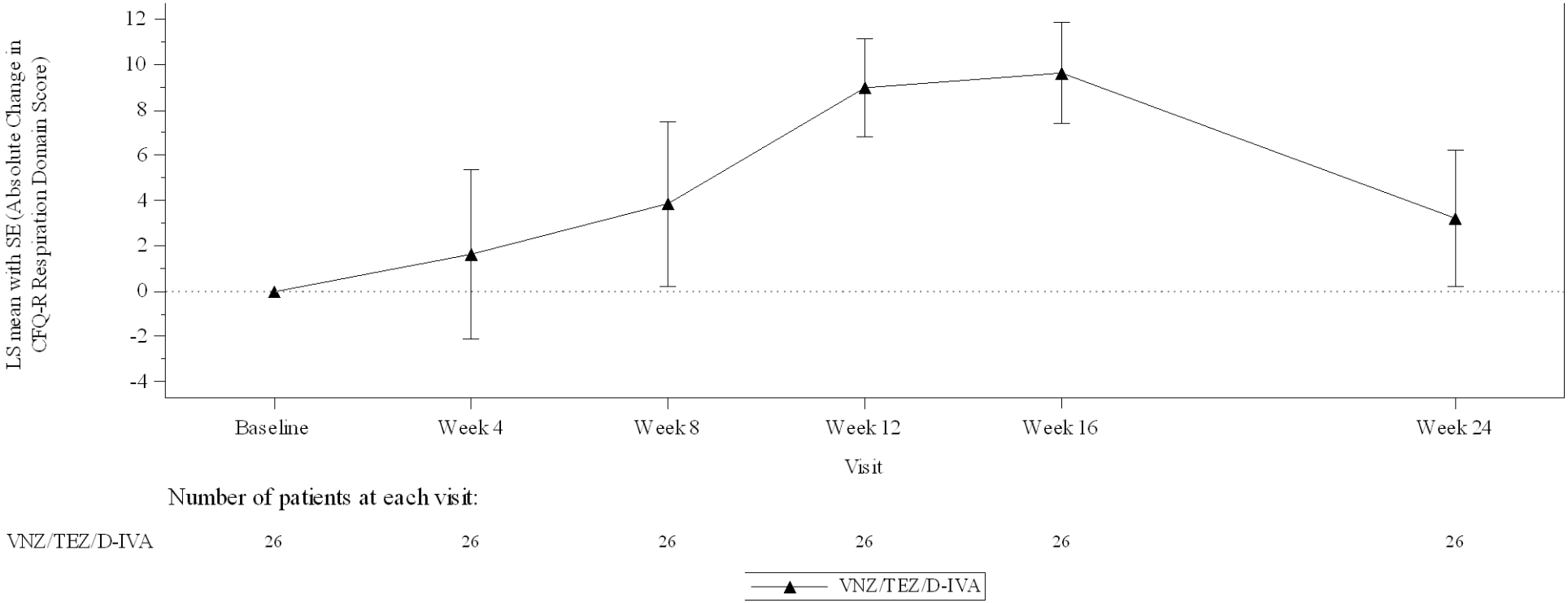
- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms.

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration
Sex = Male



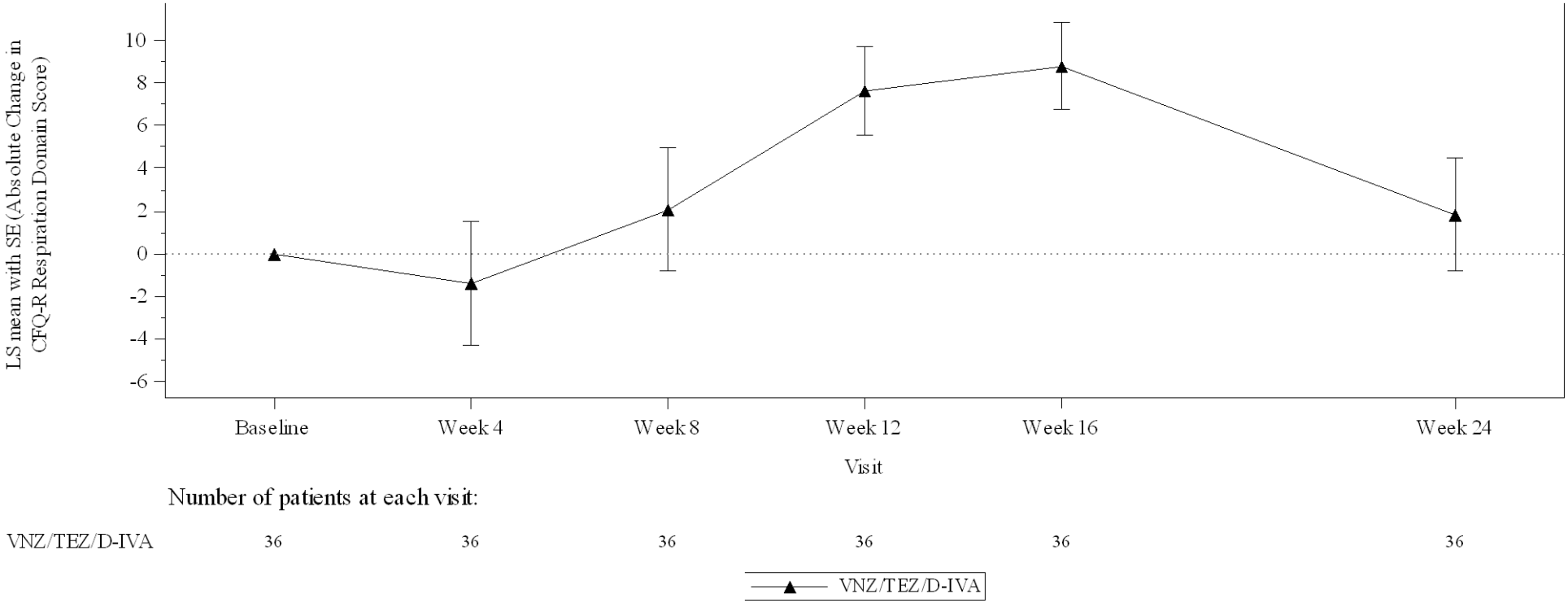
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration
Sex = Female



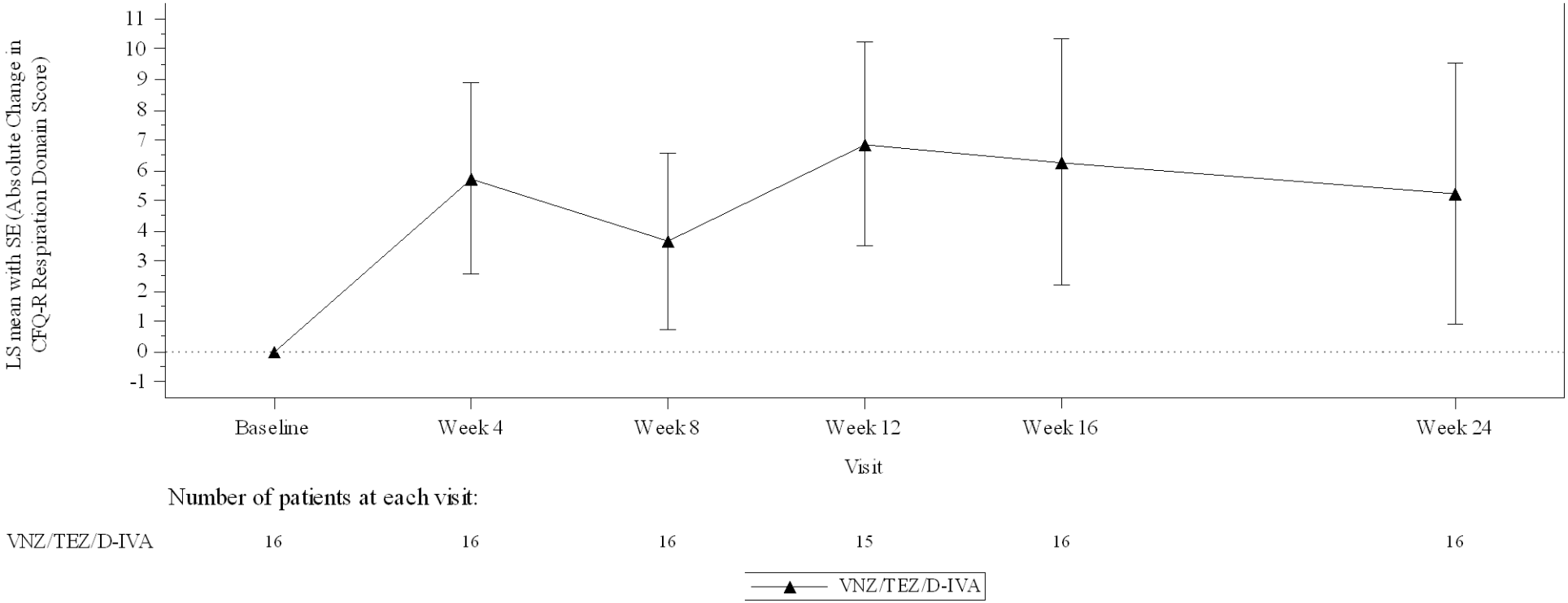
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

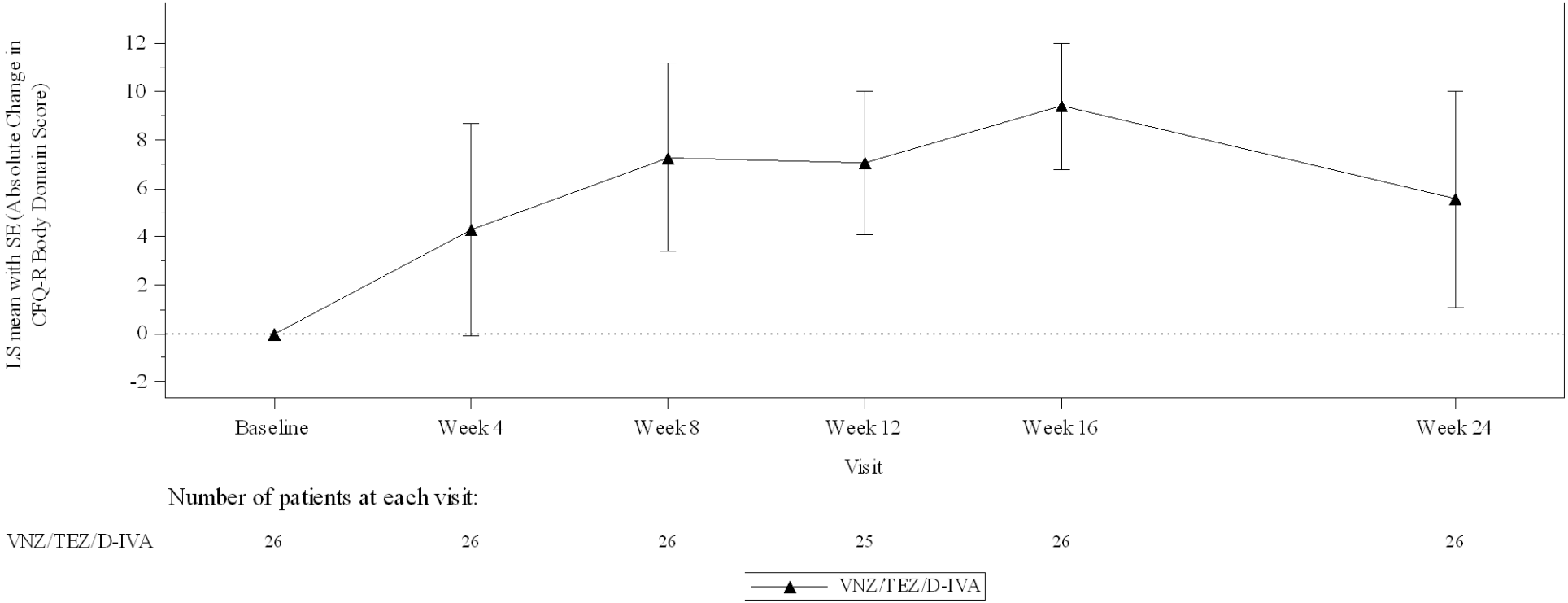
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

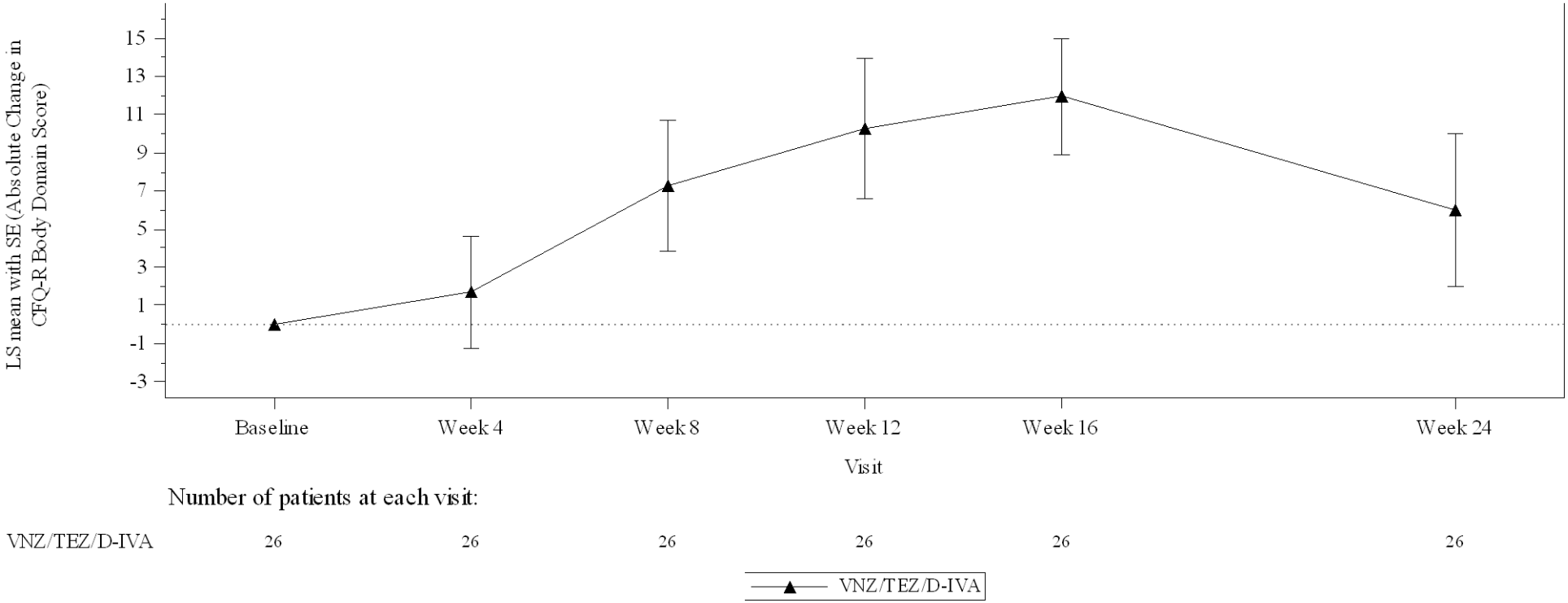
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body
Sex = Male



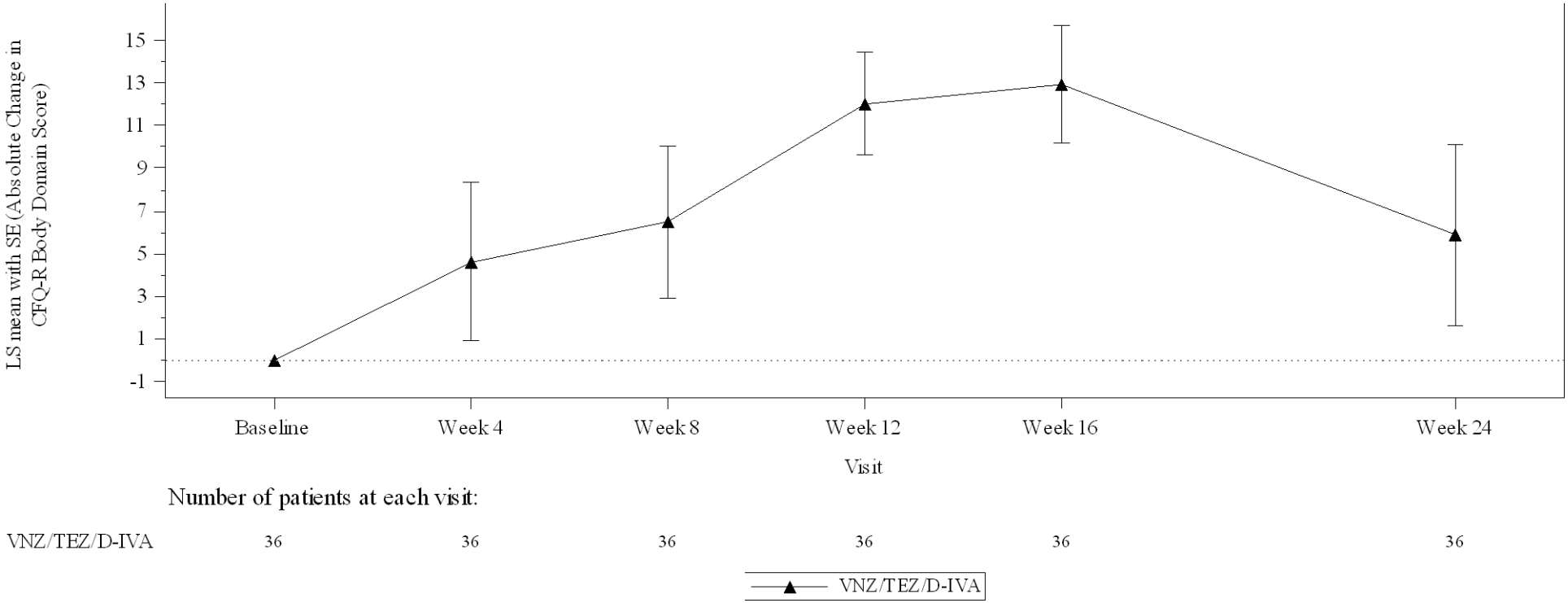
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body
Sex = Female



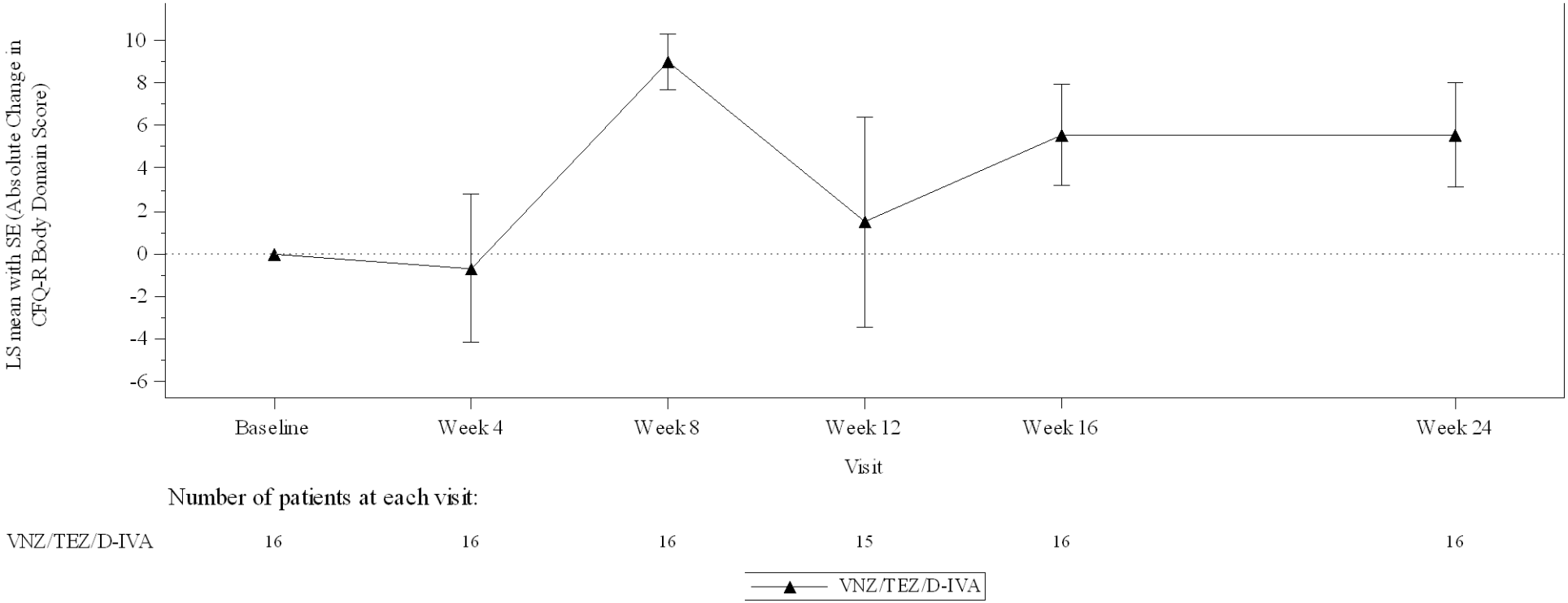
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

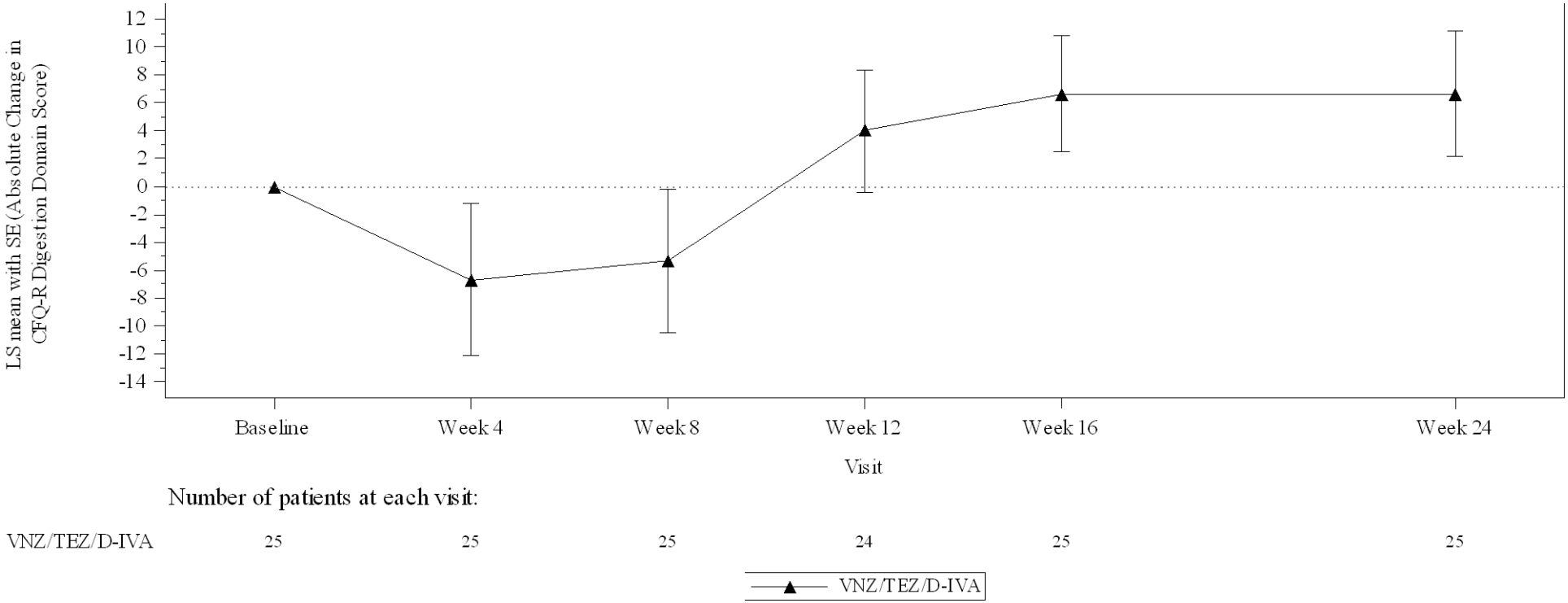
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

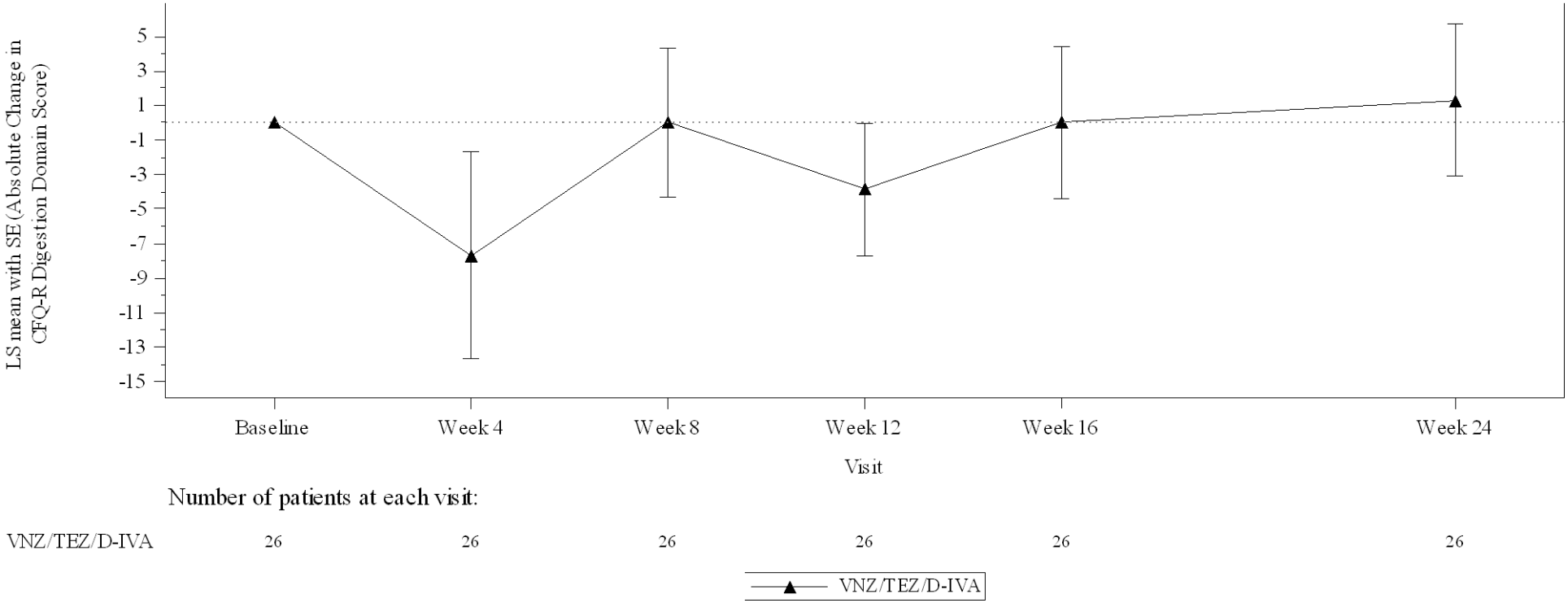
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion
Sex = Male



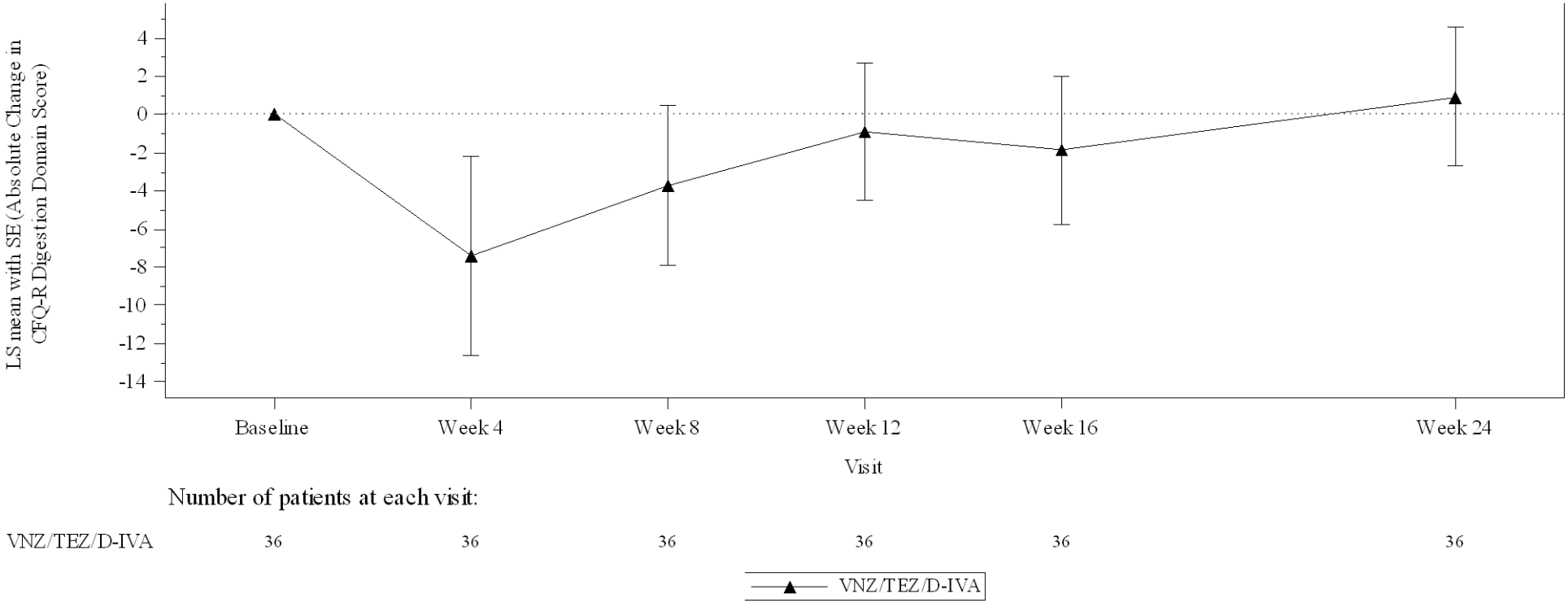
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion
Sex = Female



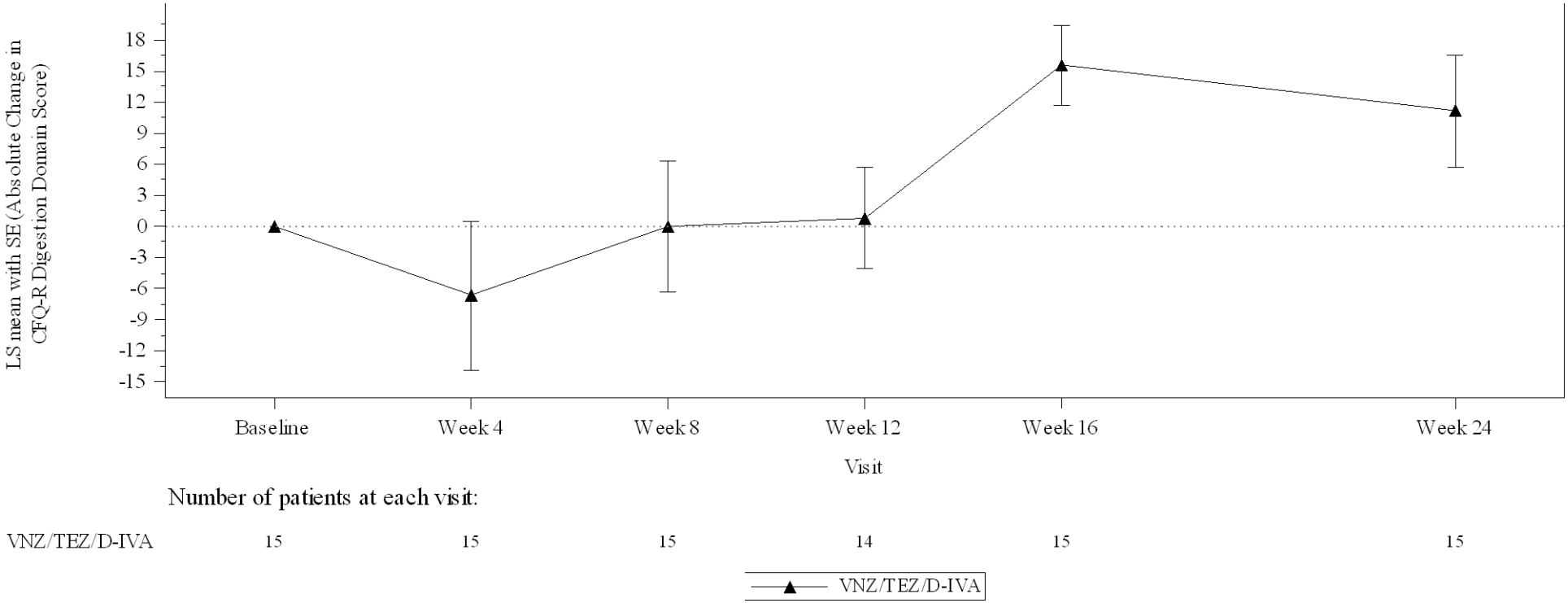
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion
$LCI_{2.5}$ at baseline <7.5

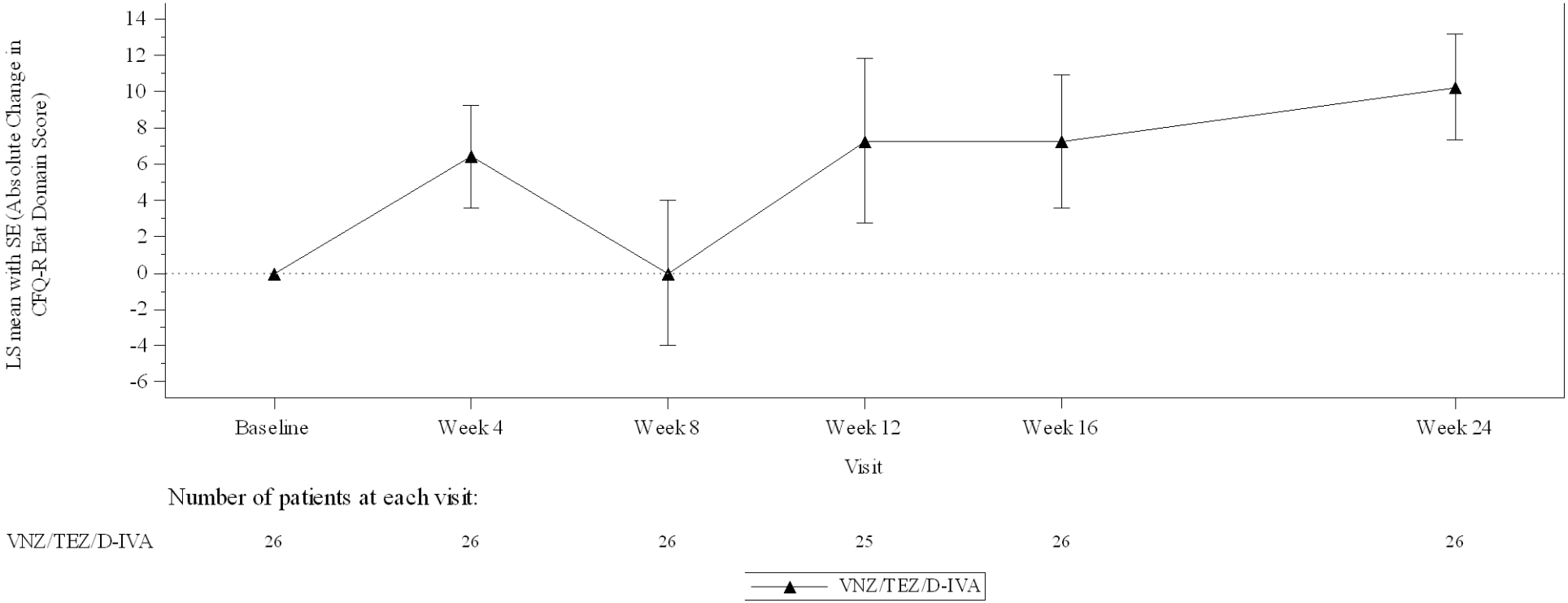
Subgroup criteria are not met for this subgroup factor.

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

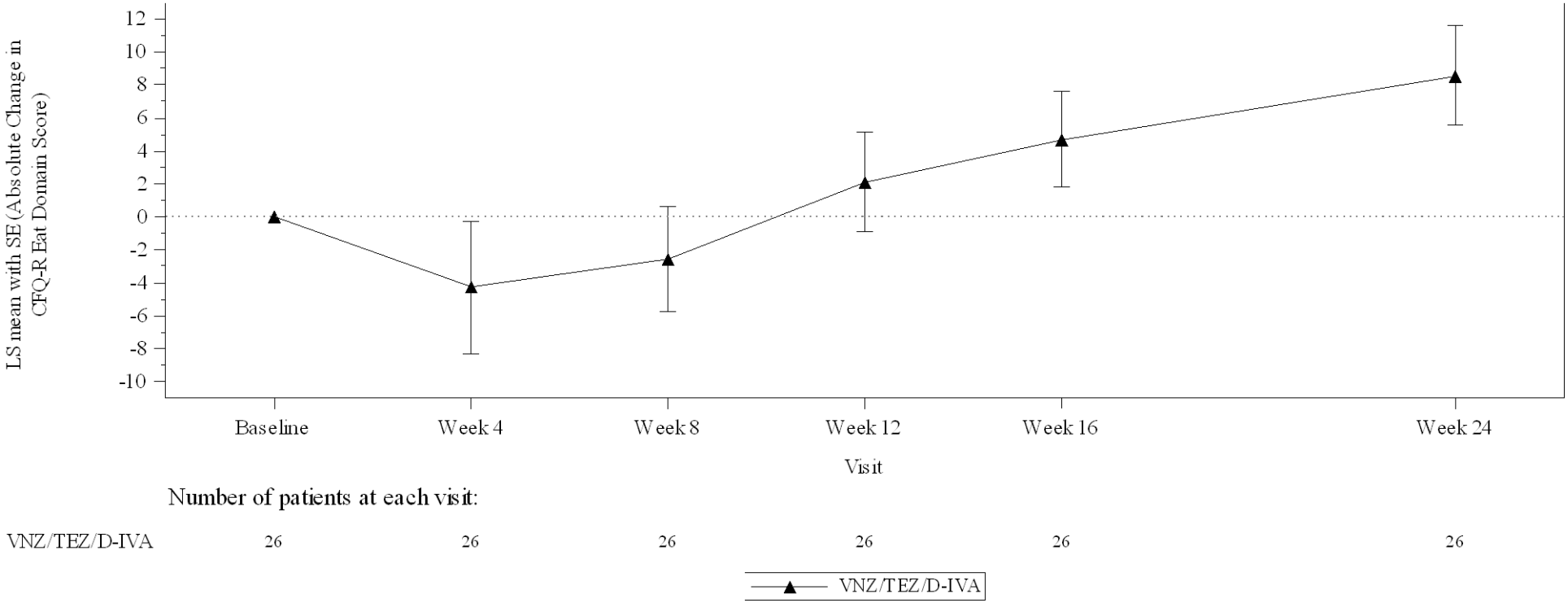
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat
Sex = Male



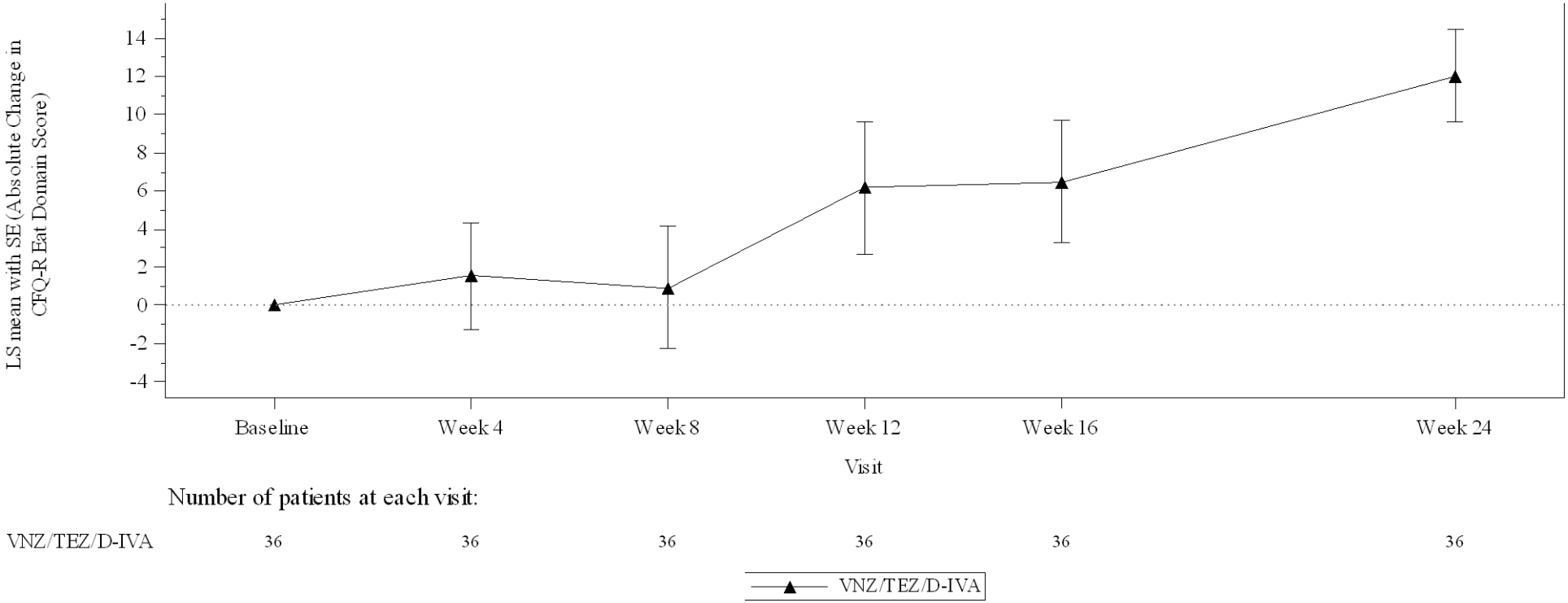
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat
Sex = Female



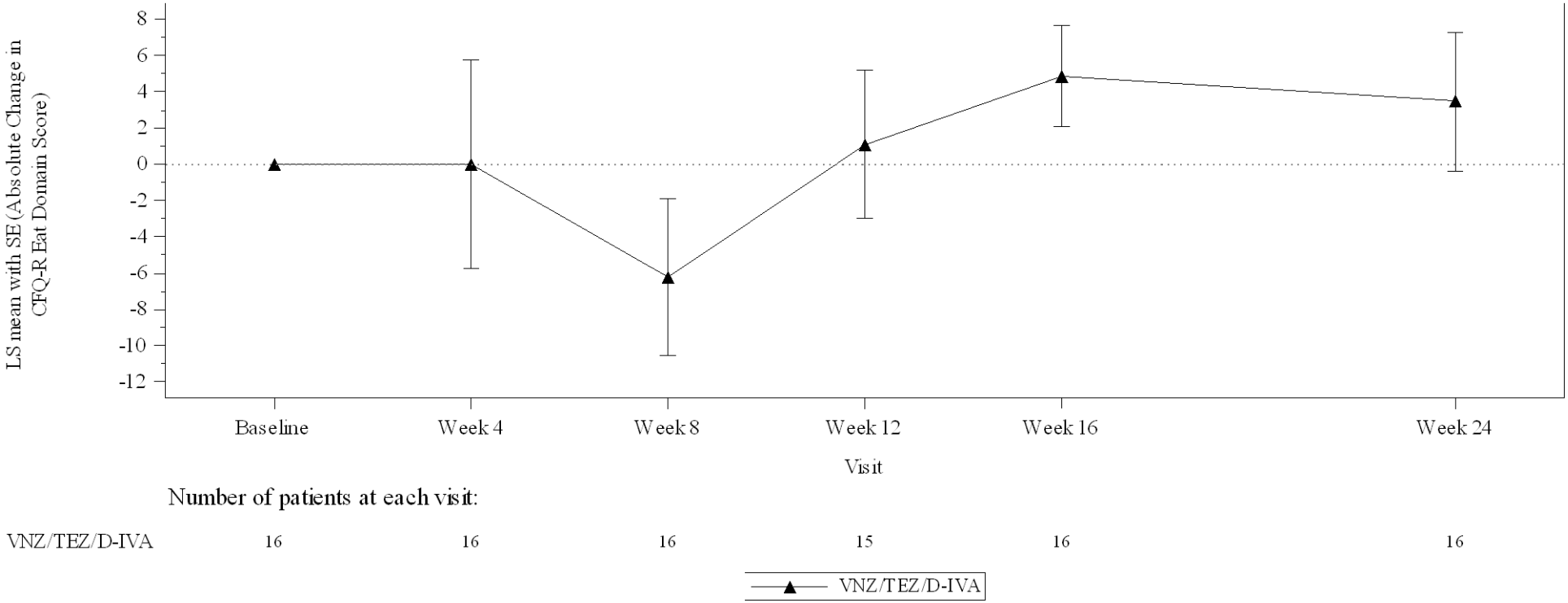
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

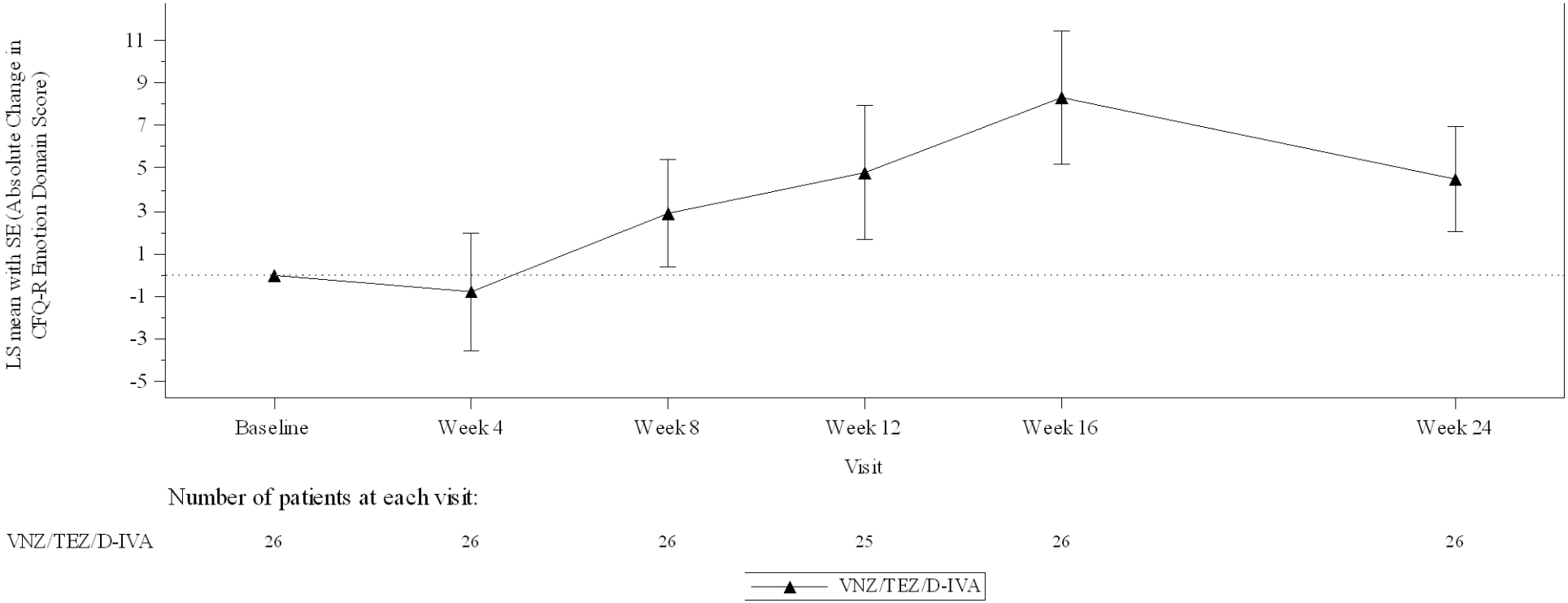
Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5

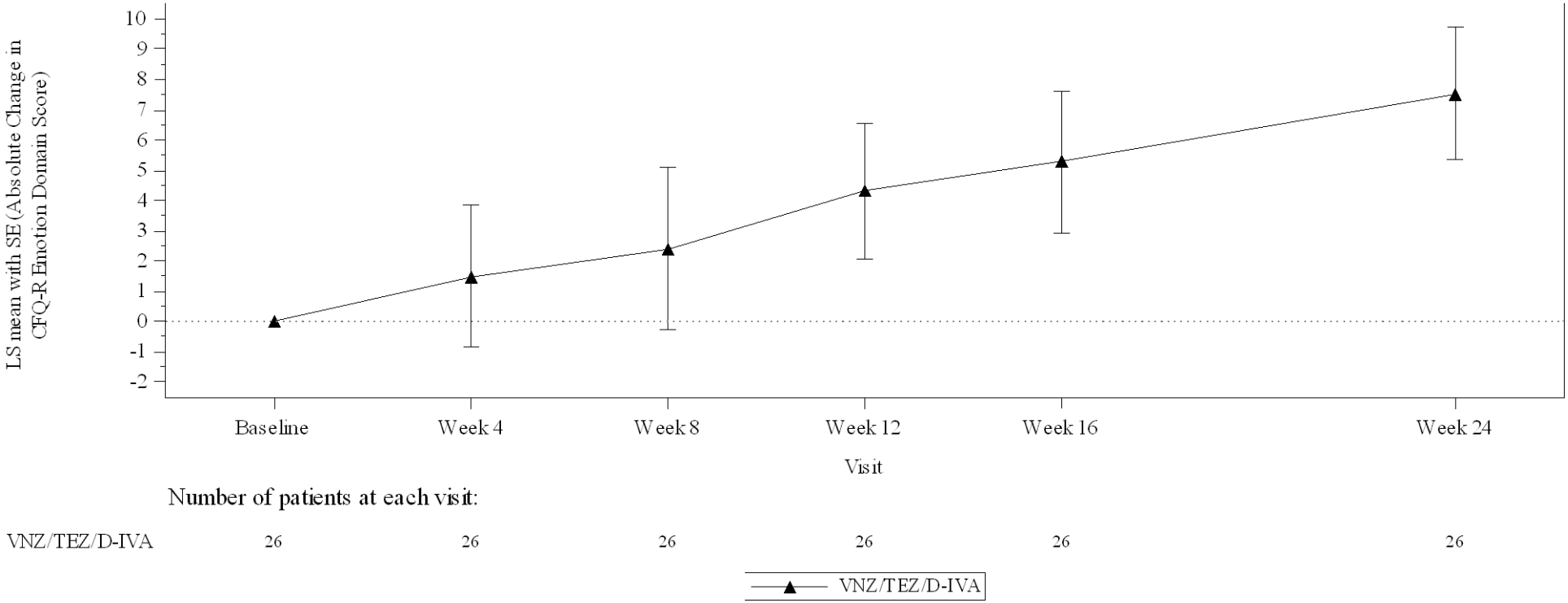
Subgroup criteria are not met for this subgroup factor.

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion
Sex = Male



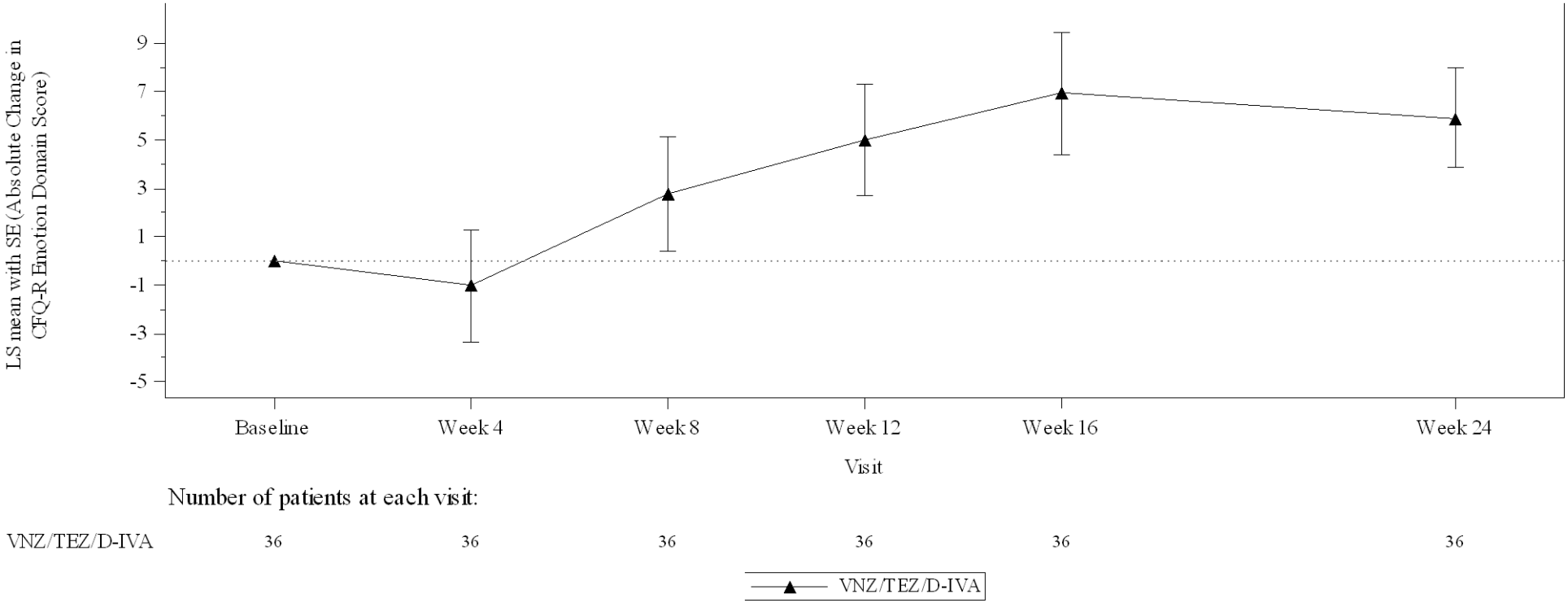
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion
Sex = Female



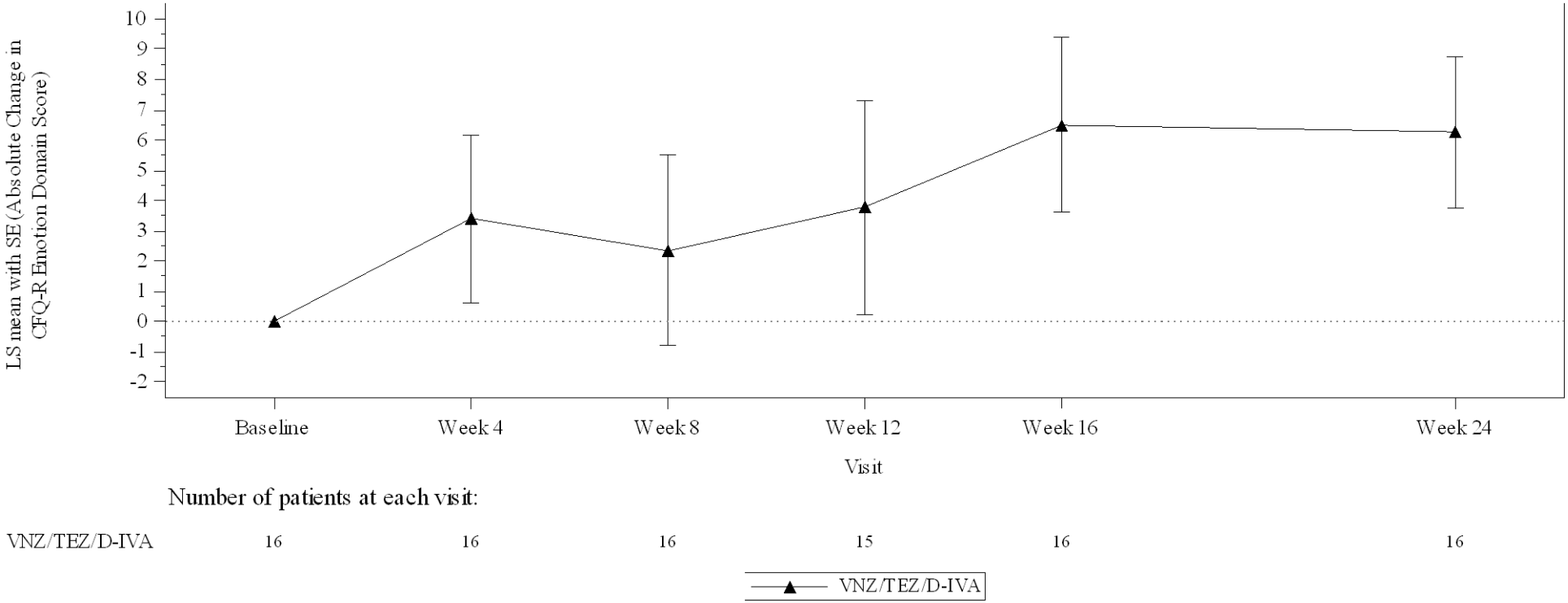
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

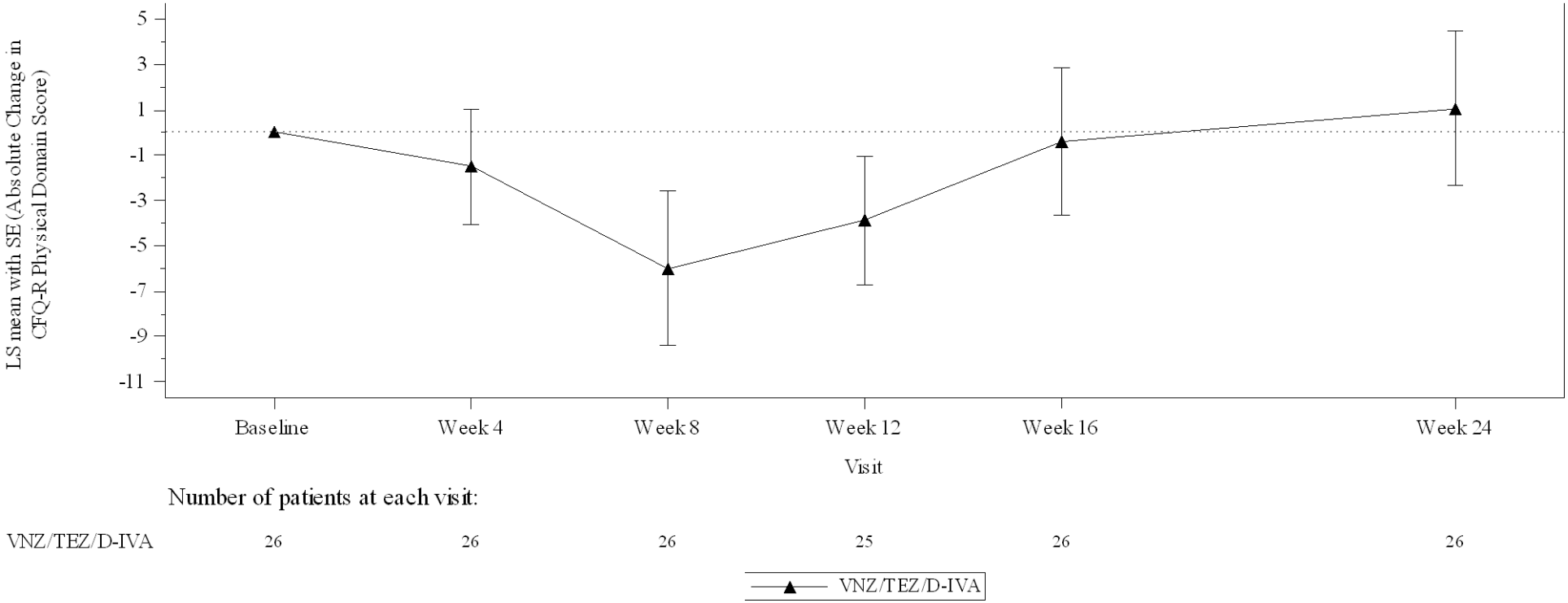
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

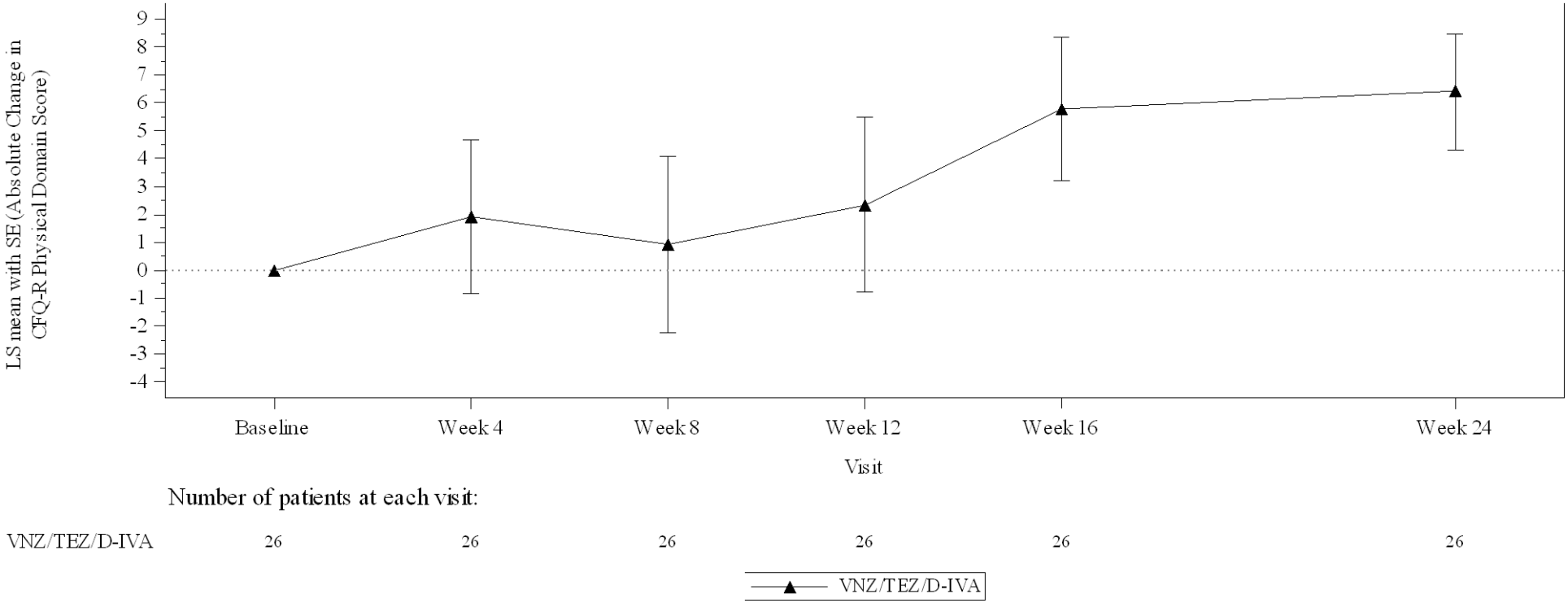
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical
Sex = Male



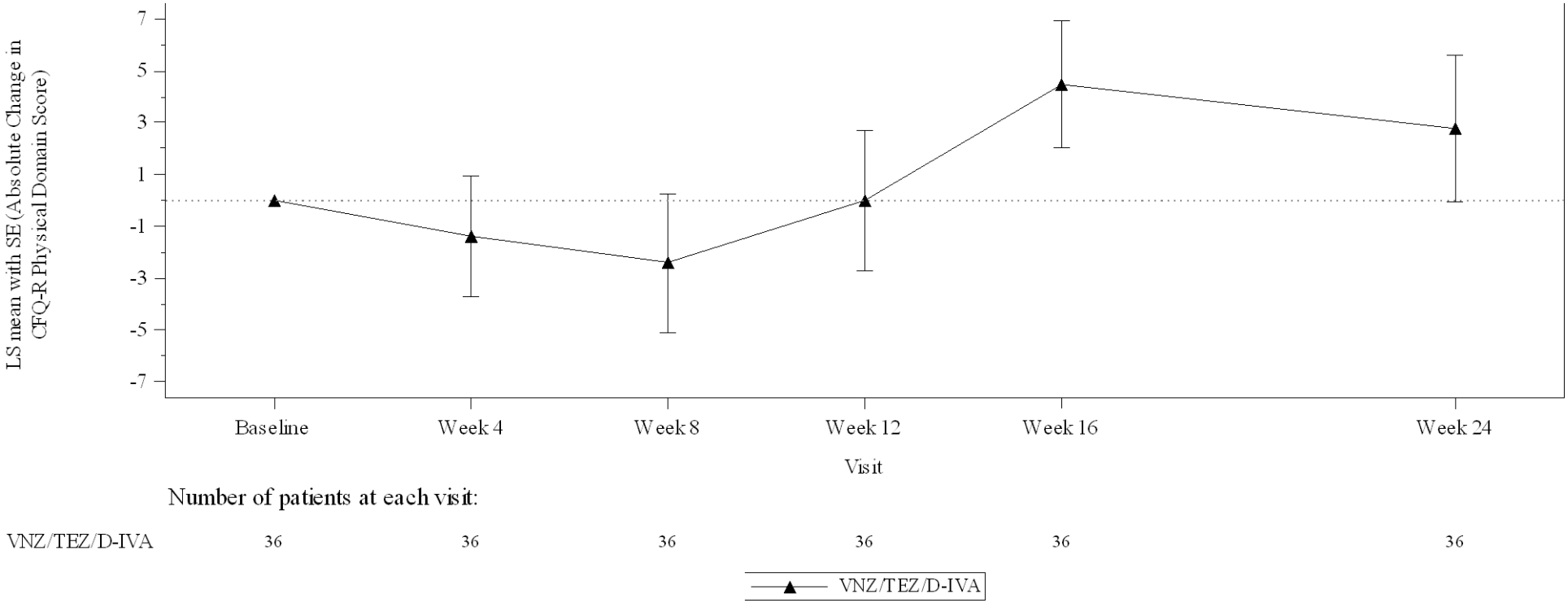
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical
Sex = Female



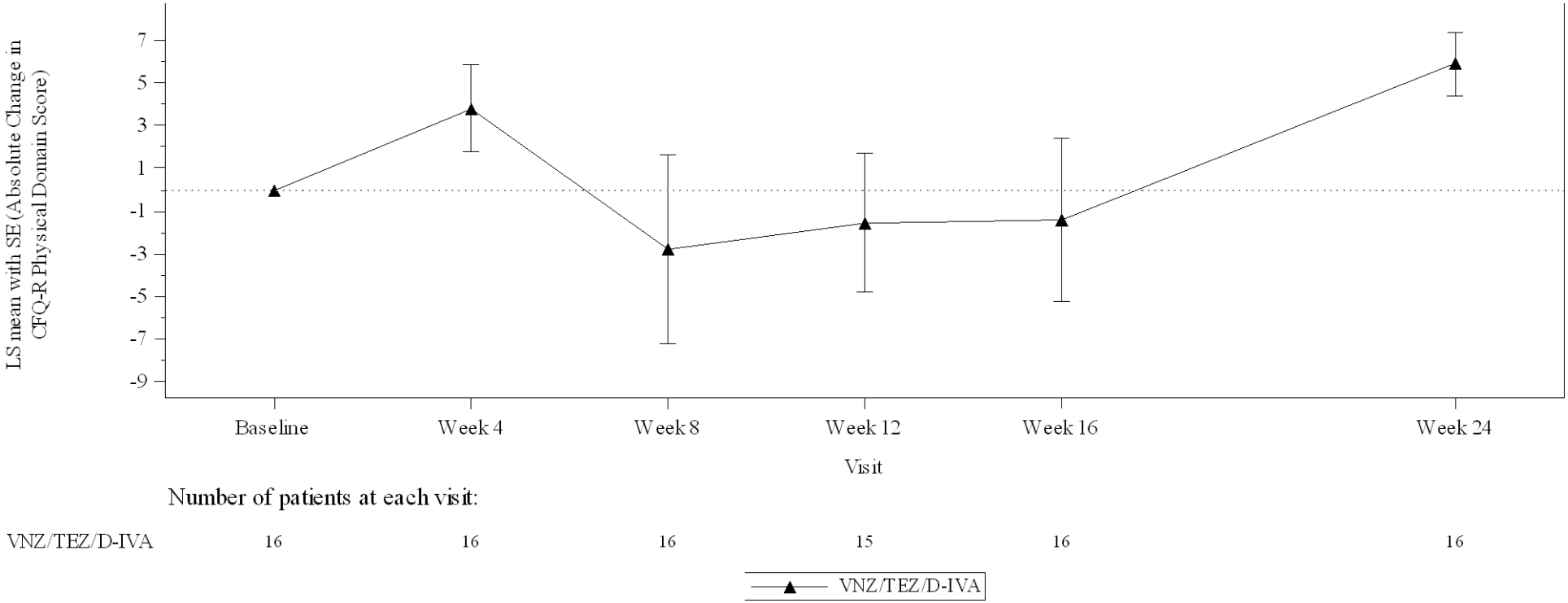
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical
$LCI_{2.5}$ at baseline <7.5

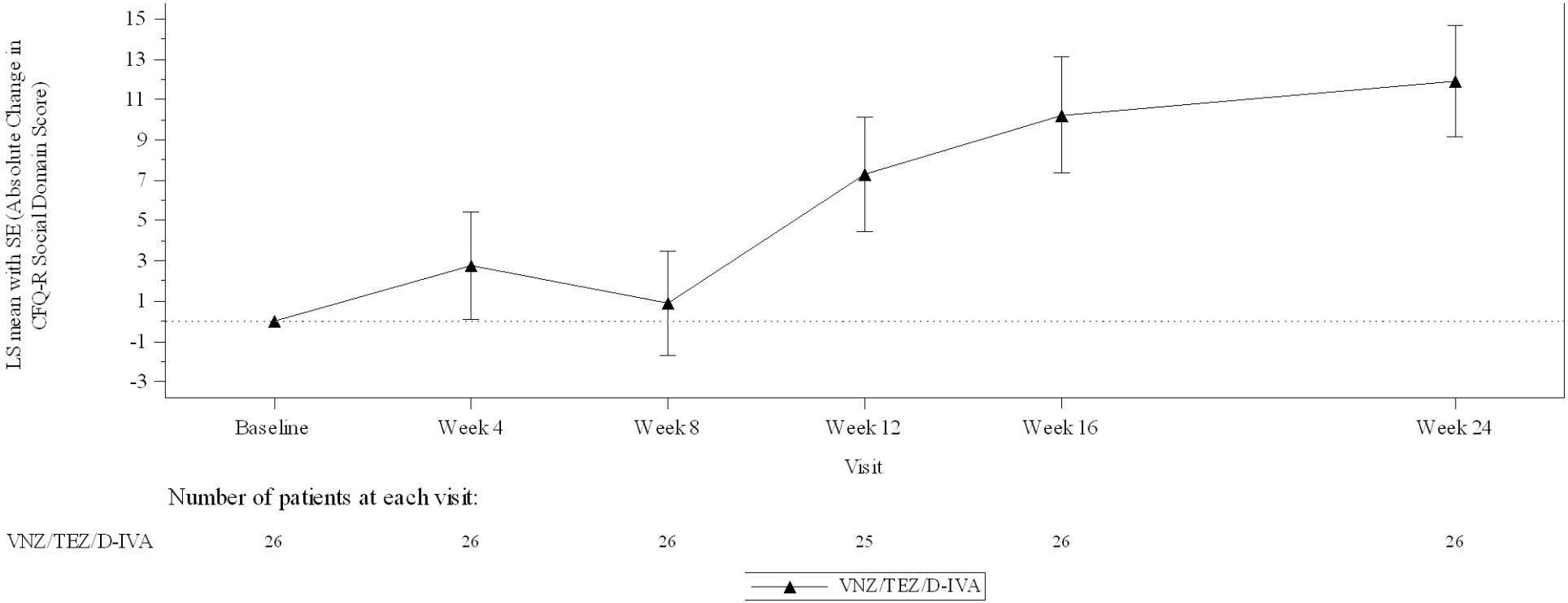
Subgroup criteria are not met for this subgroup factor.

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

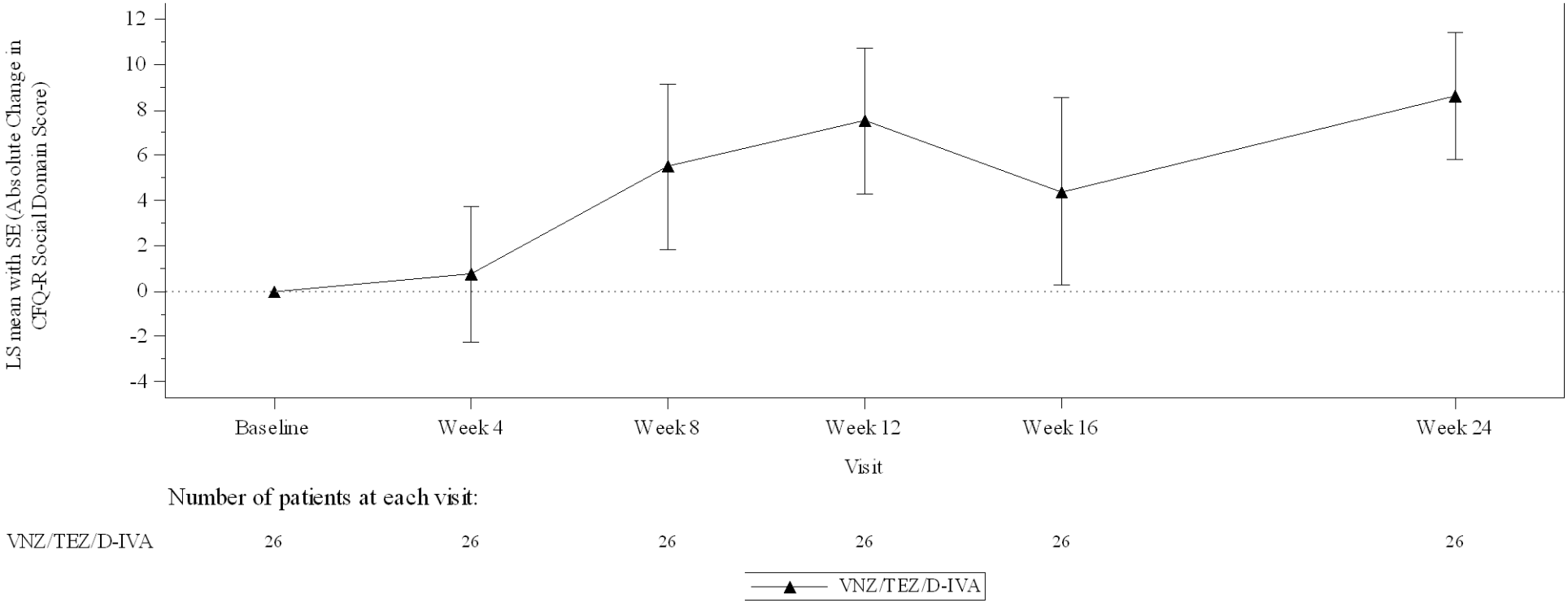
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Social
Sex = Male



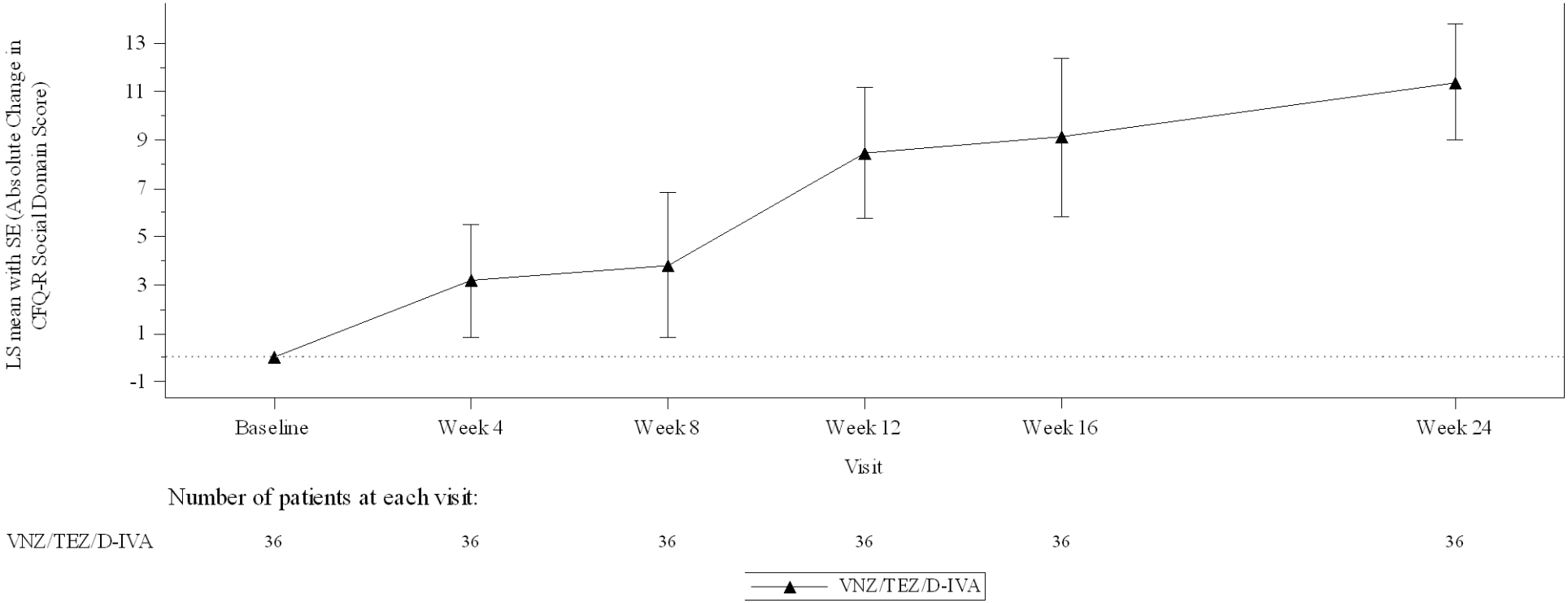
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Social
Sex = Female



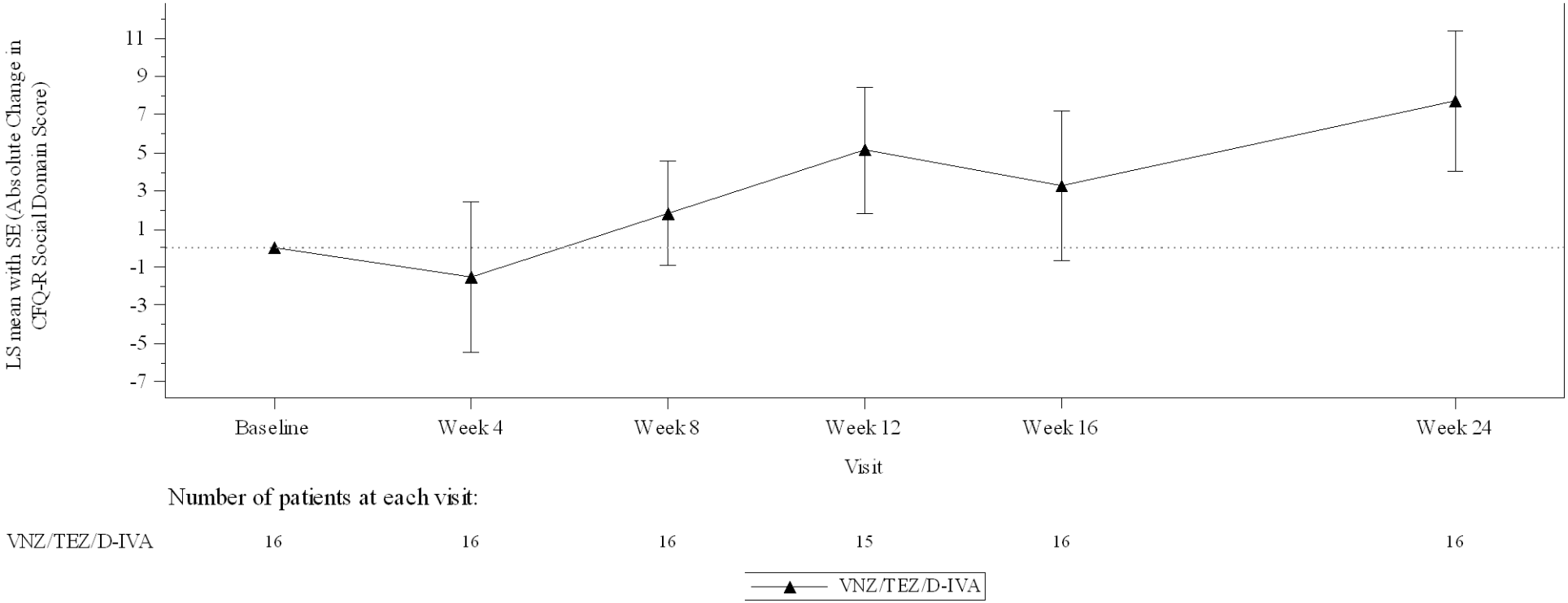
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Social
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Social
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Social
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

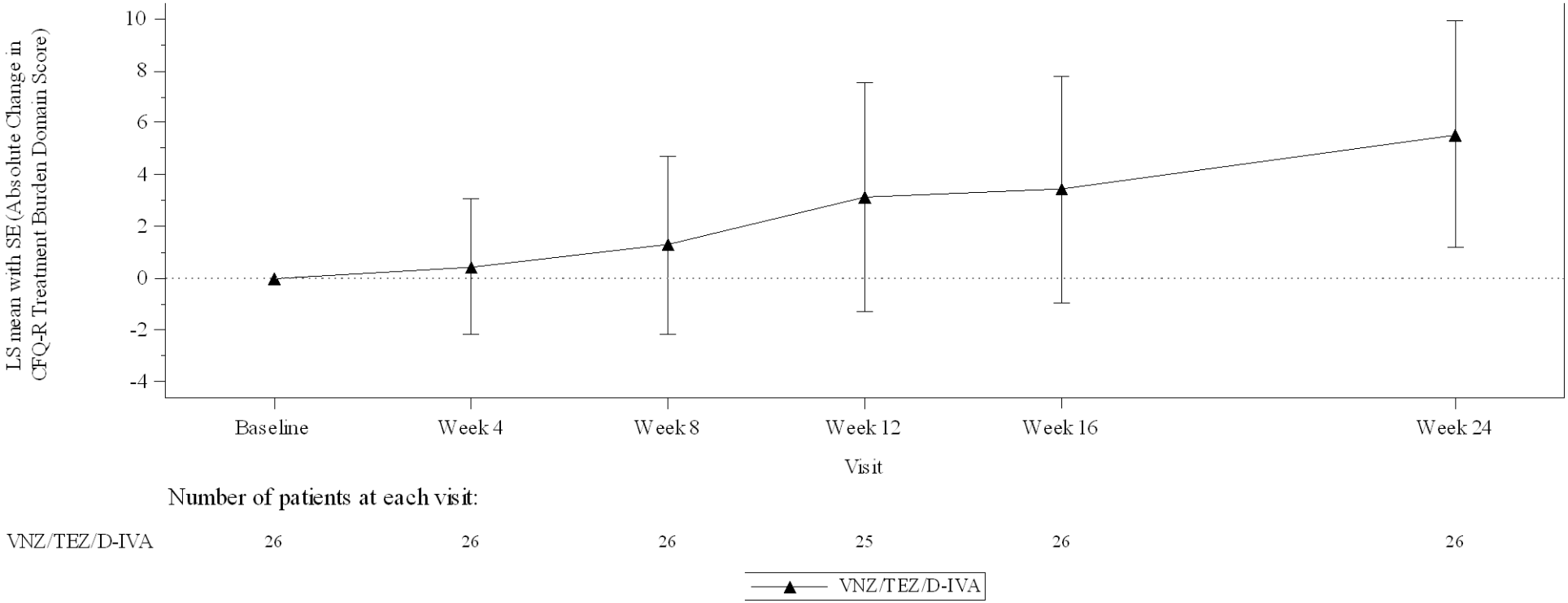
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Social
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

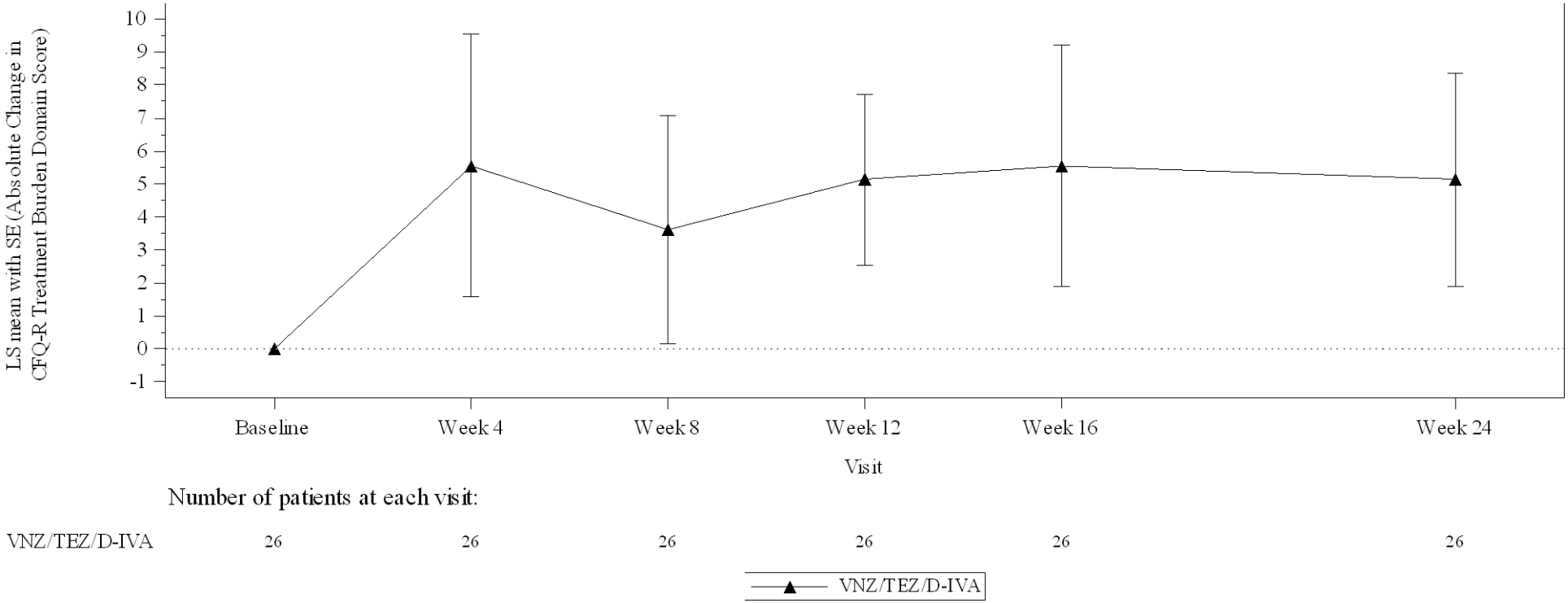
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden
Sex = Male



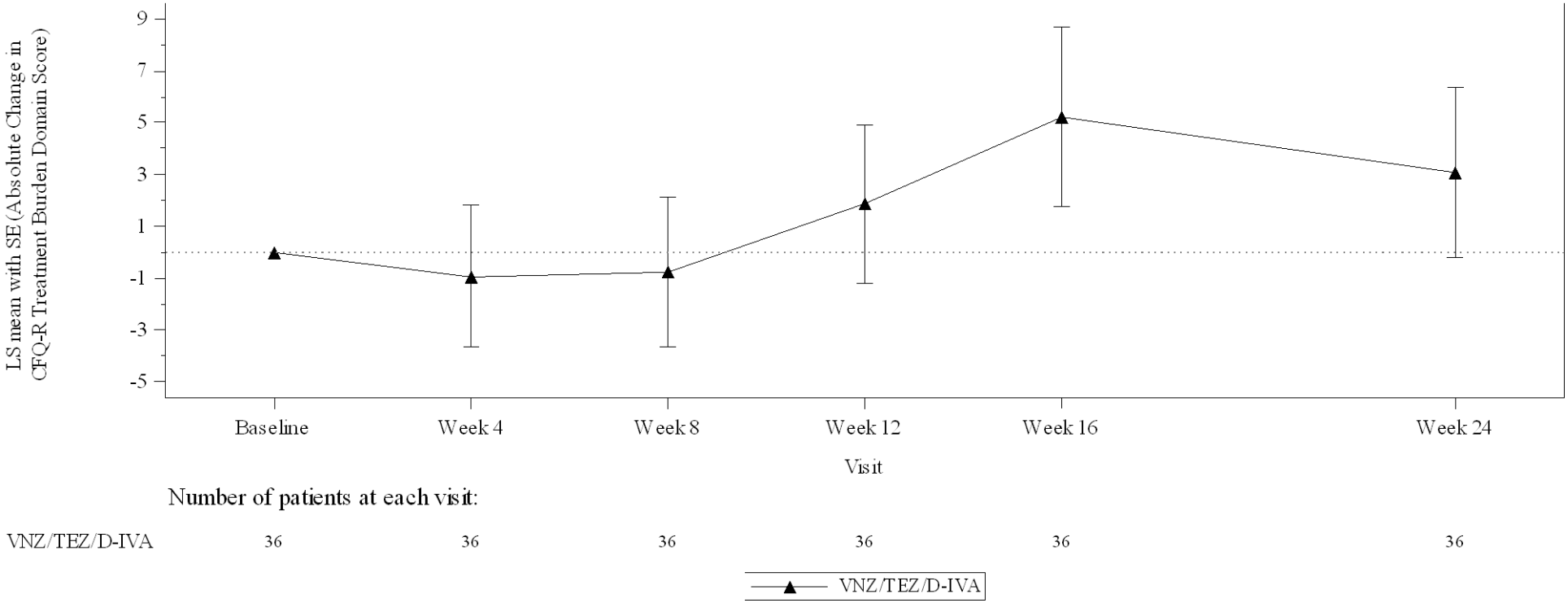
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden
Sex = Female



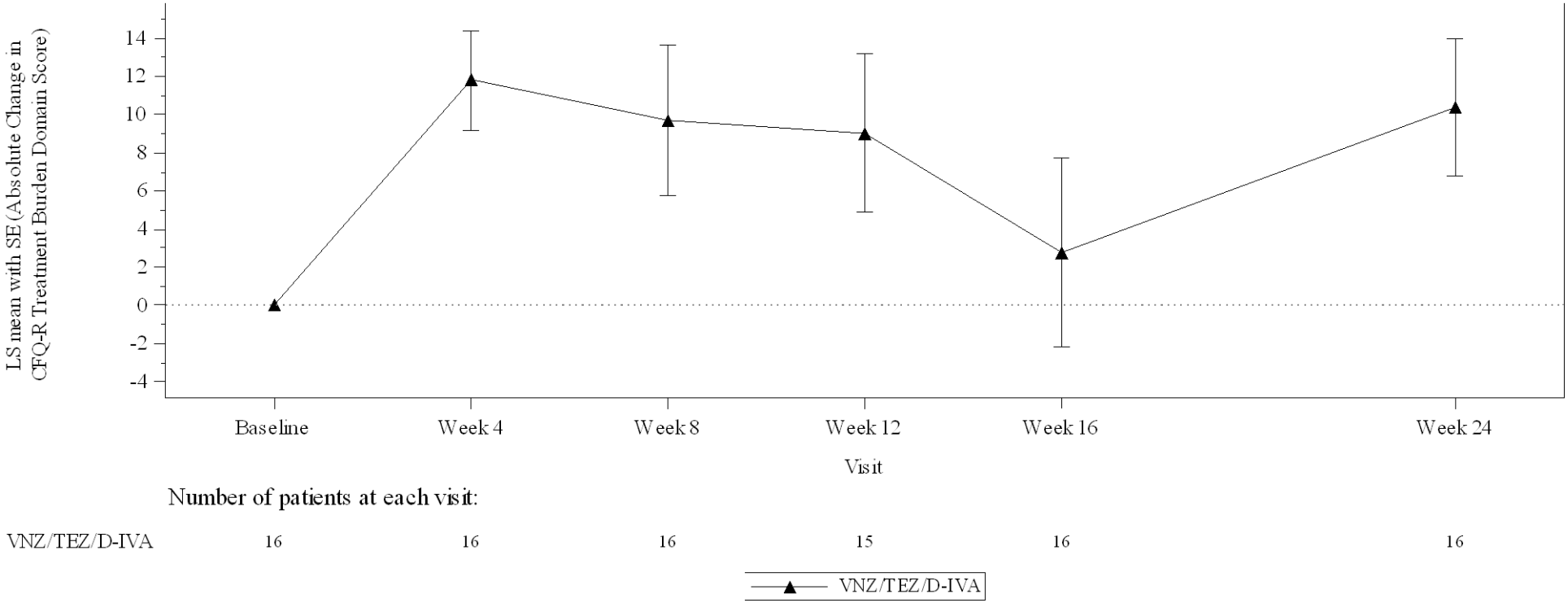
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

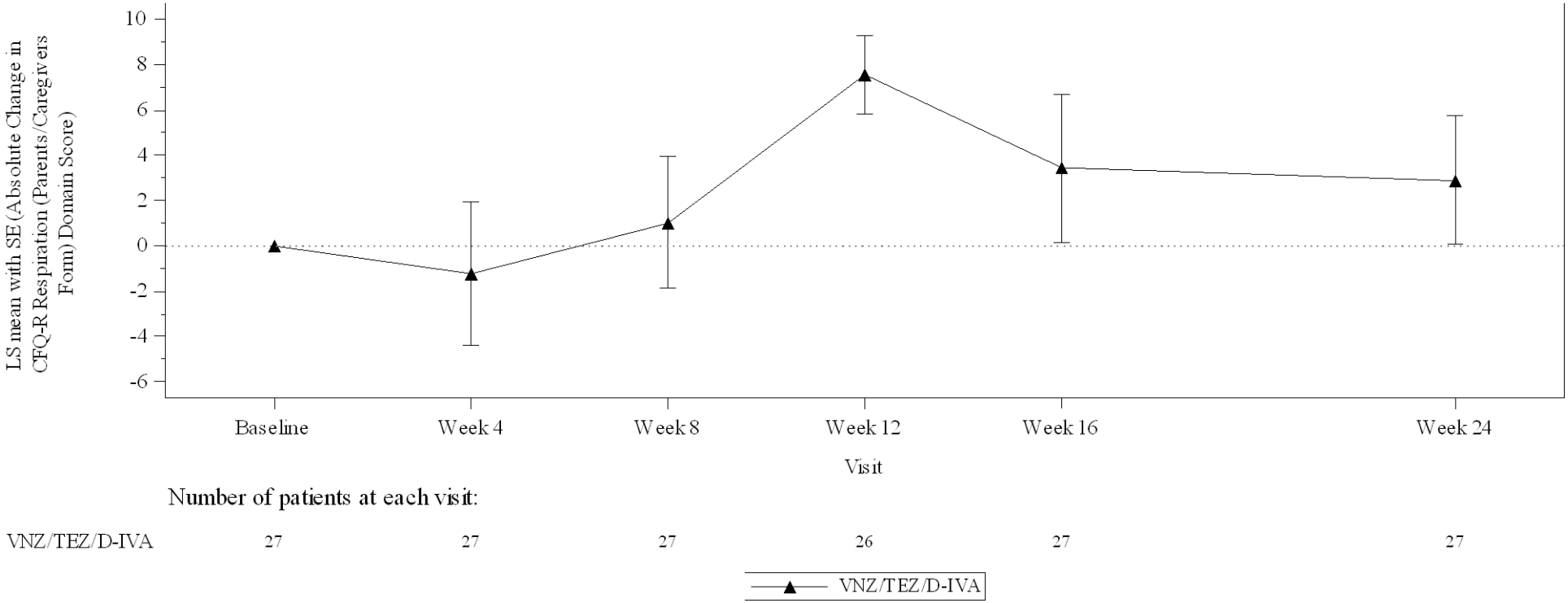
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

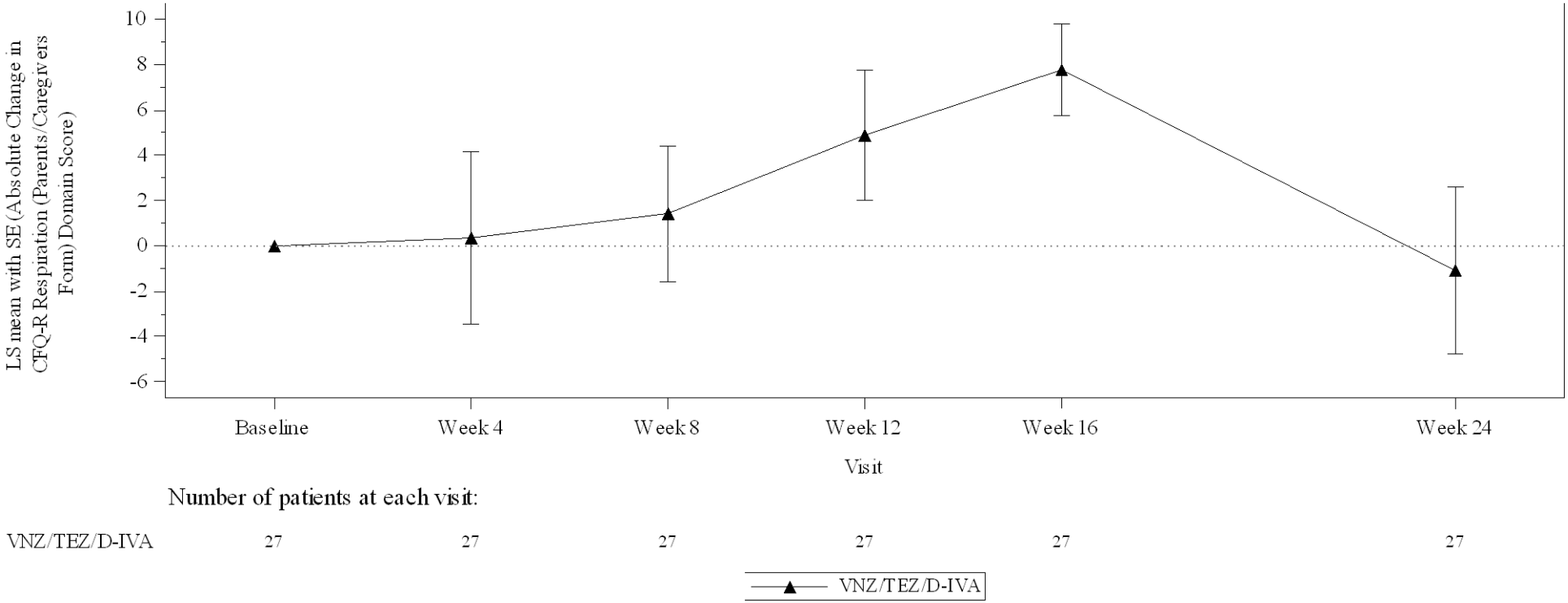
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Sex = Male



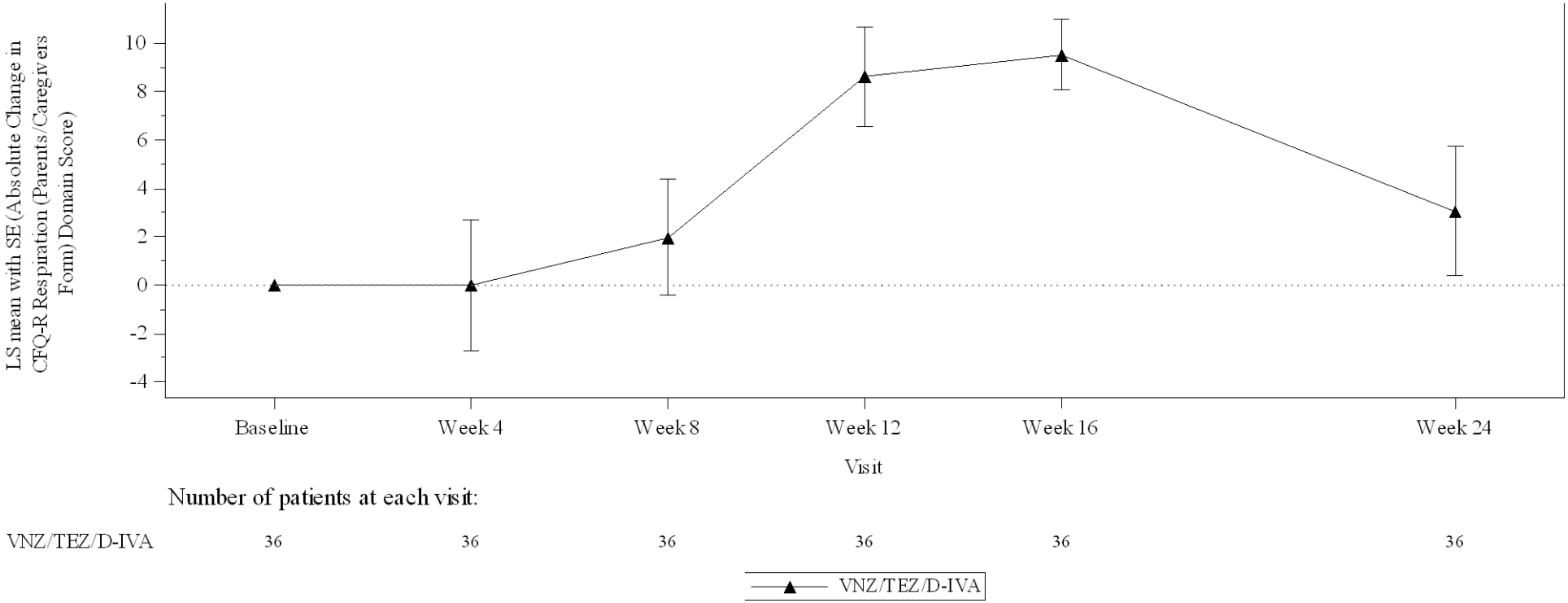
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Sex = Female



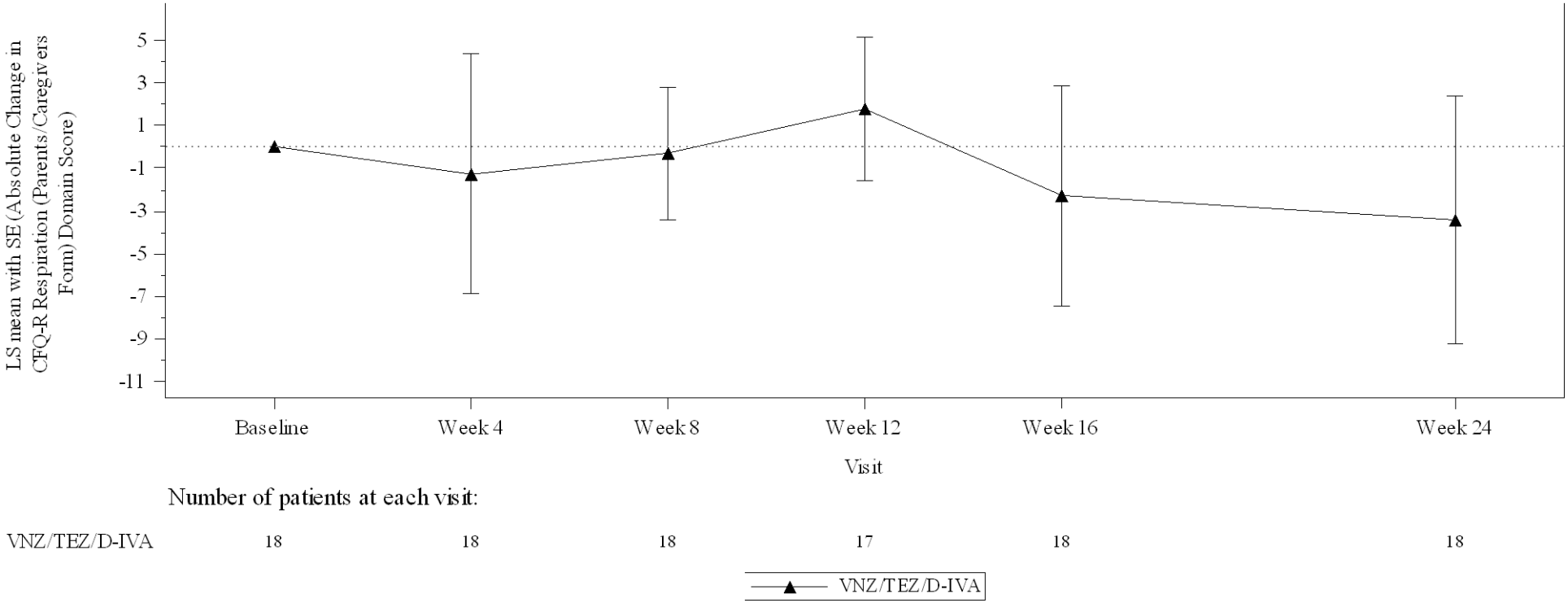
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

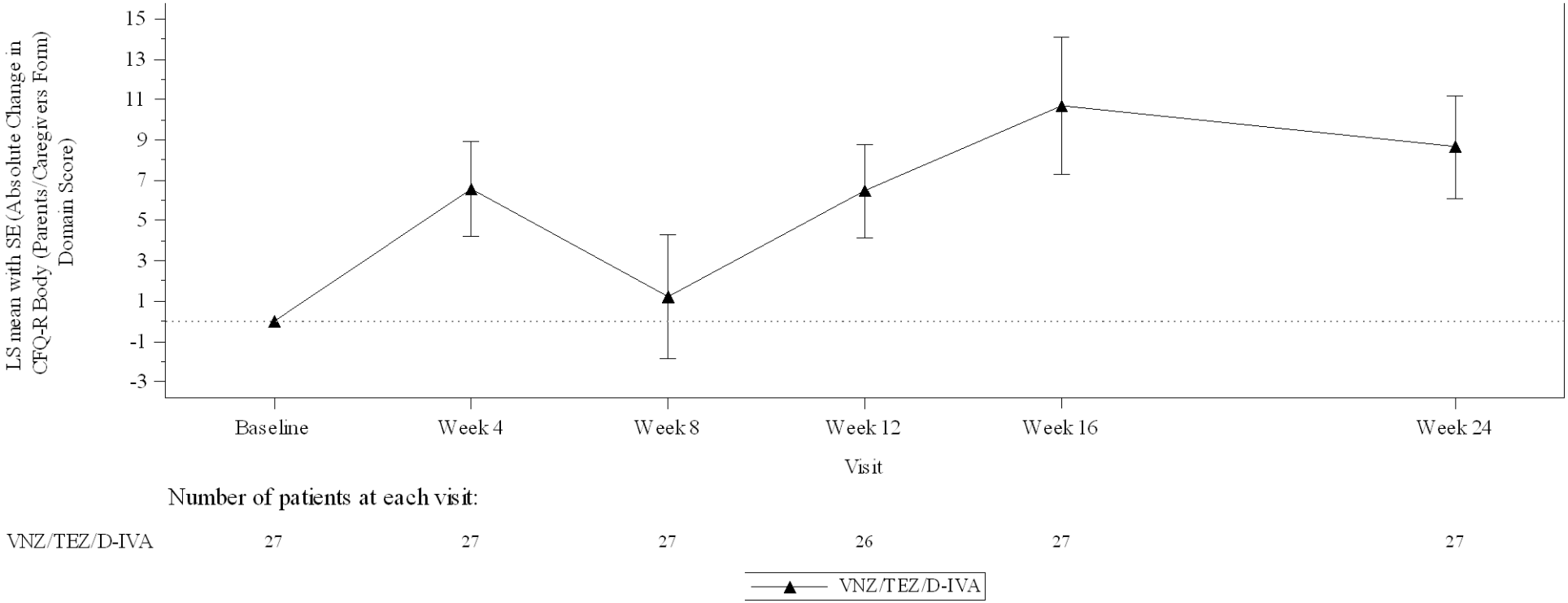
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

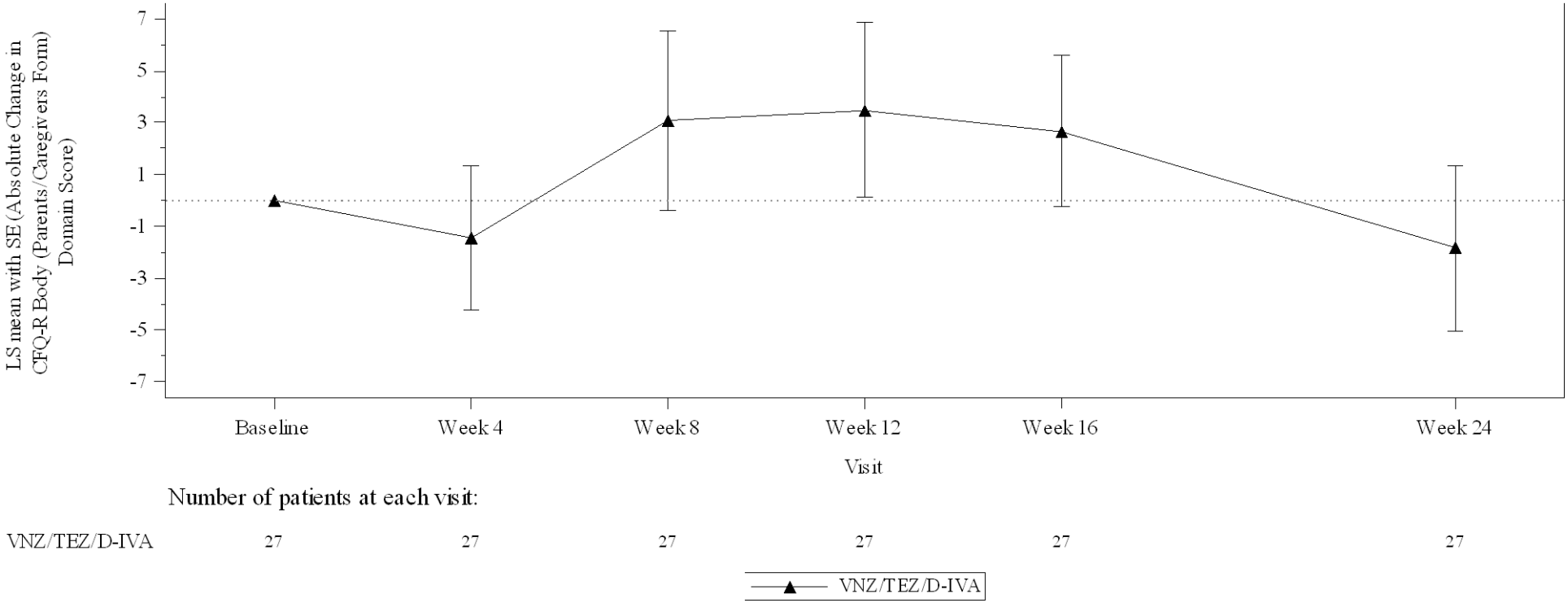
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Sex = Male



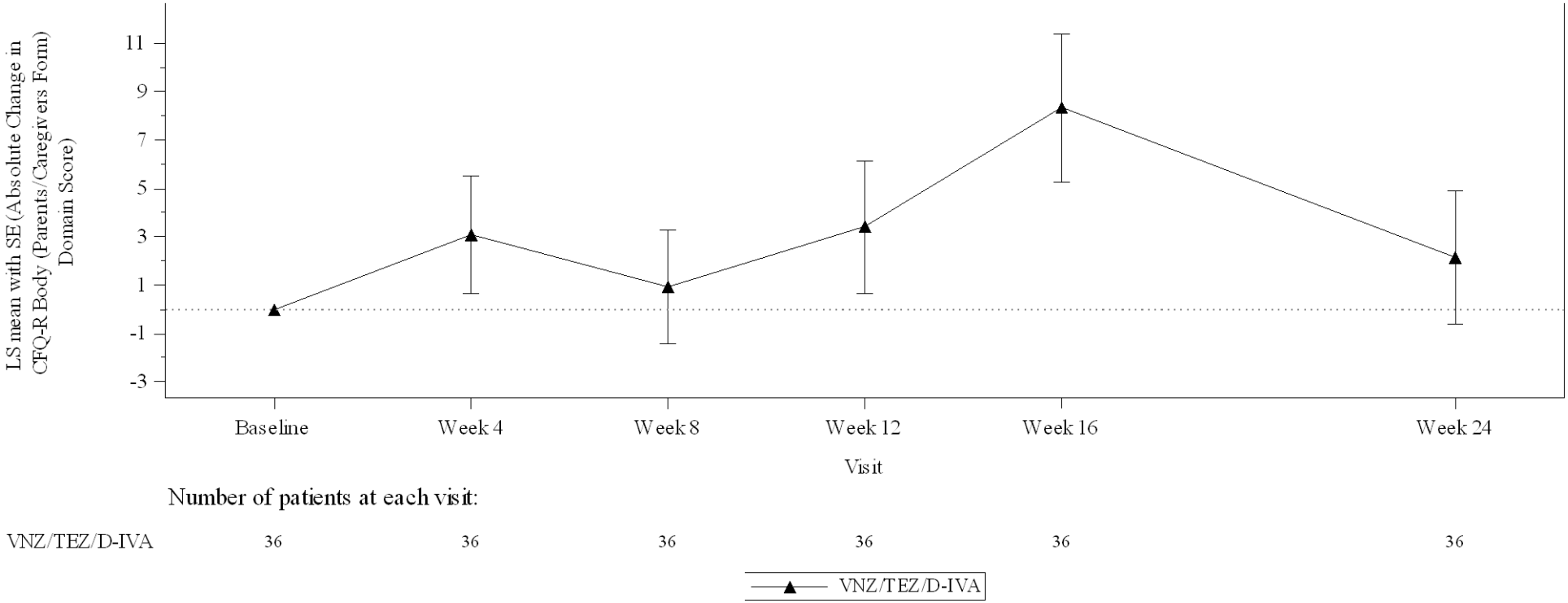
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Sex = Female



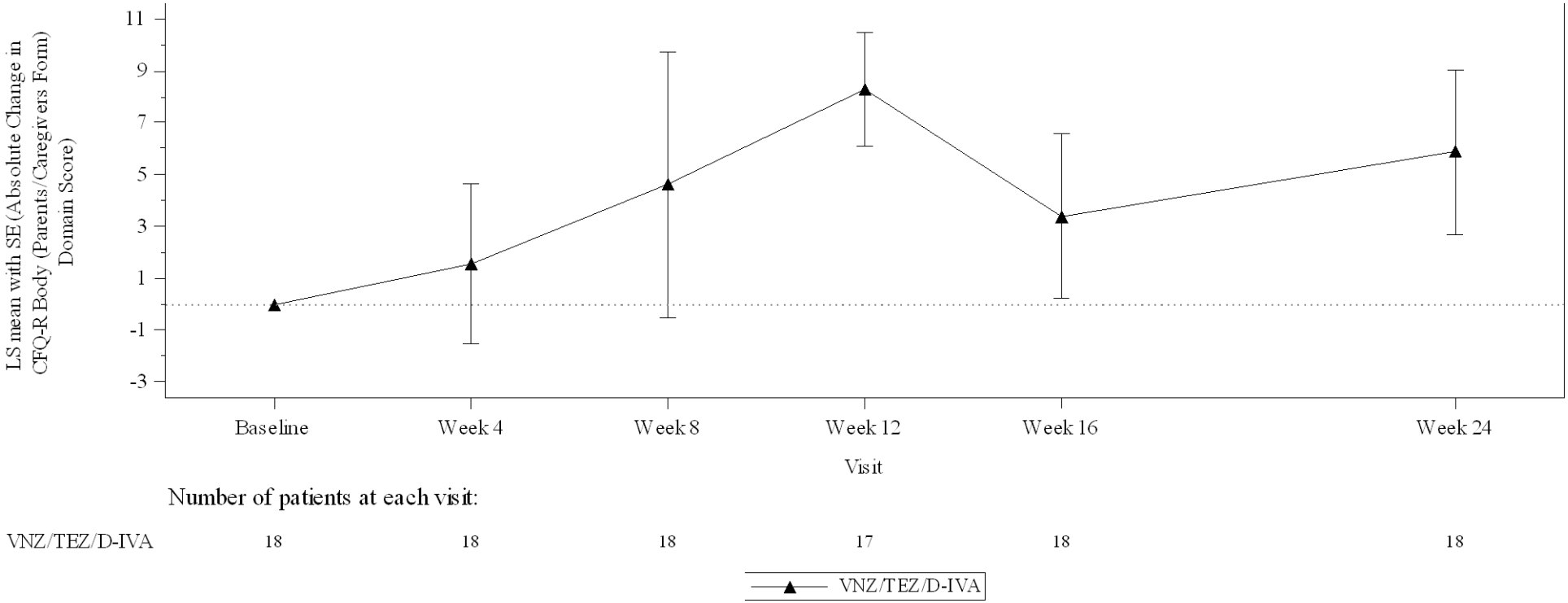
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

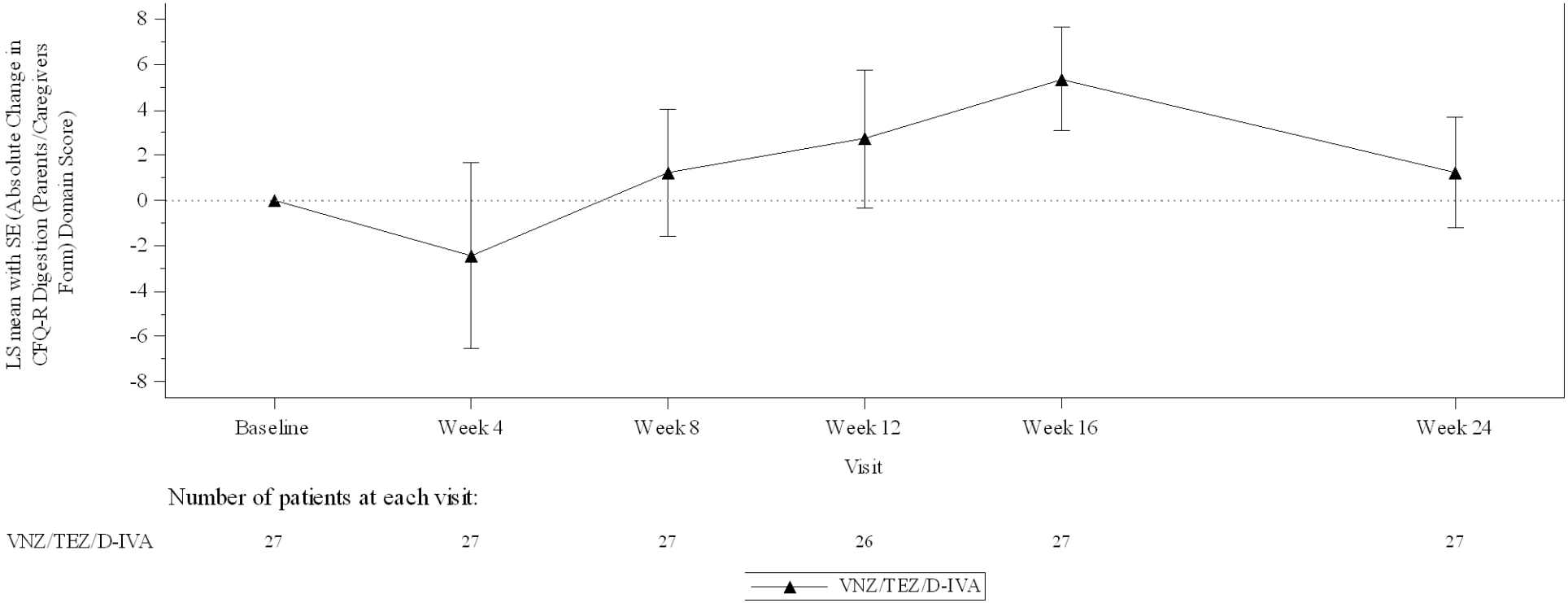
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

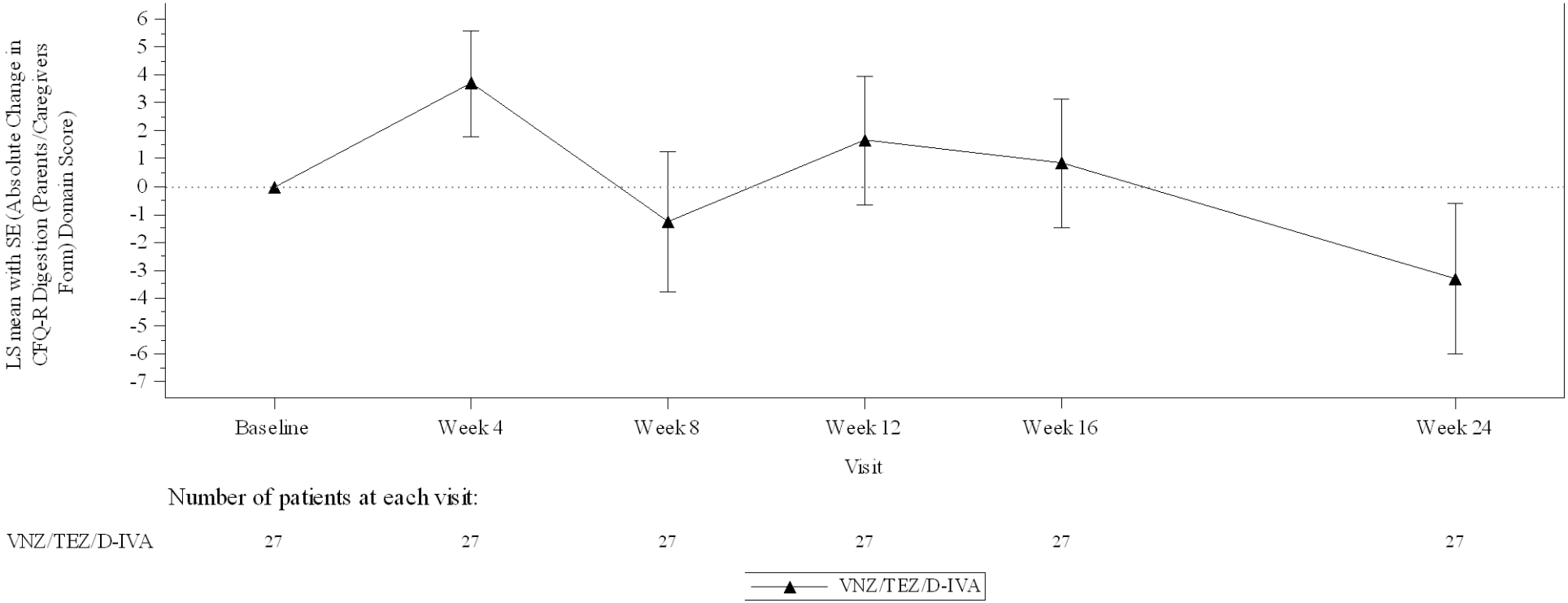
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Sex = Male



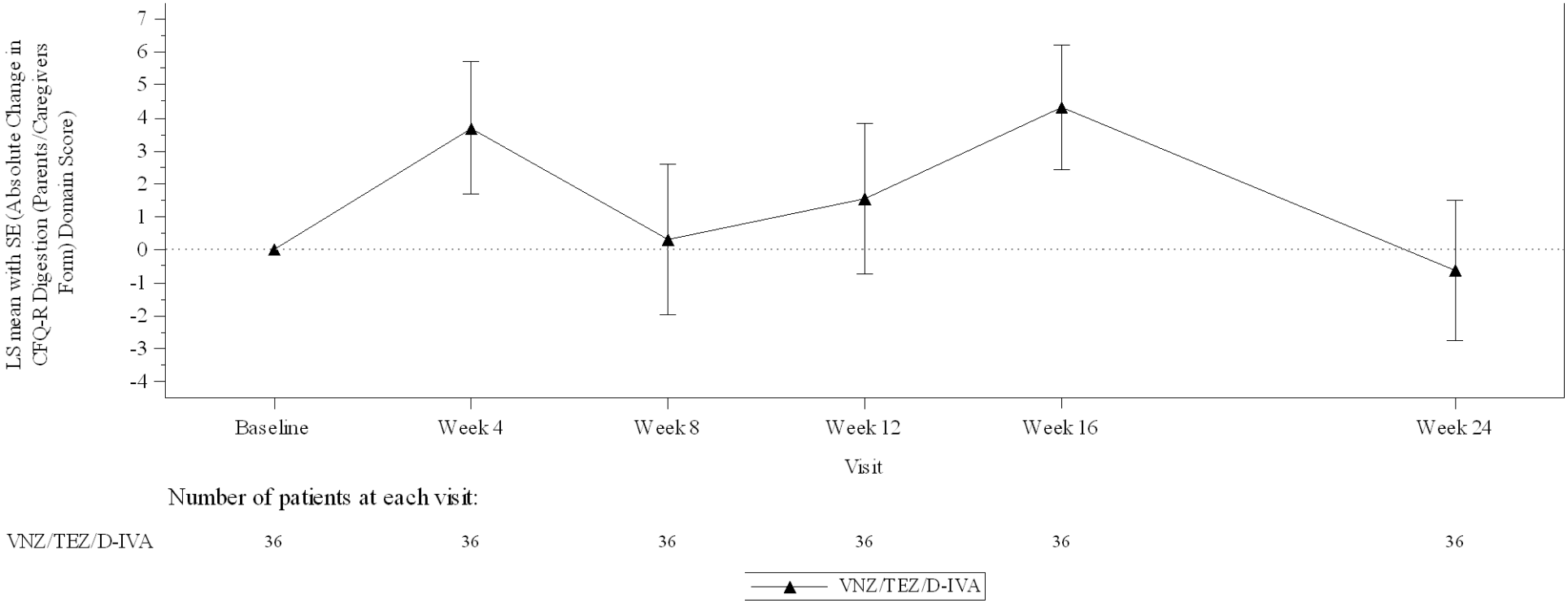
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Sex = Female



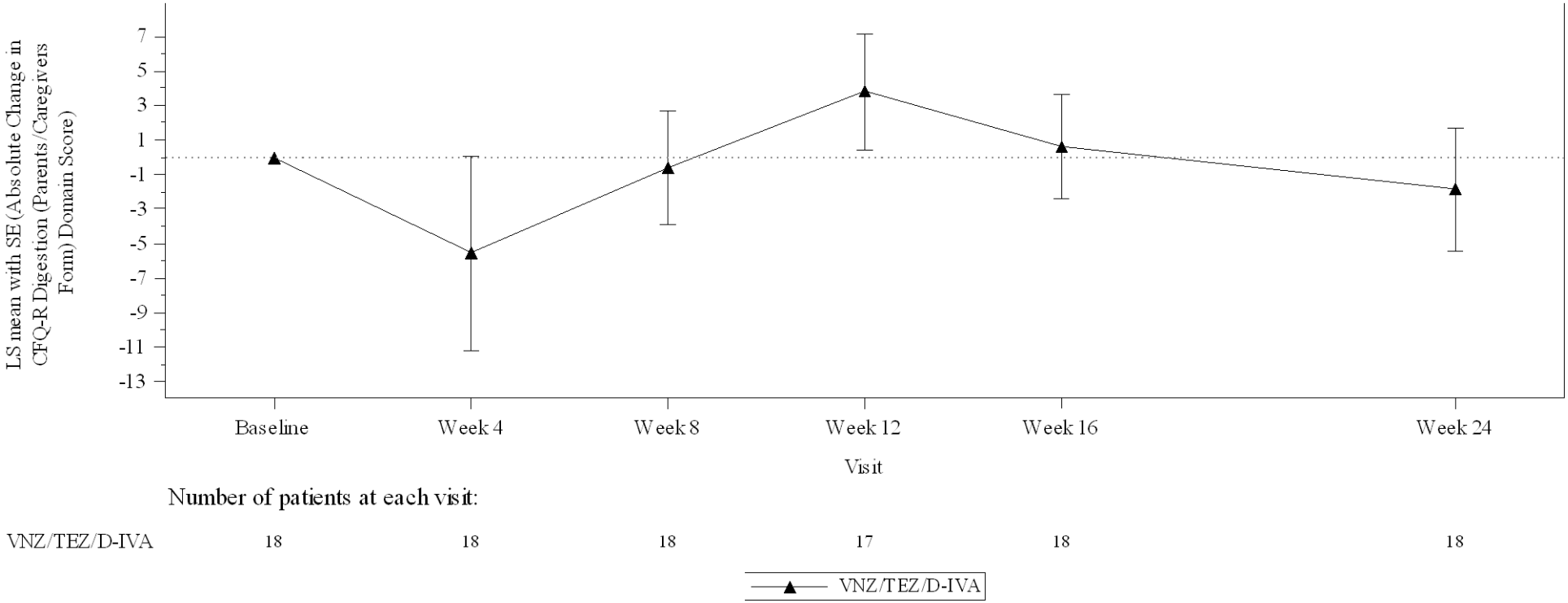
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Region = North America



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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World



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Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

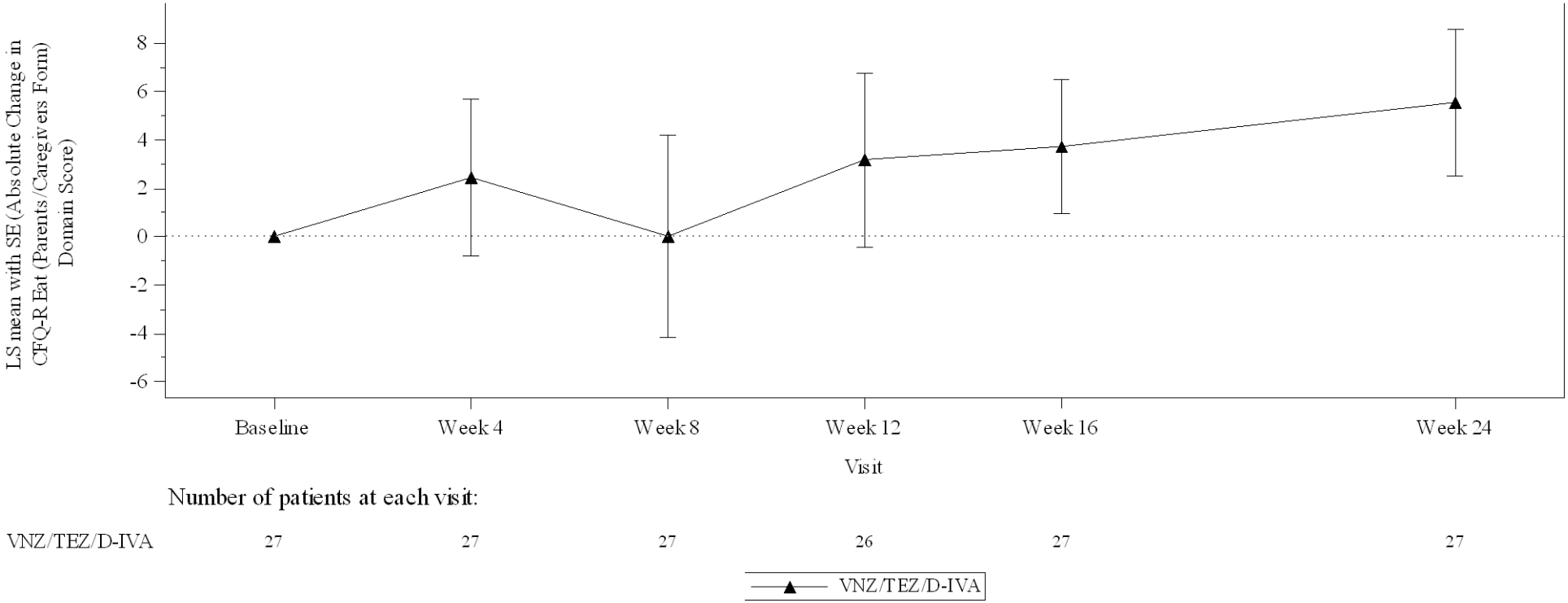
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Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

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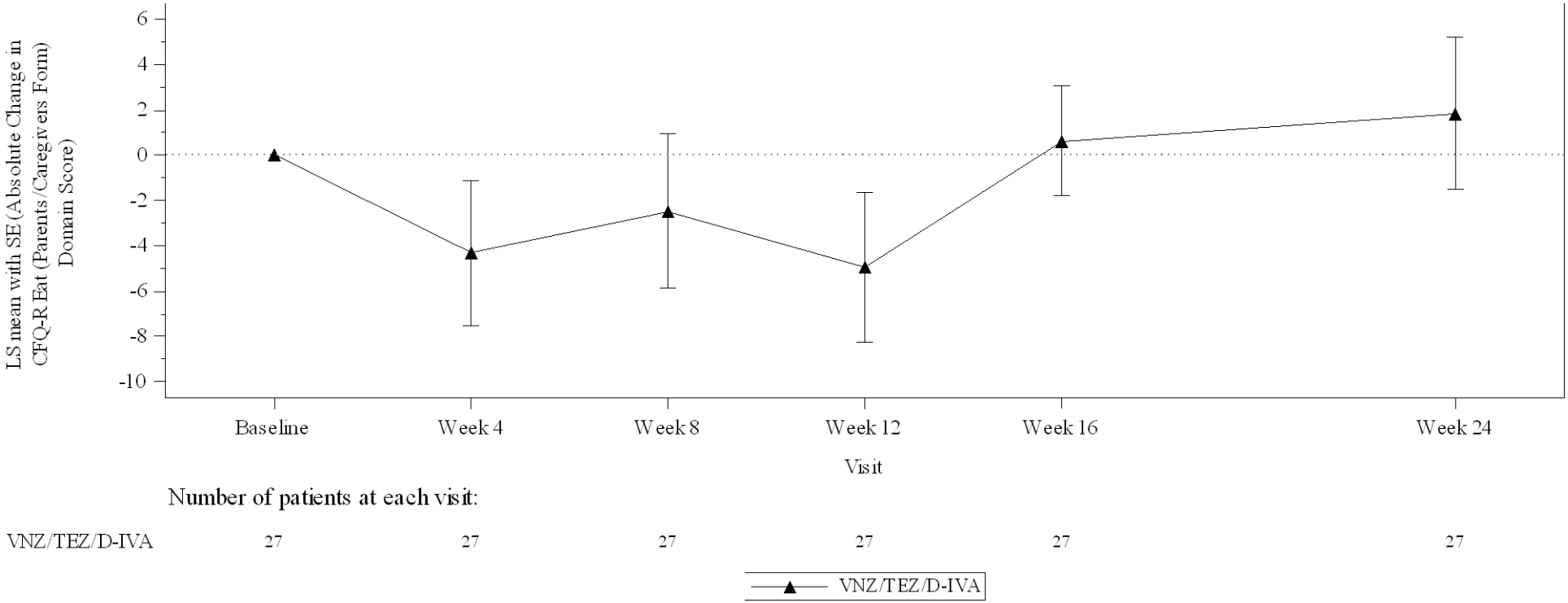
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Sex = Male



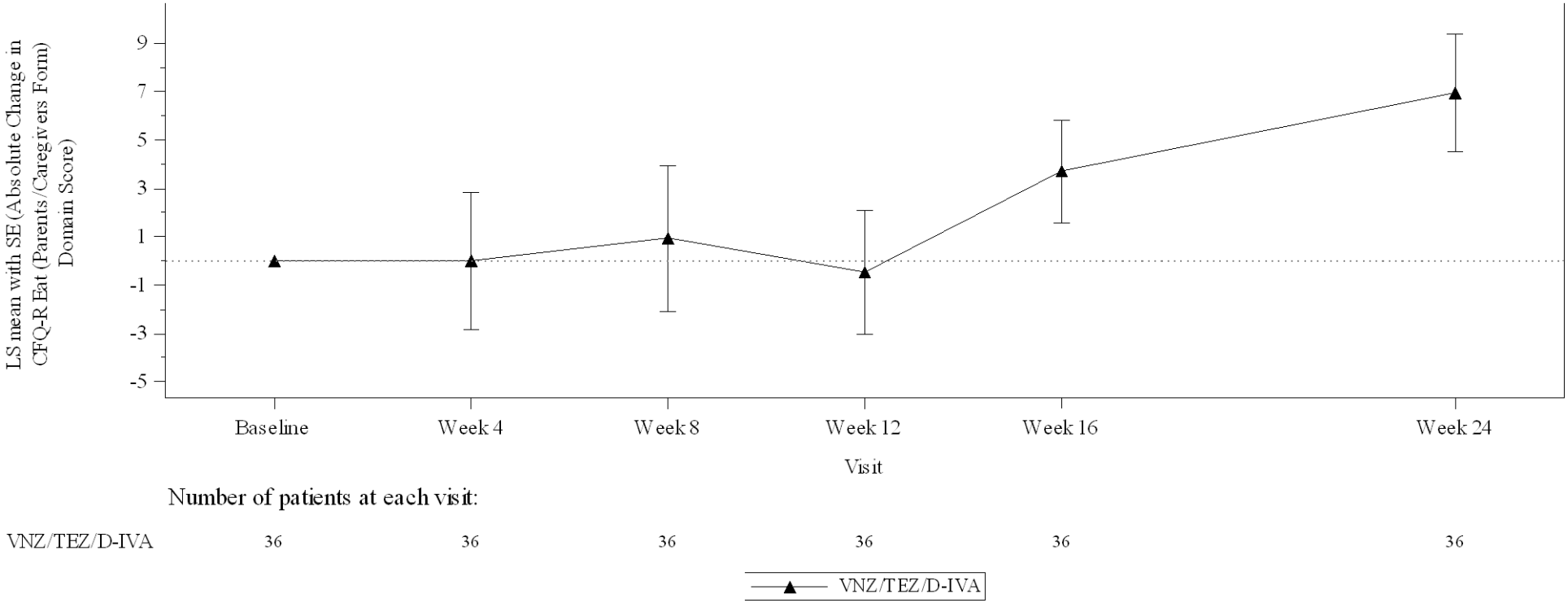
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Sex = Female



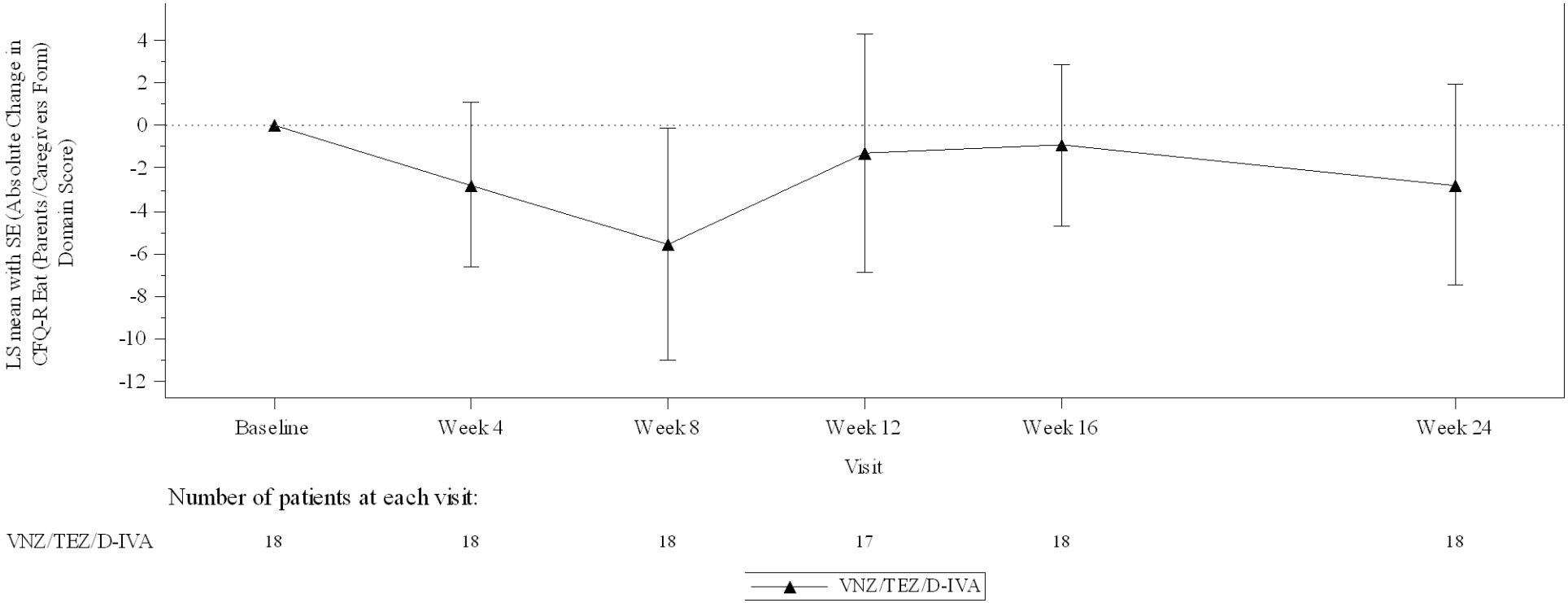
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Region = North America



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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Region = Rest of World



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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

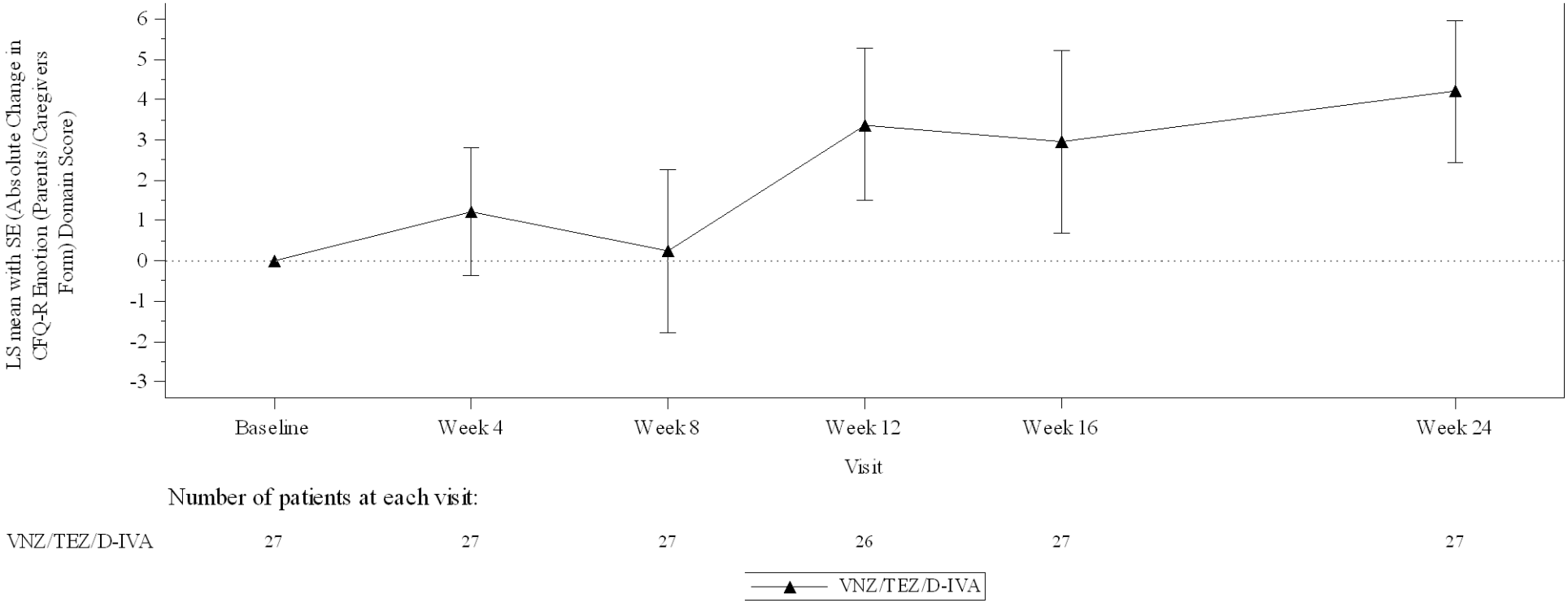
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

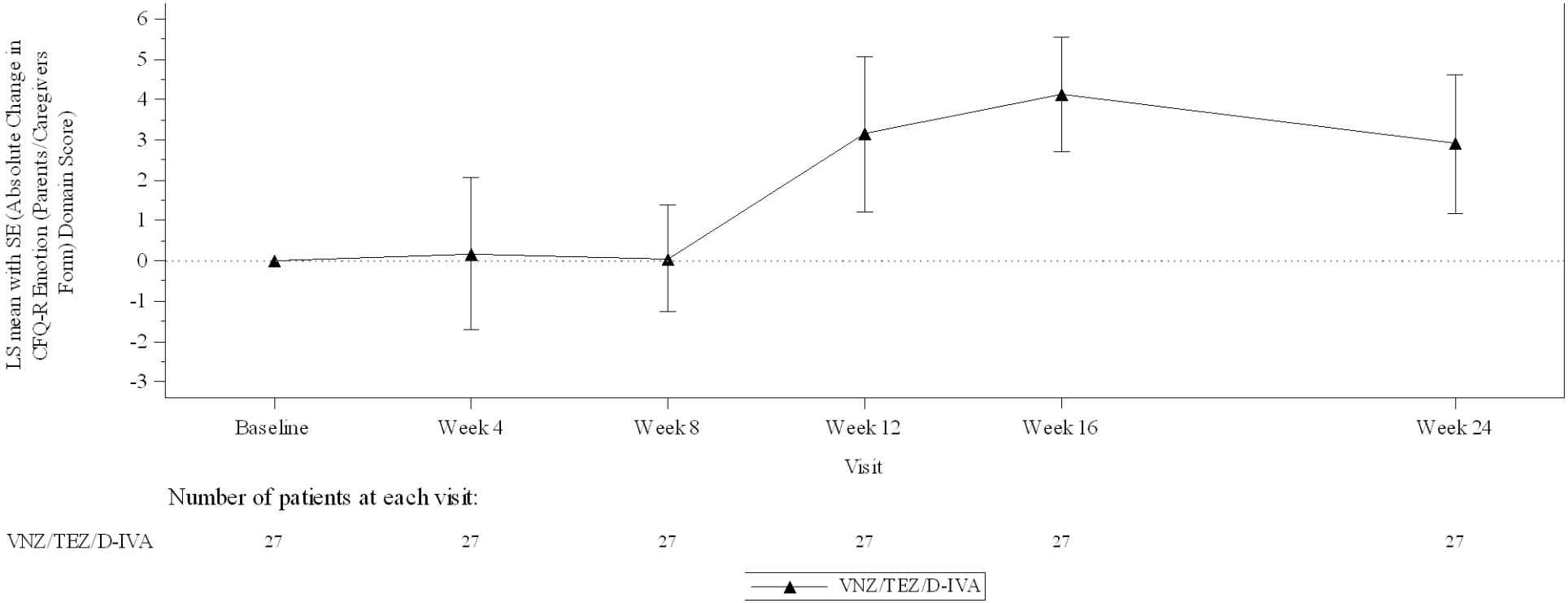
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Sex = Male



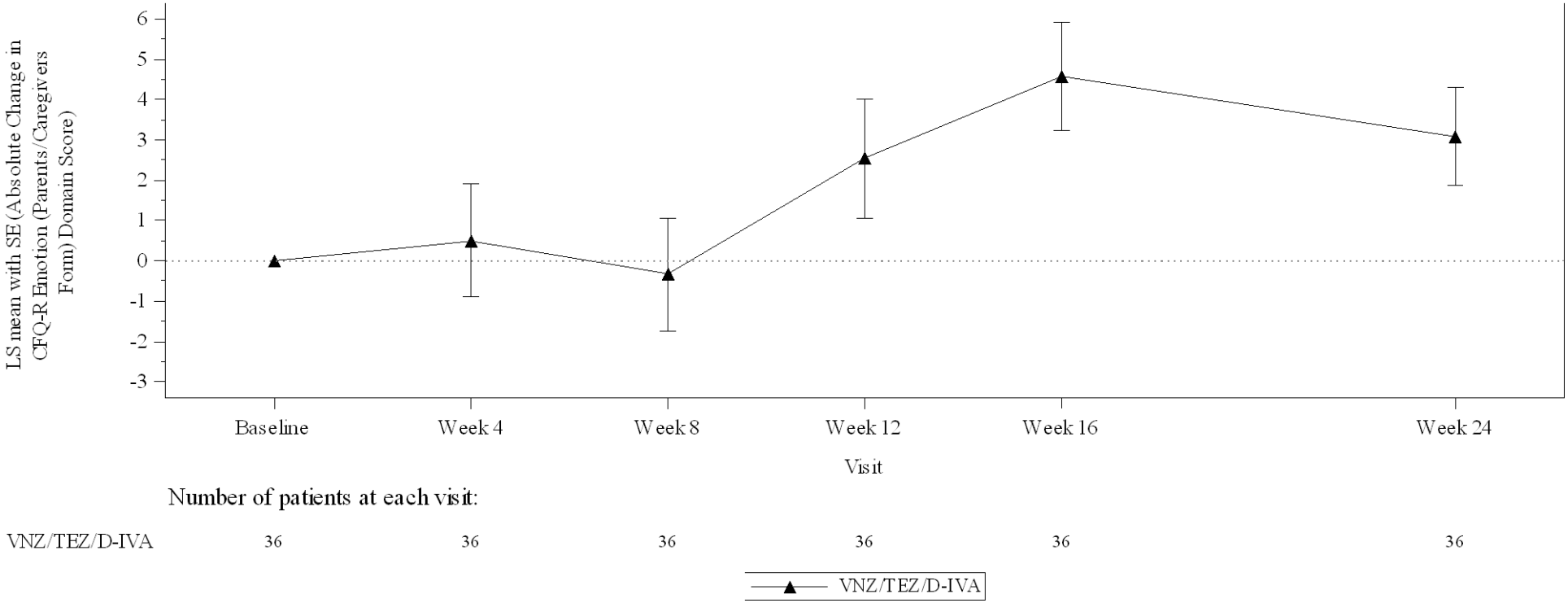
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Sex = Female



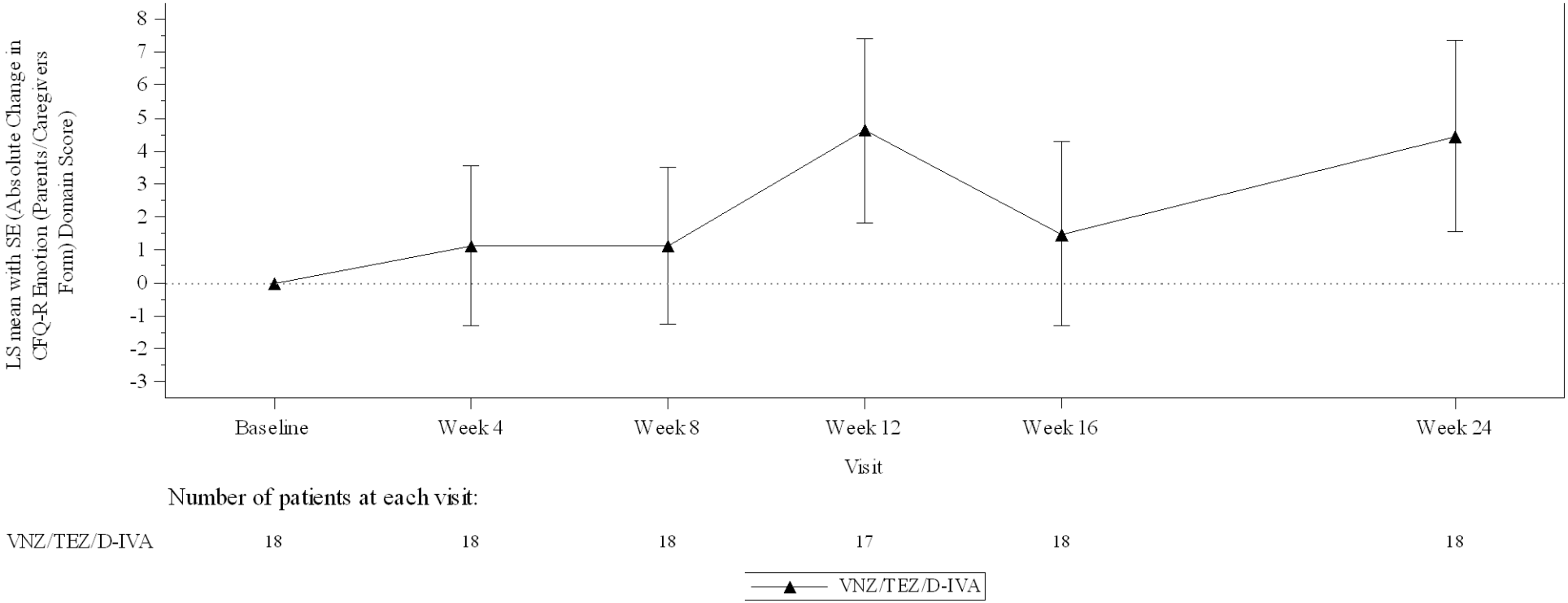
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Region = North America



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non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World



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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

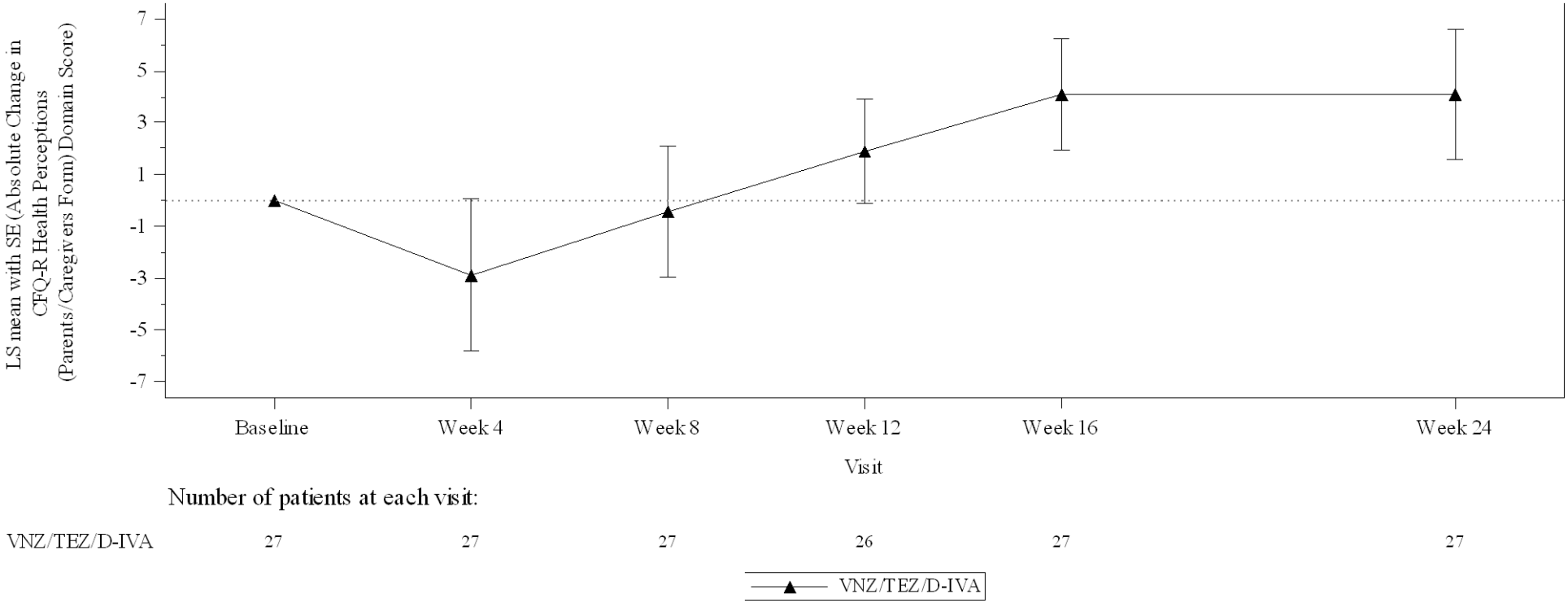
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non-(F/MF)
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Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

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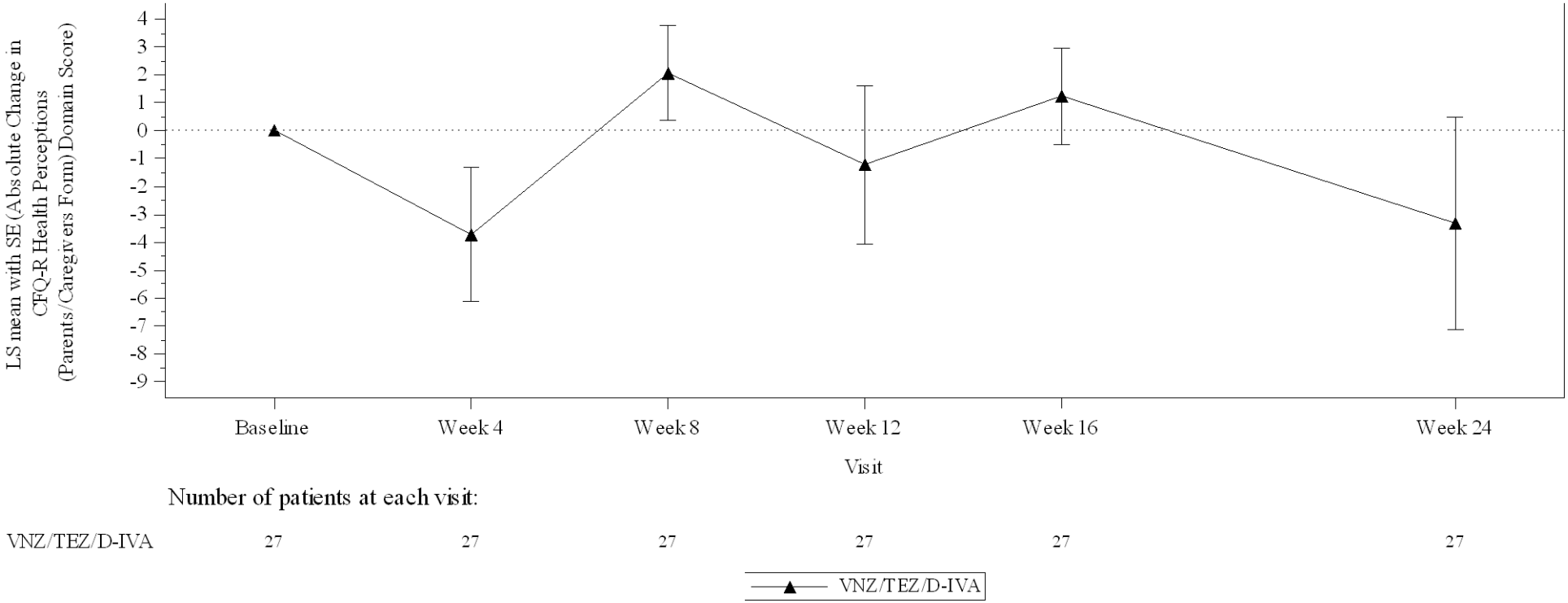
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male



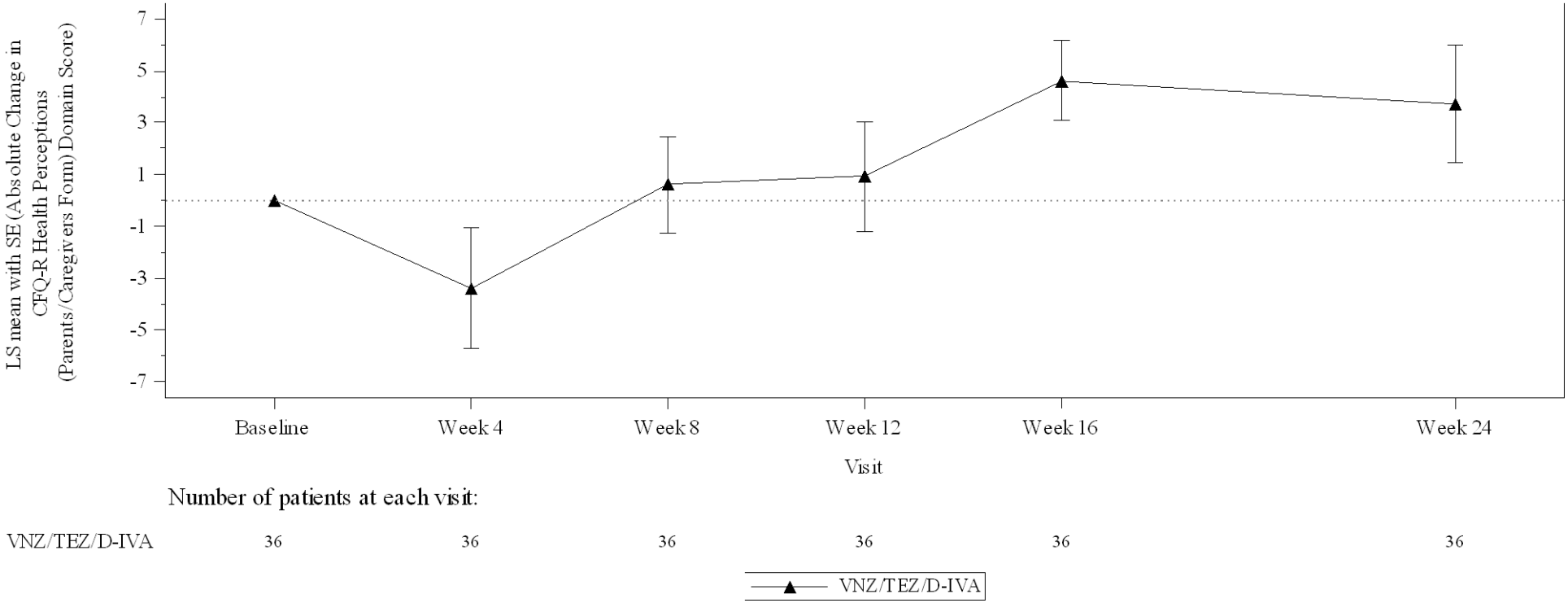
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female



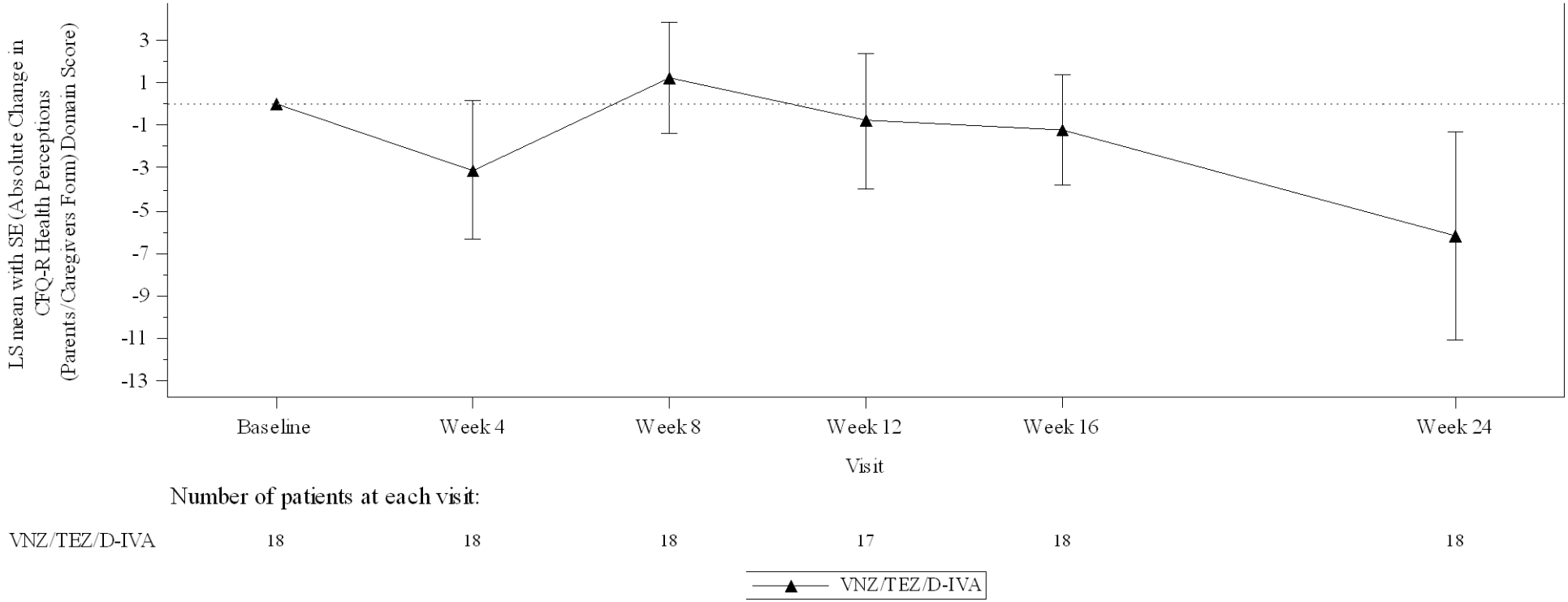
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America



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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

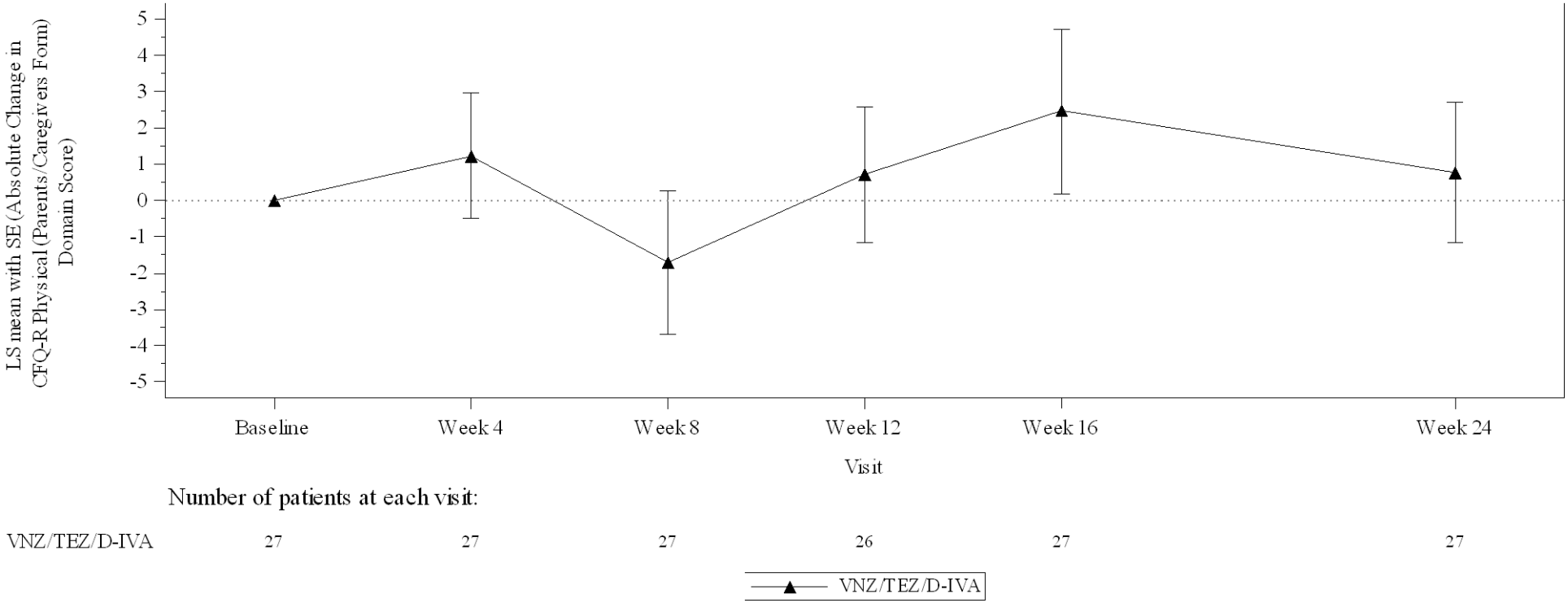
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

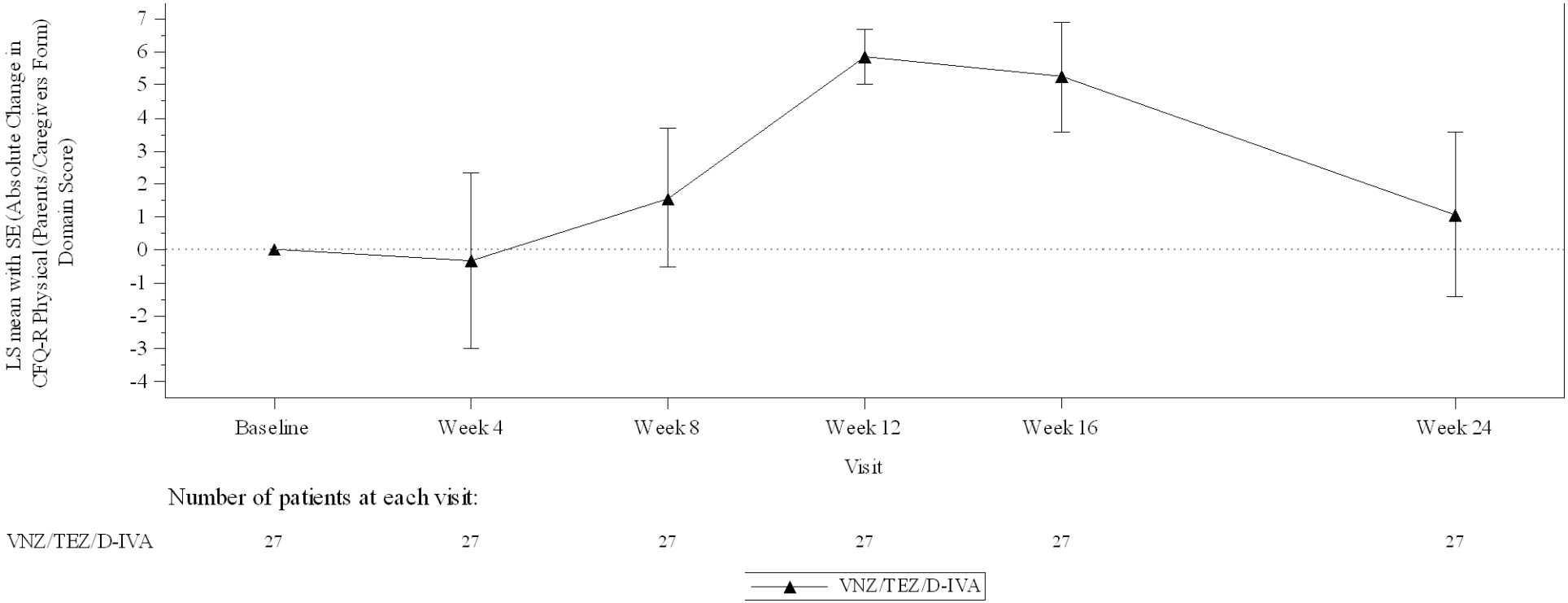
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Sex = Male



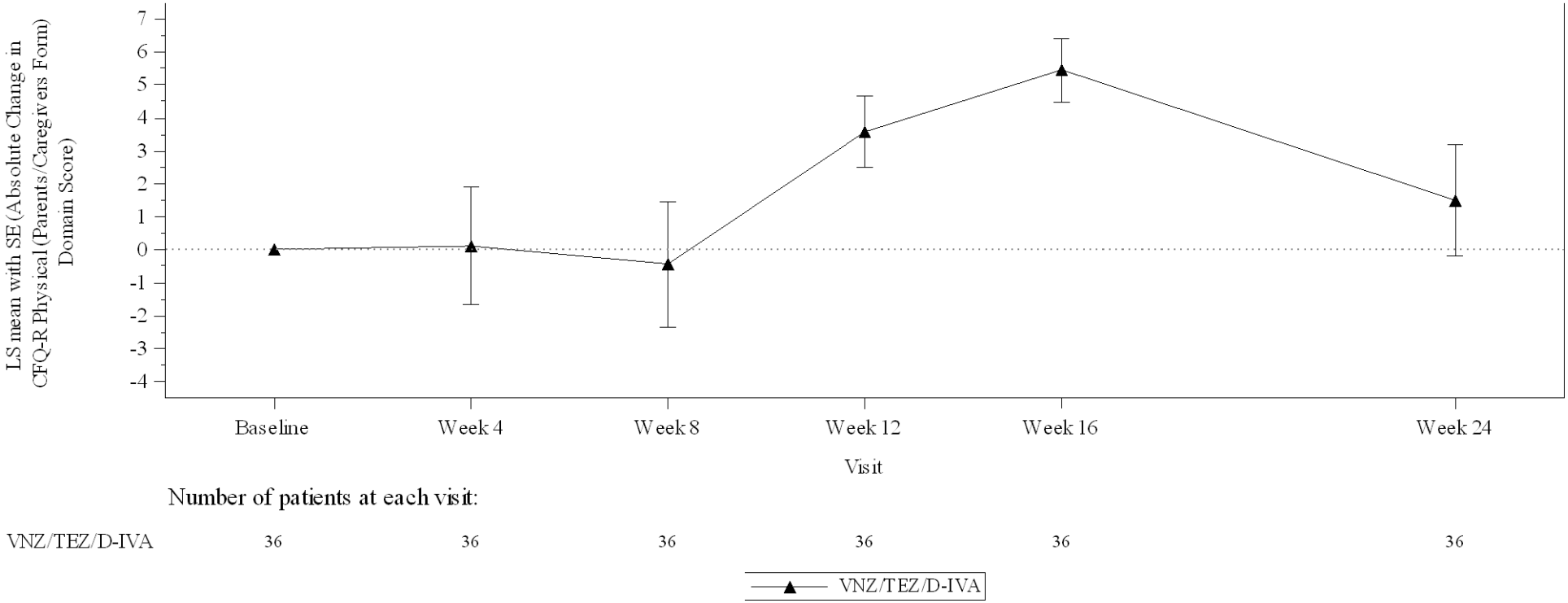
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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Sex = Female



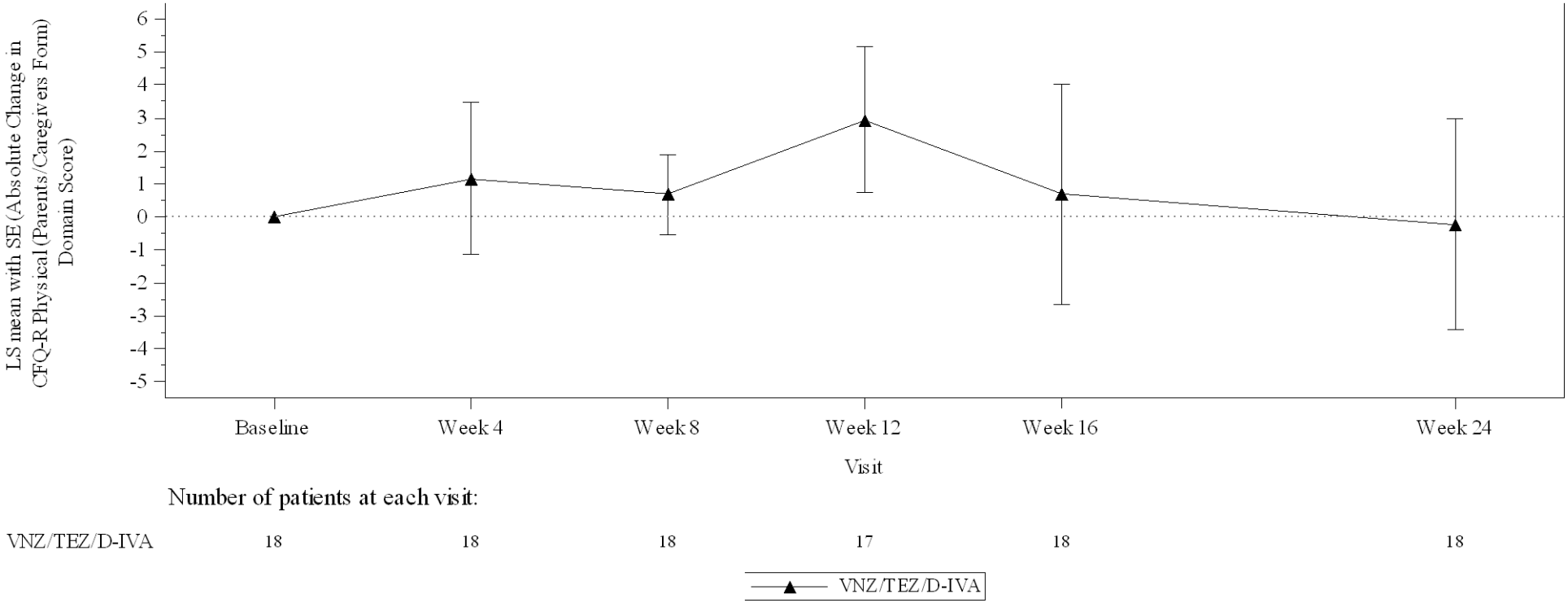
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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

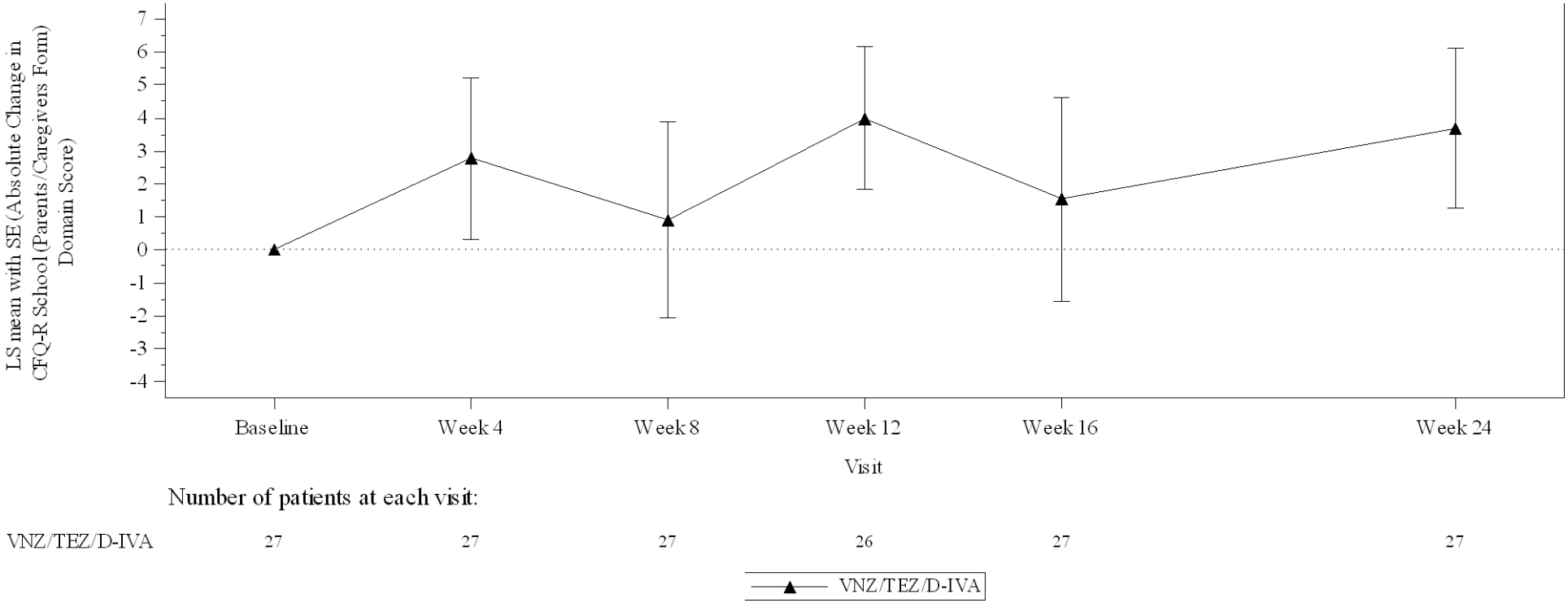
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

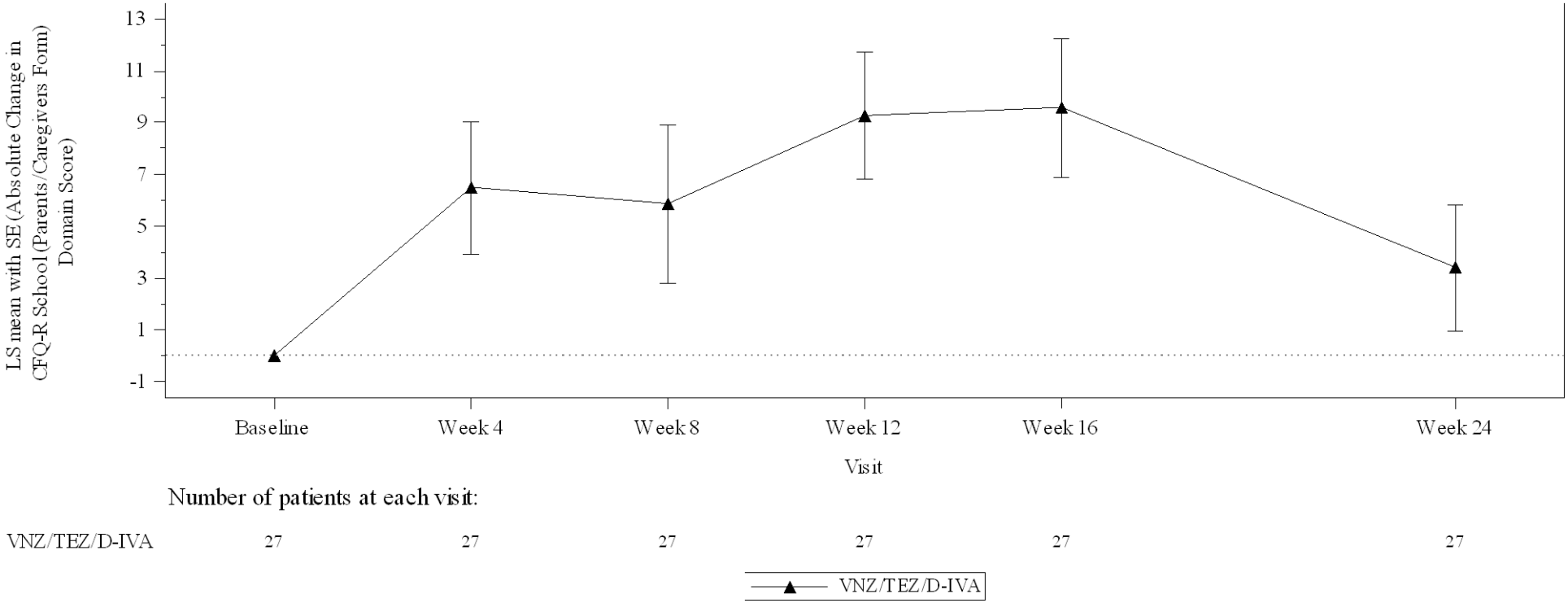
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Sex = Male



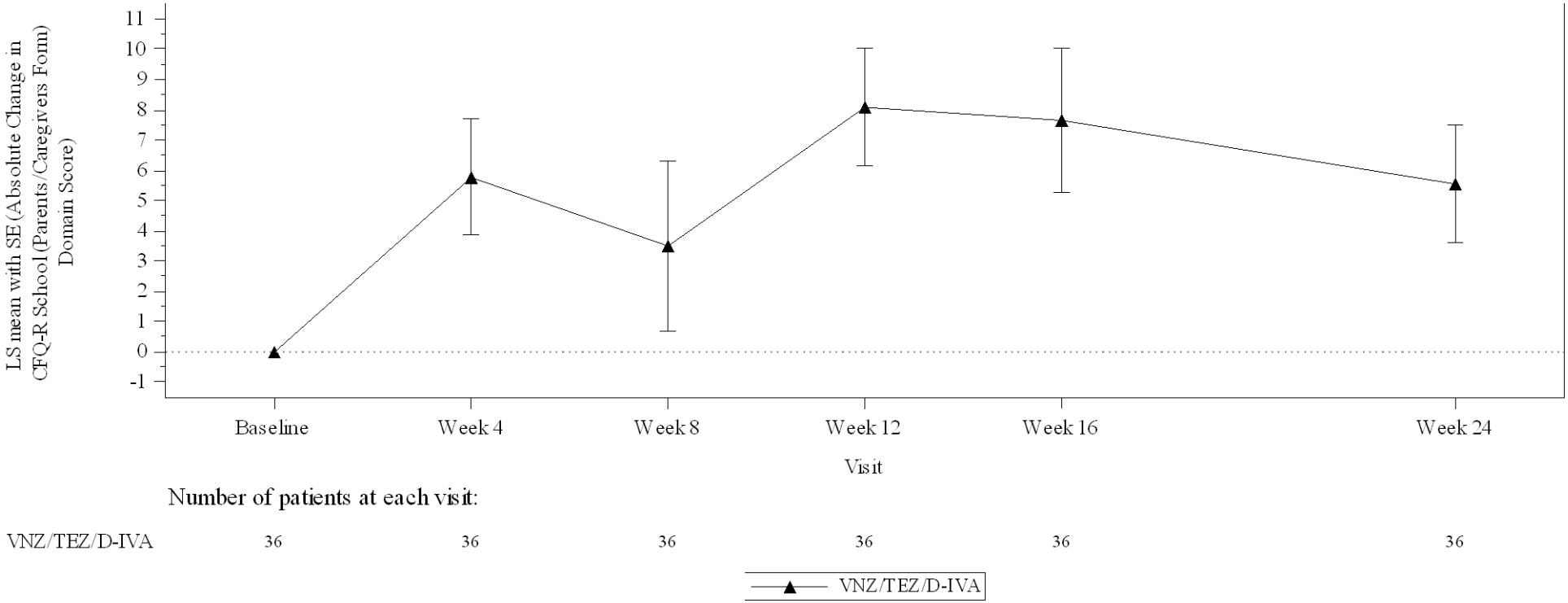
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Sex = Female



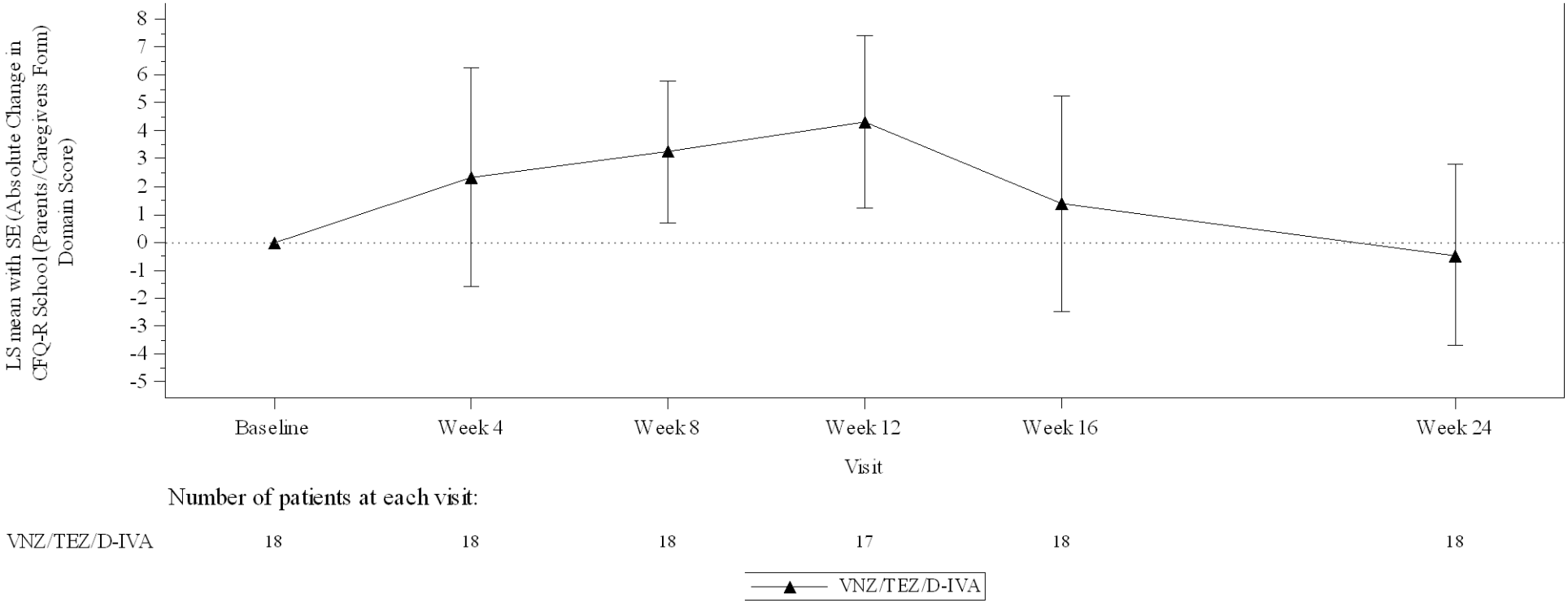
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

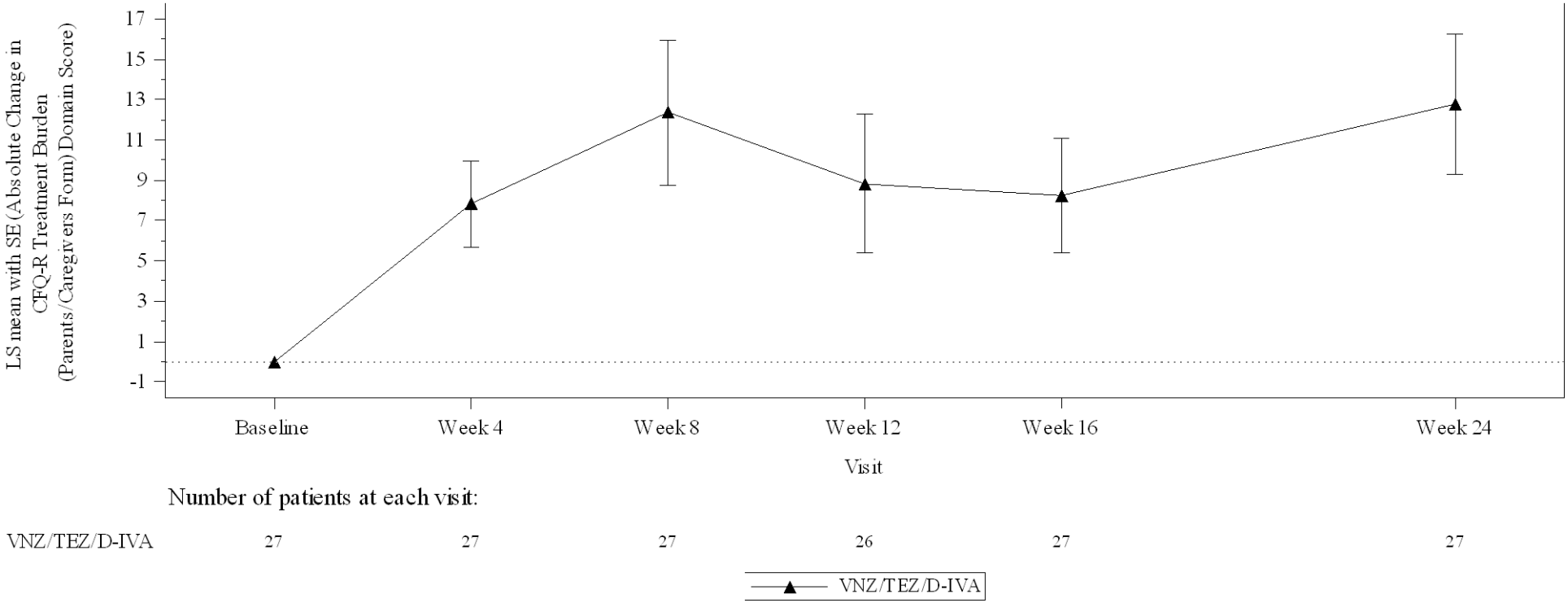
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

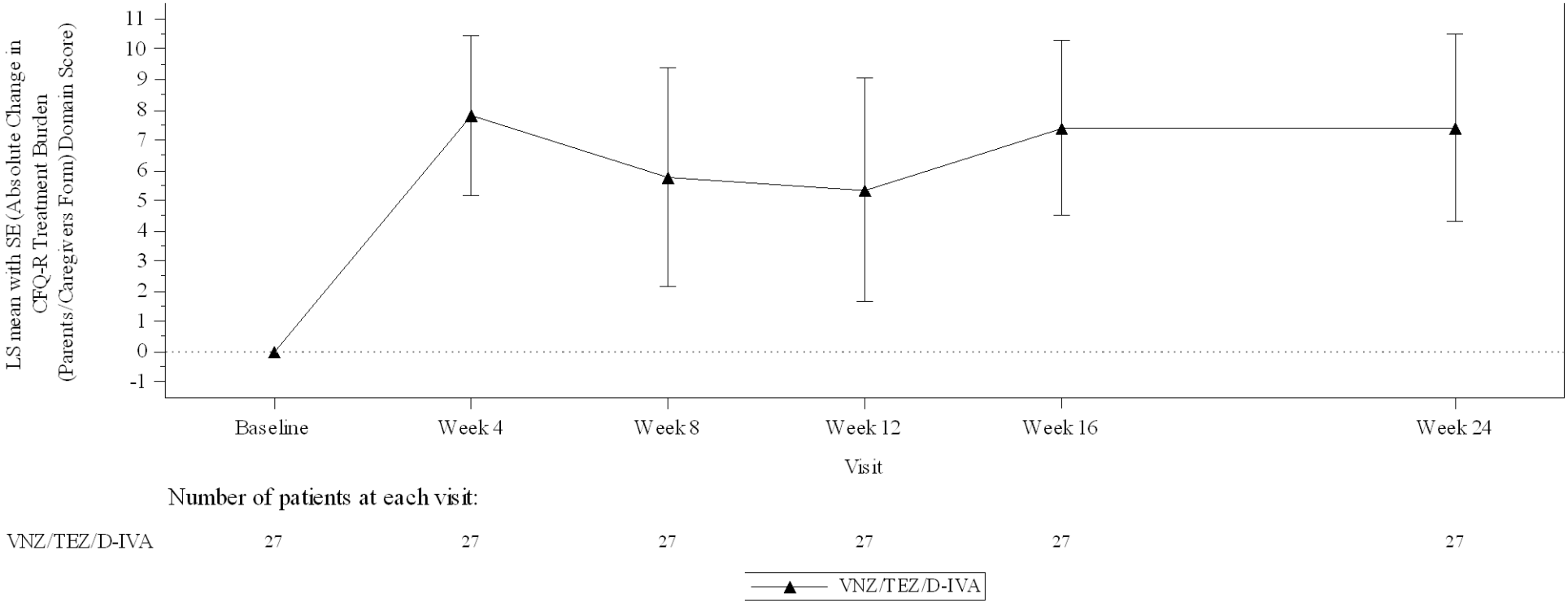
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male



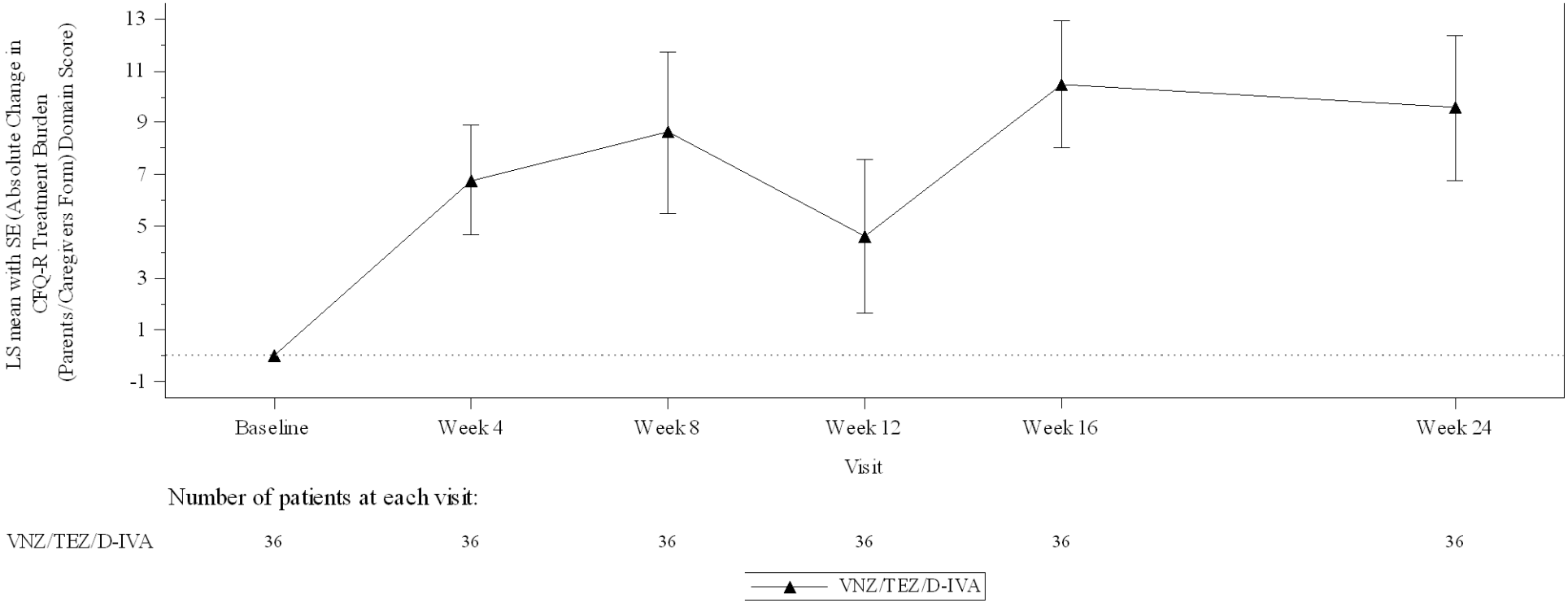
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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female



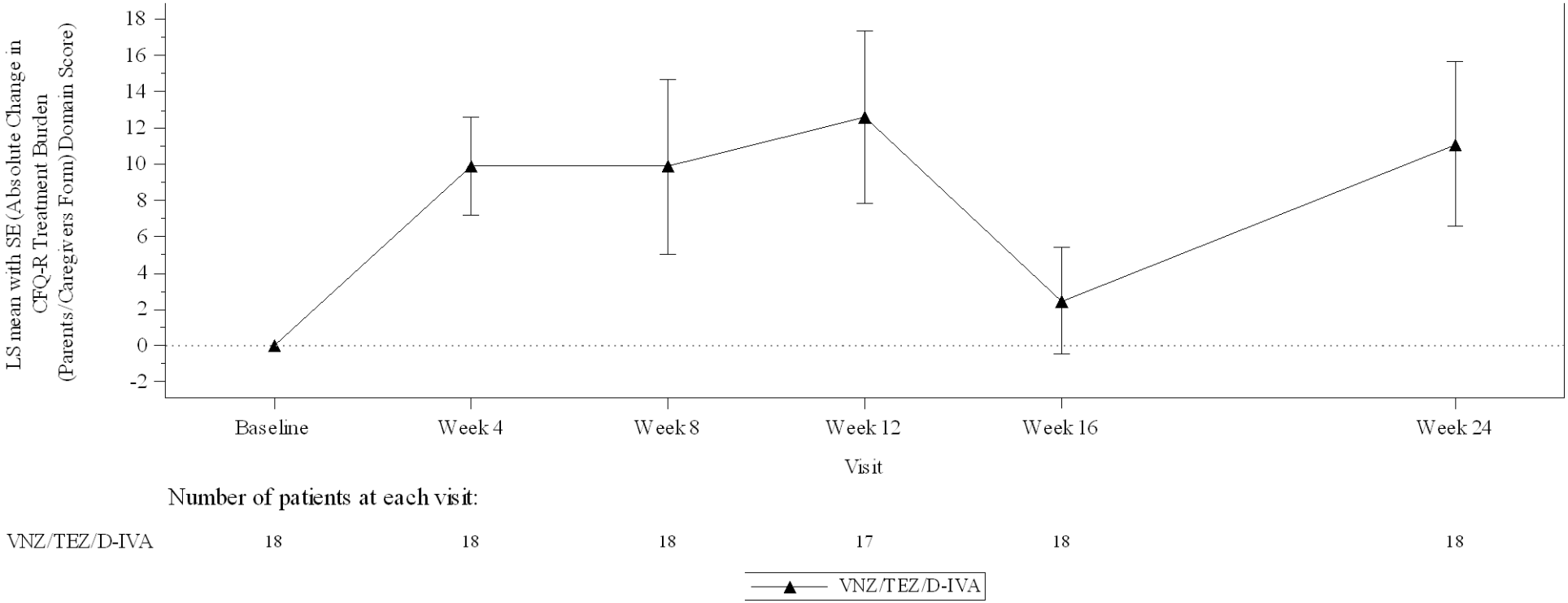
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World



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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

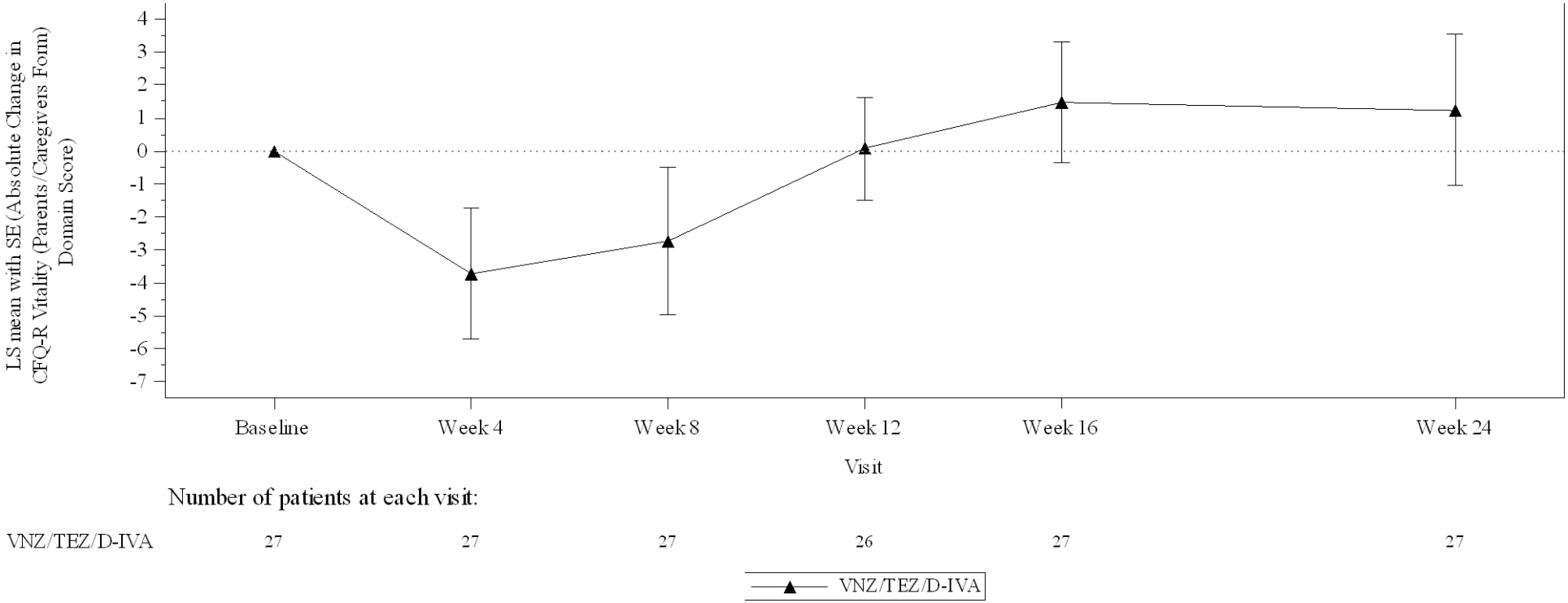
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

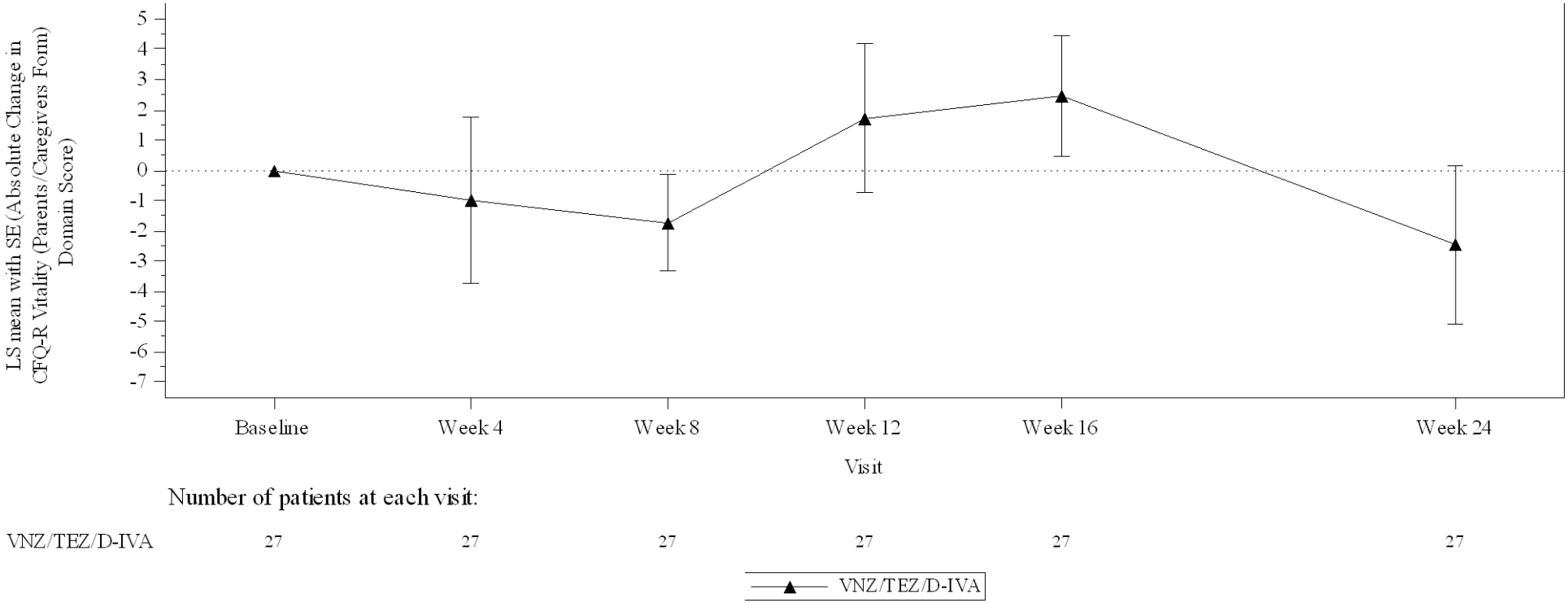
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Sex = Male



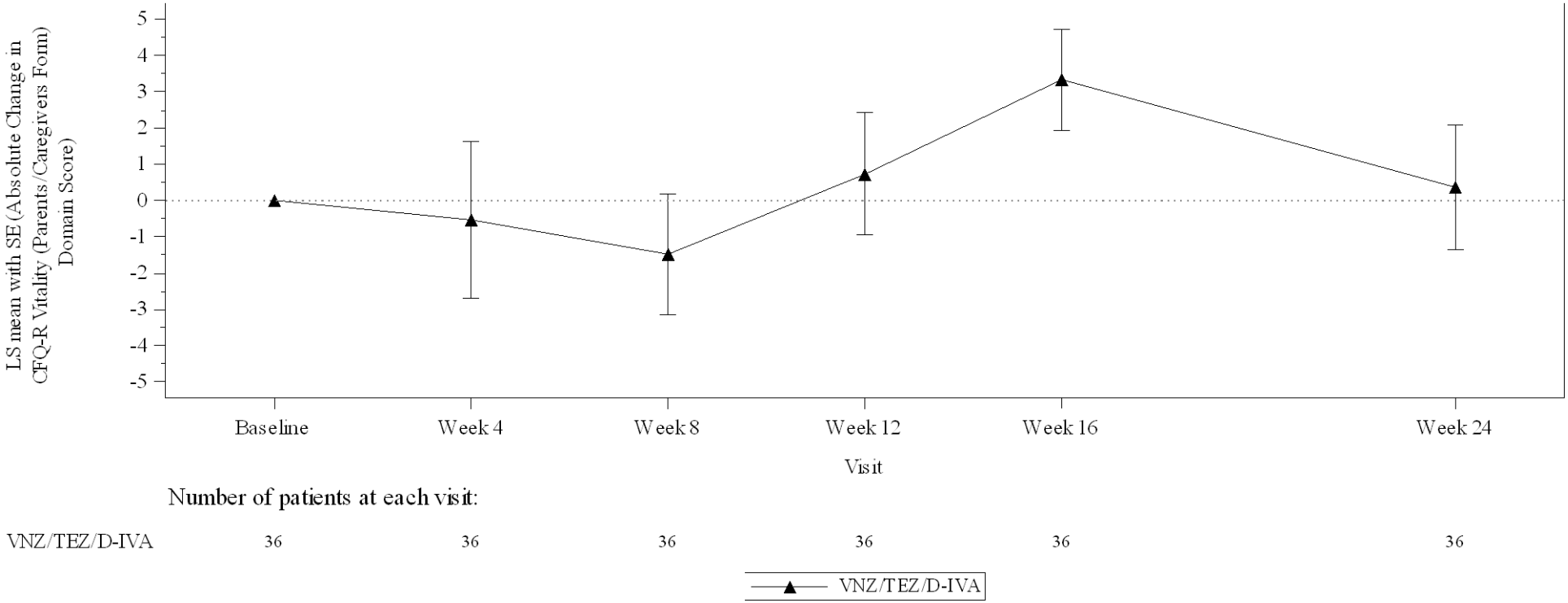
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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Sex = Female



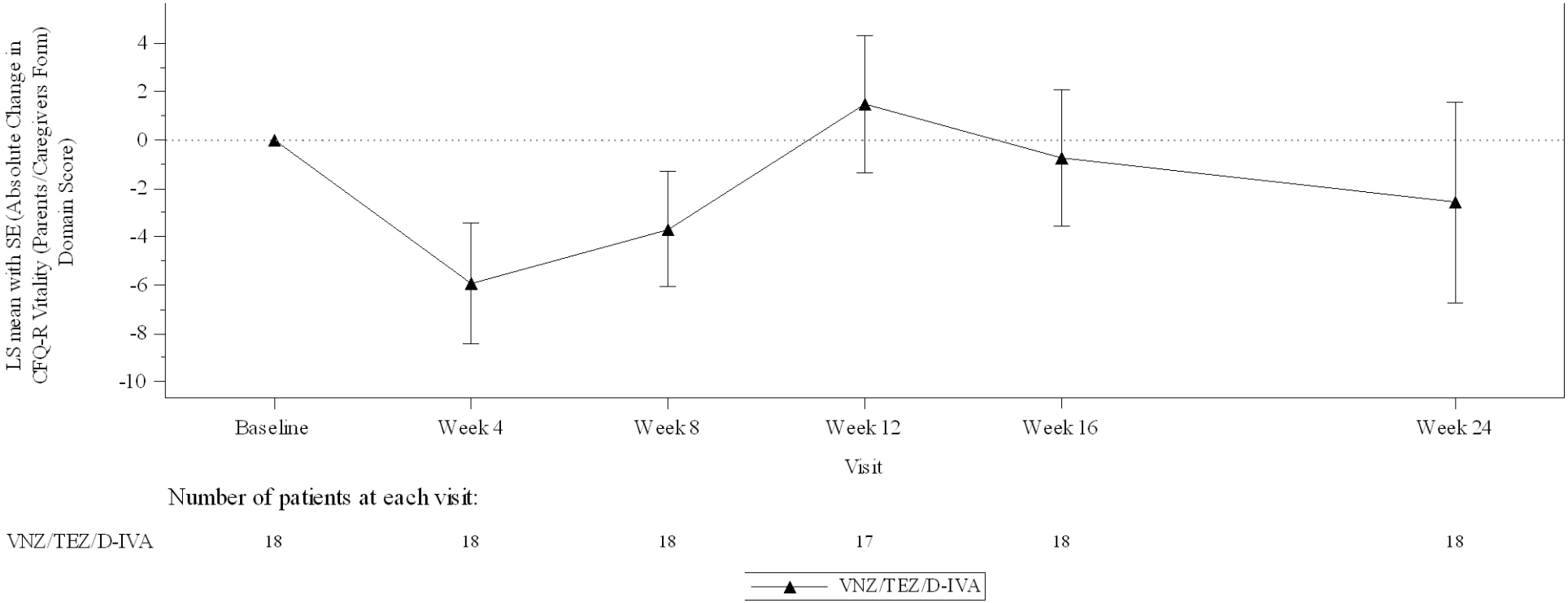
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World



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Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

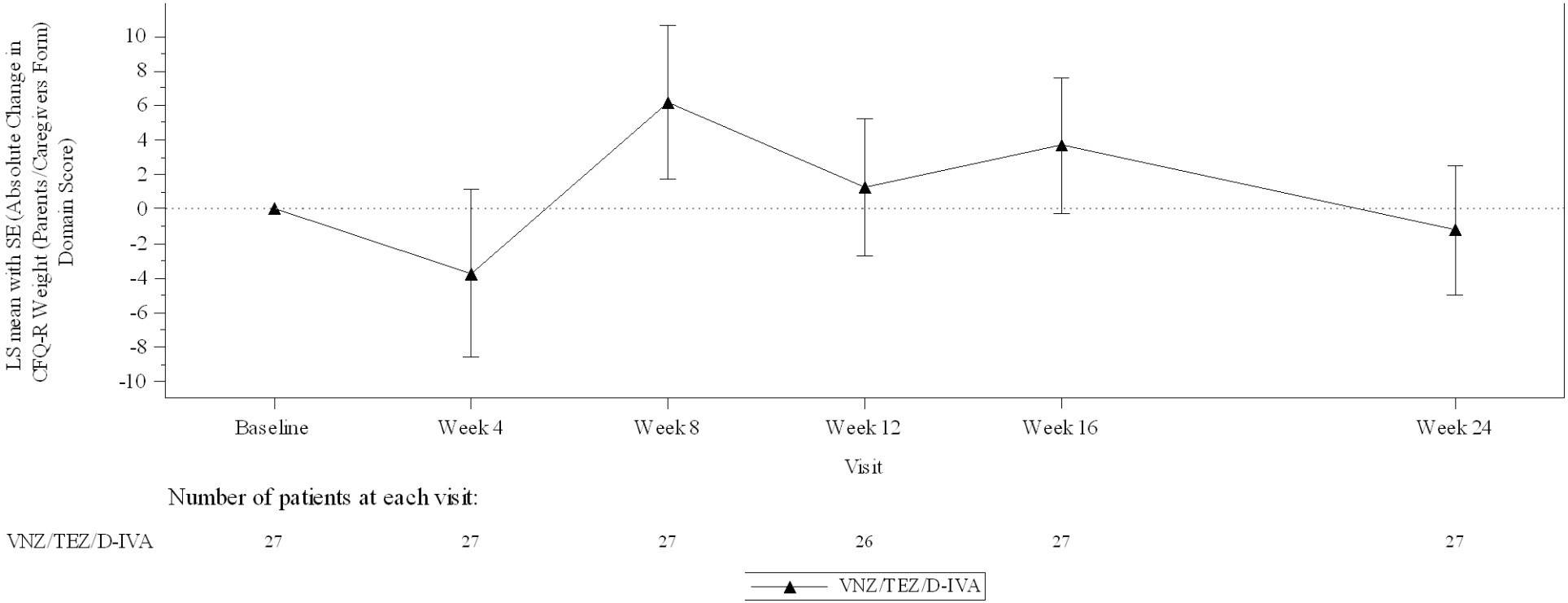
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

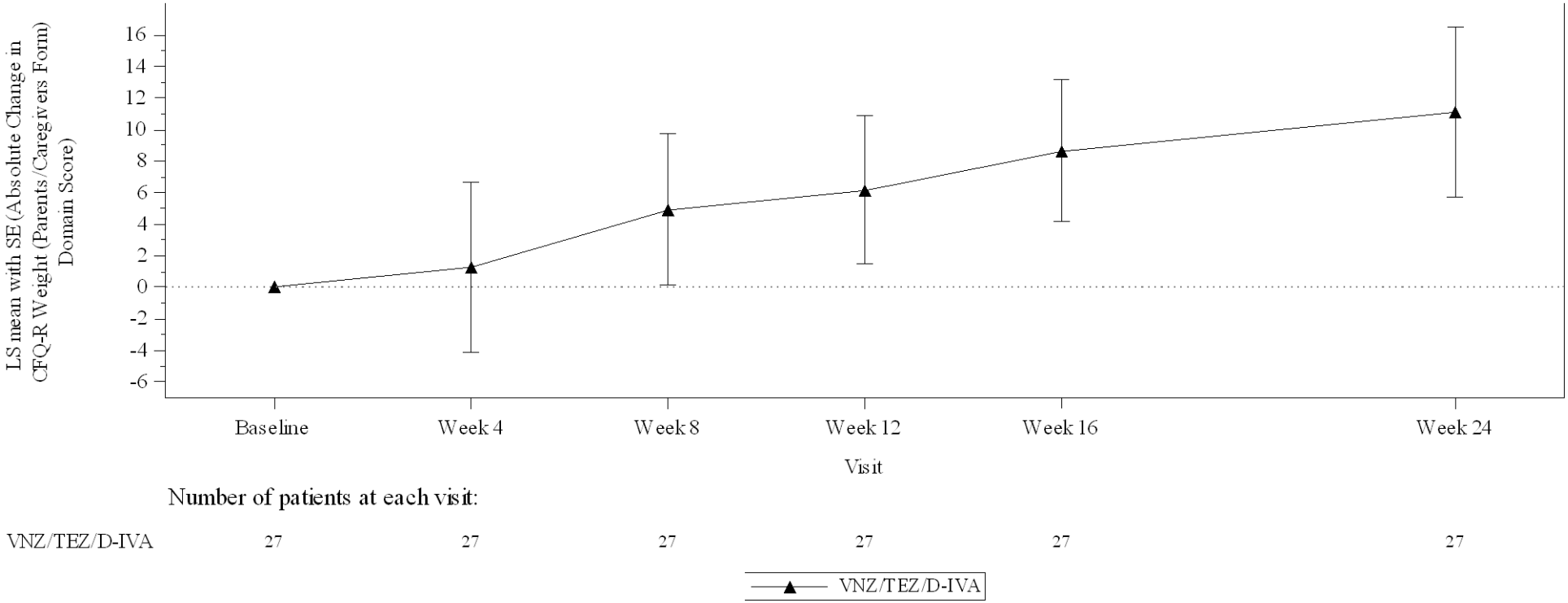
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Sex = Male



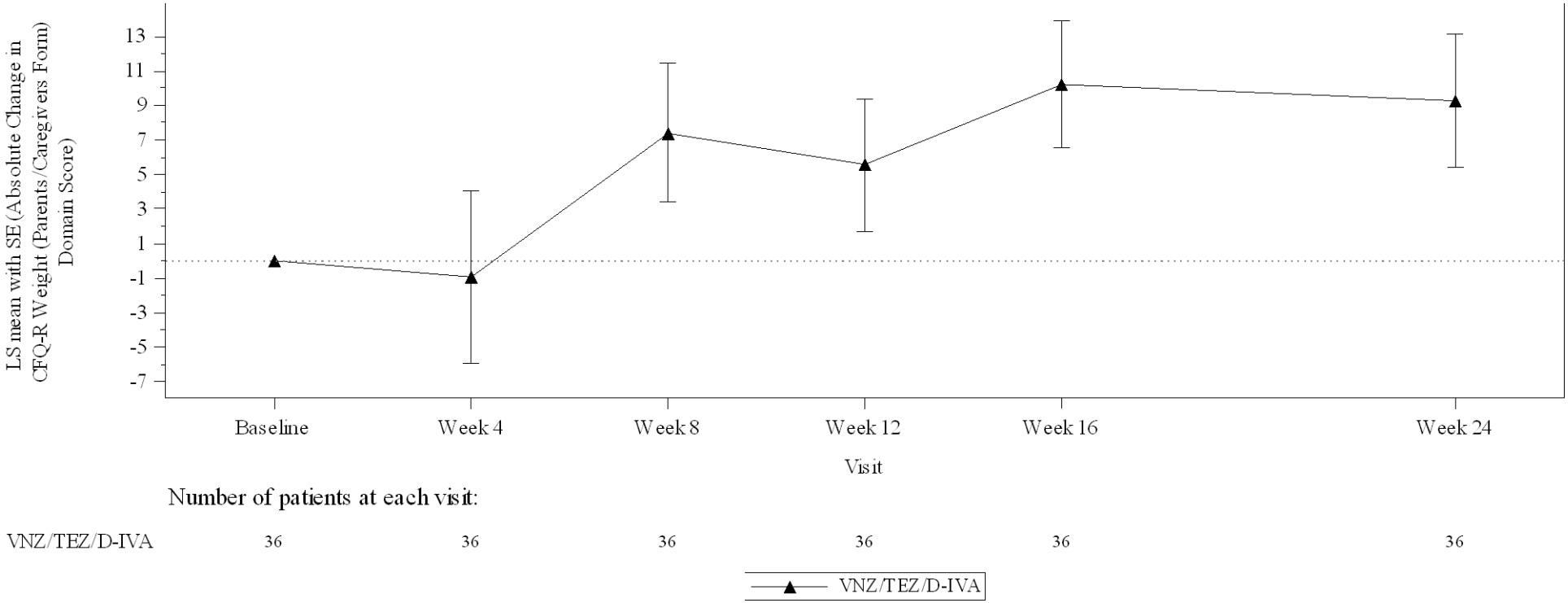
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Sex = Female



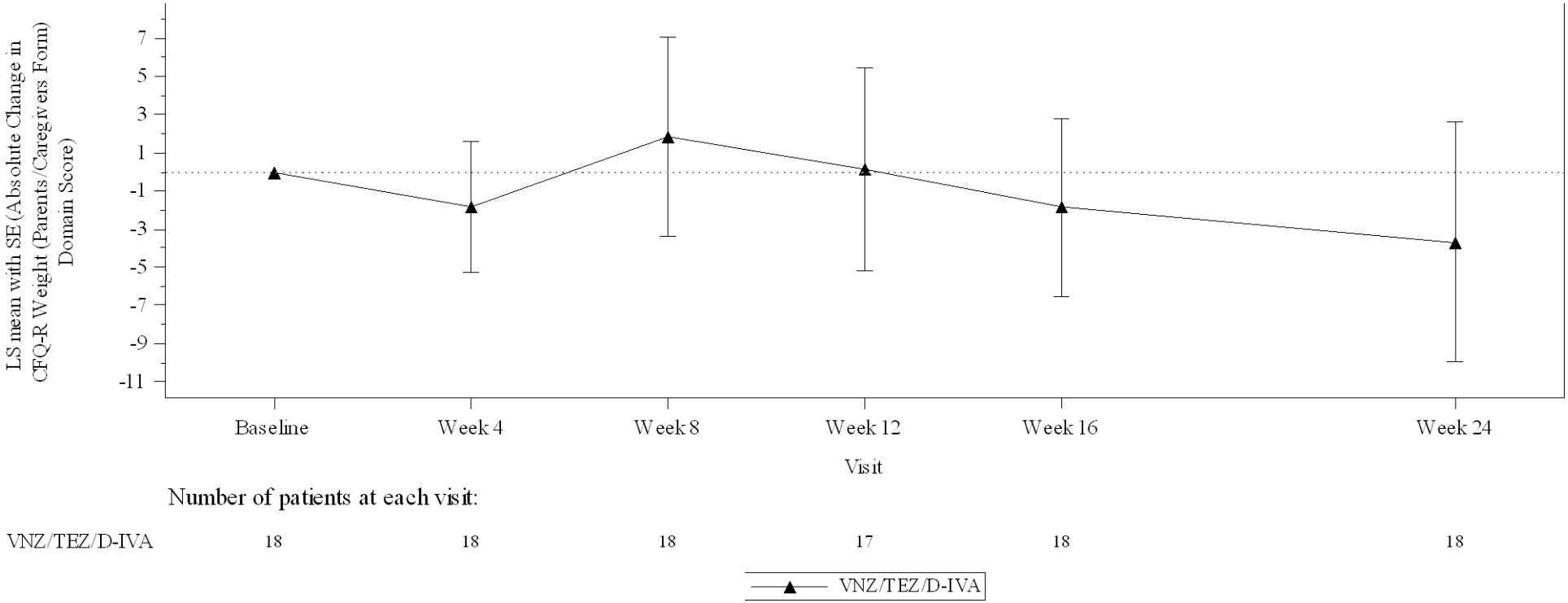
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Region = North America



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Region = Rest of World



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5

Subgroup criteria are not met for this subgroup factor.

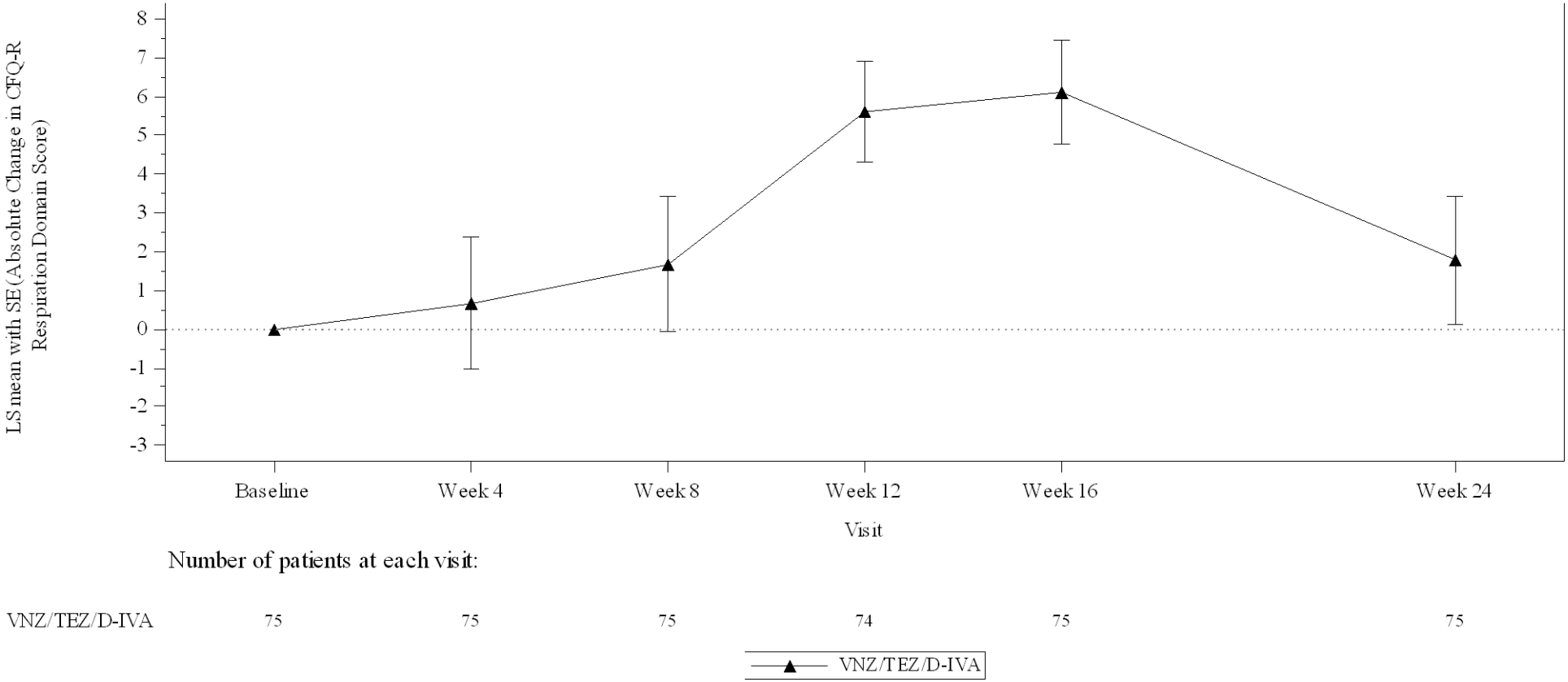
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 2.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
non-(F/MF)
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5

Subgroup criteria are not met for this subgroup factor.

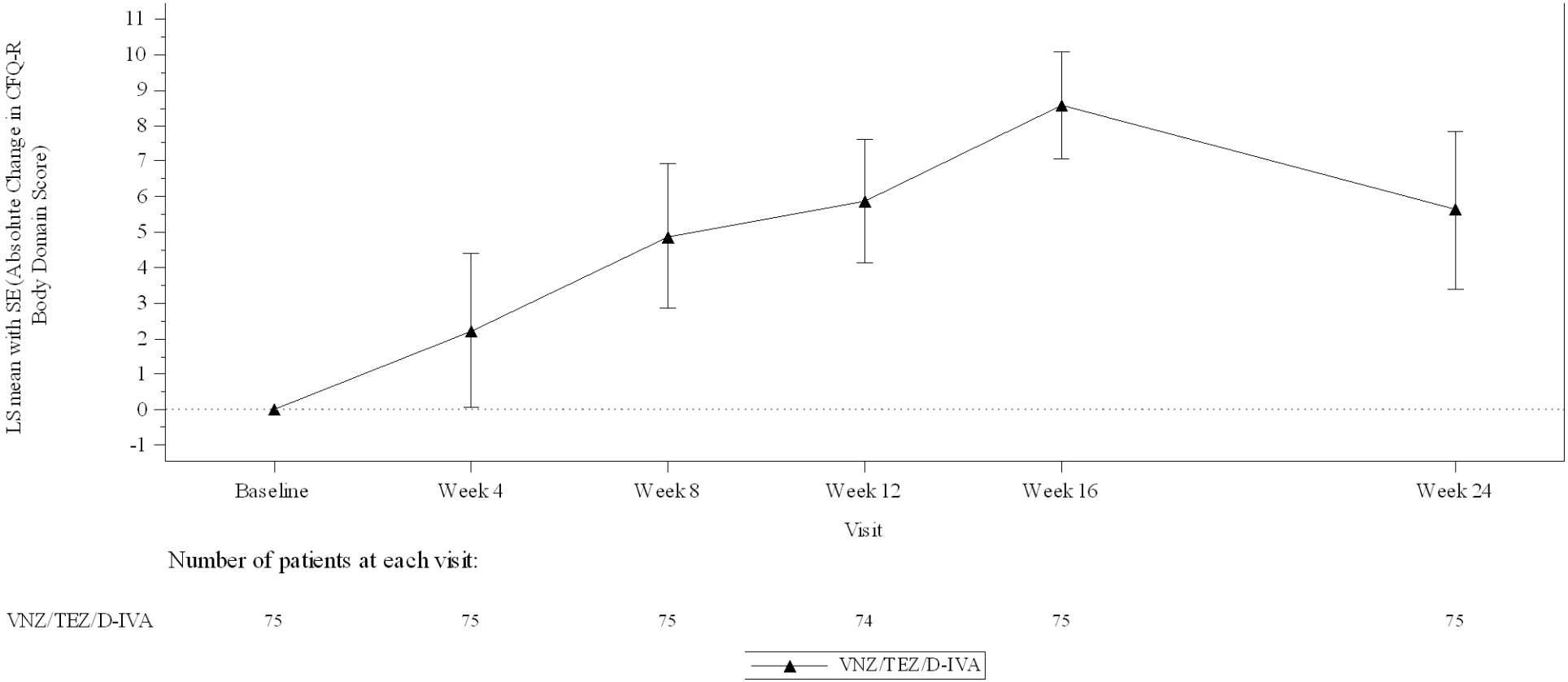
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effects for visit, with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Respiration



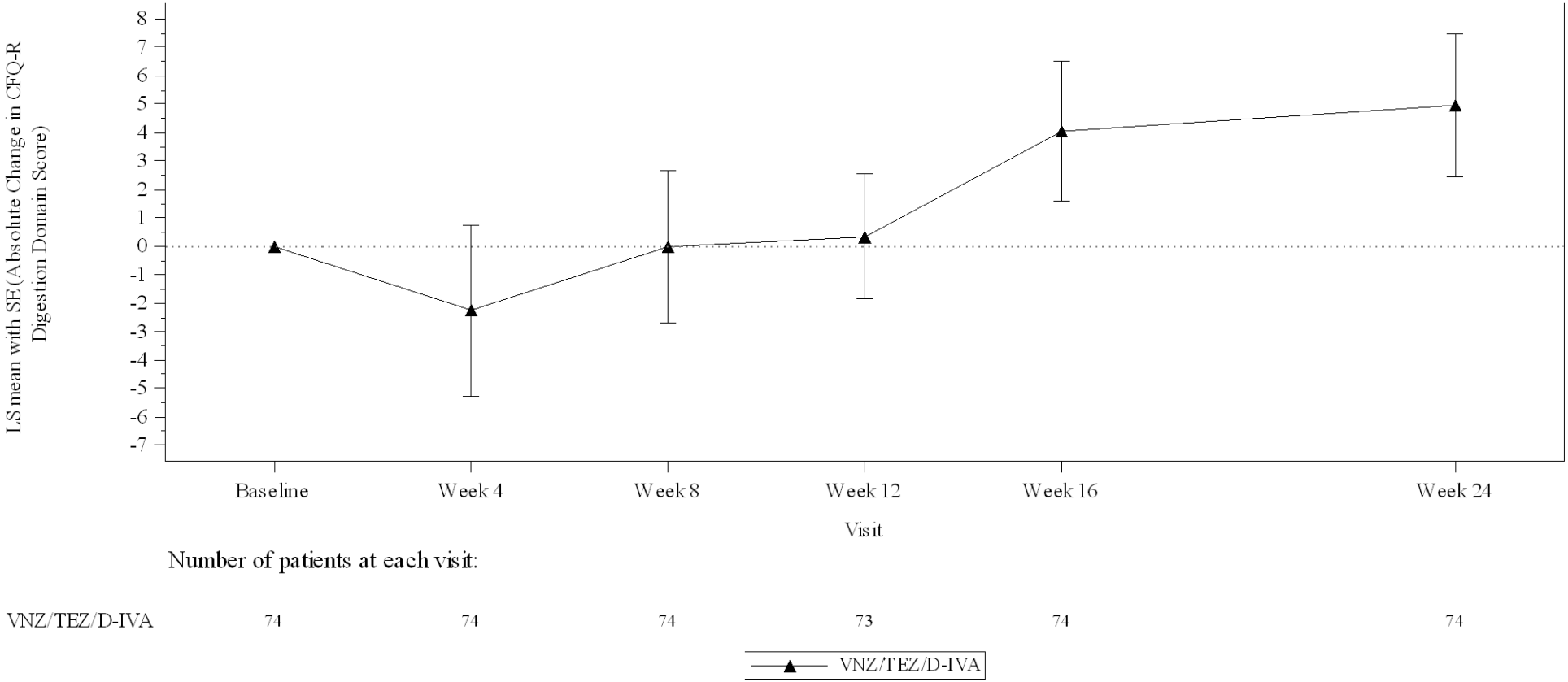
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Body



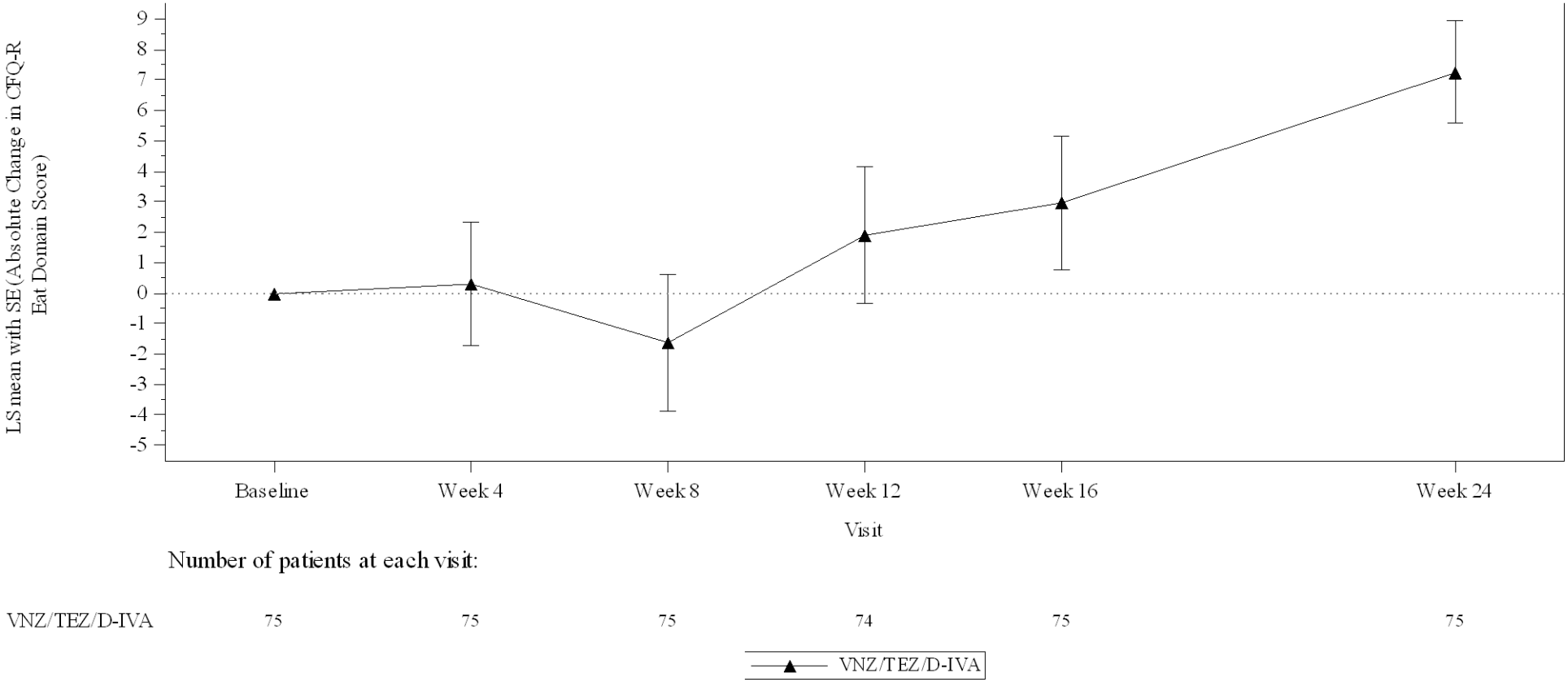
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Digestion



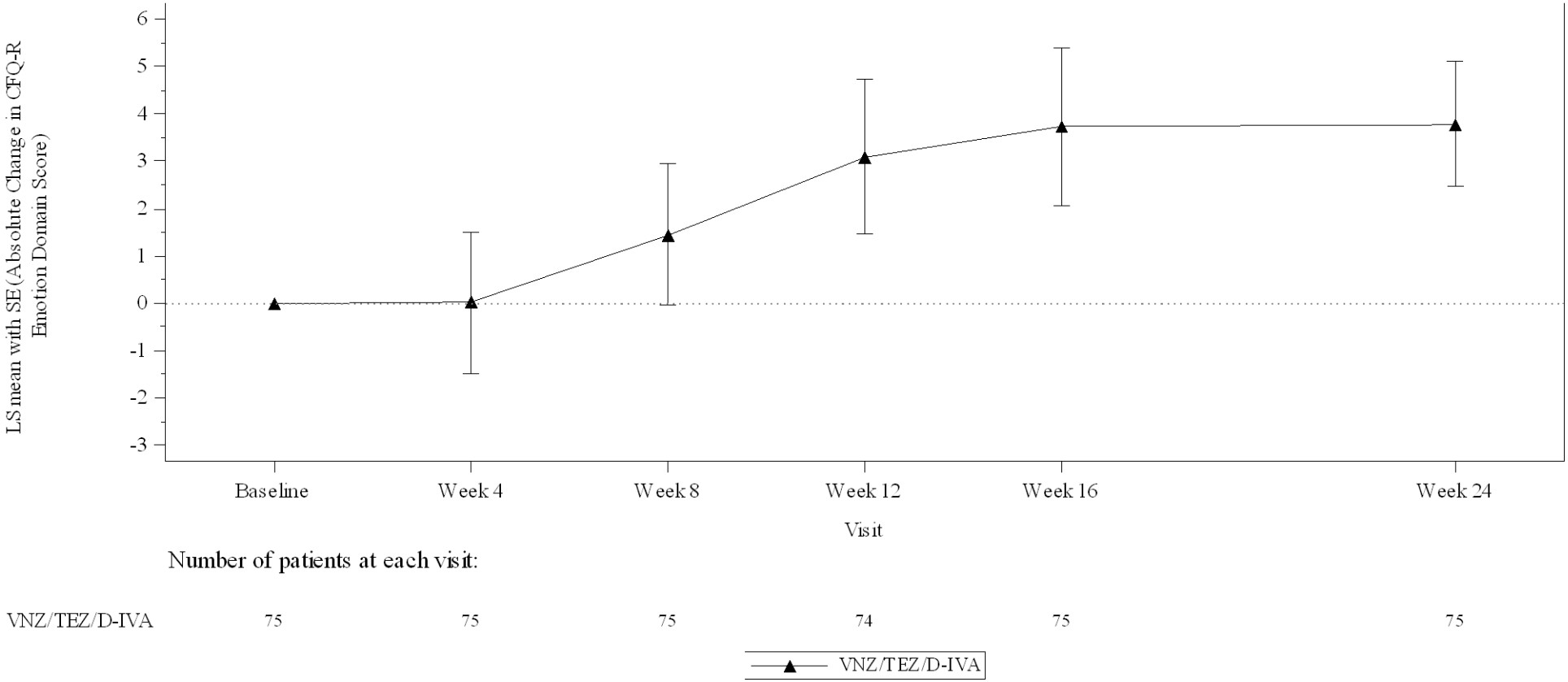
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Eat



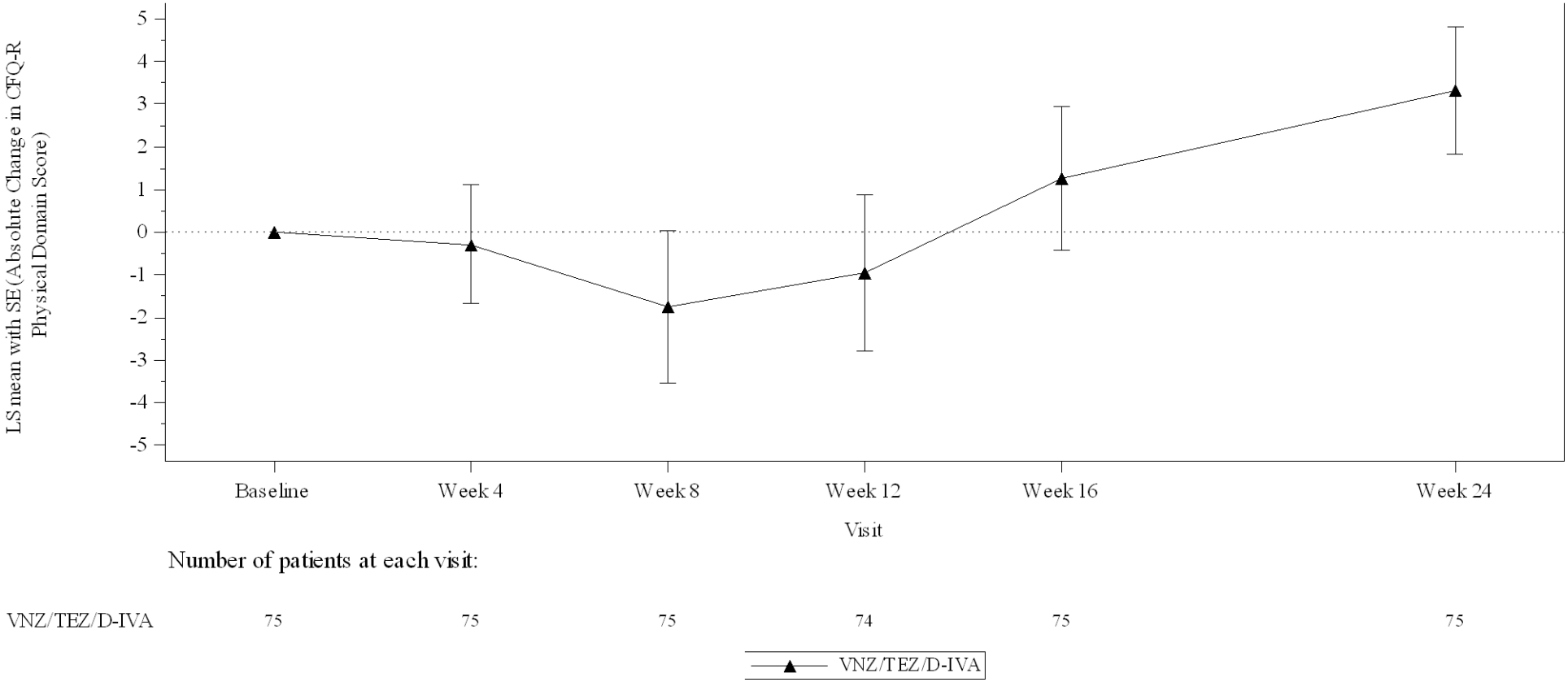
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Emotion



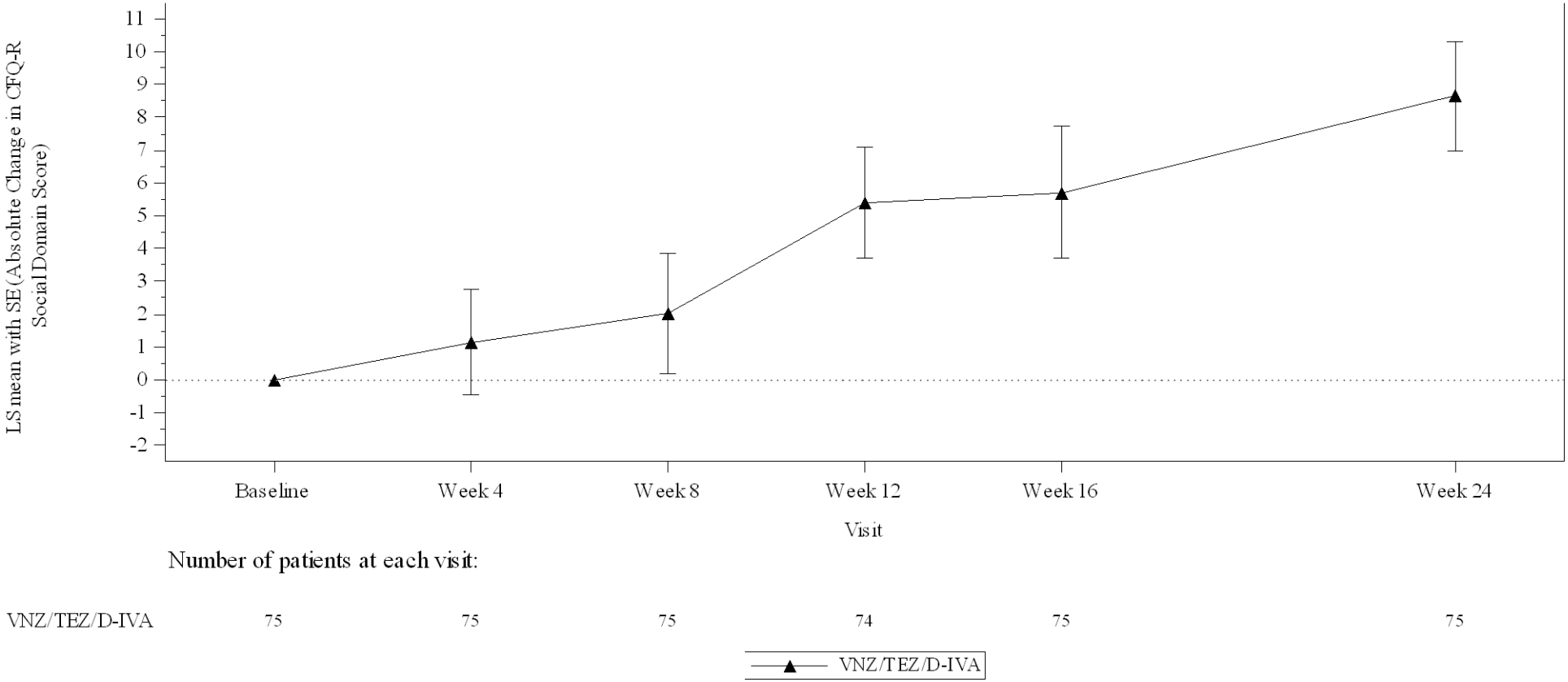
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Physical



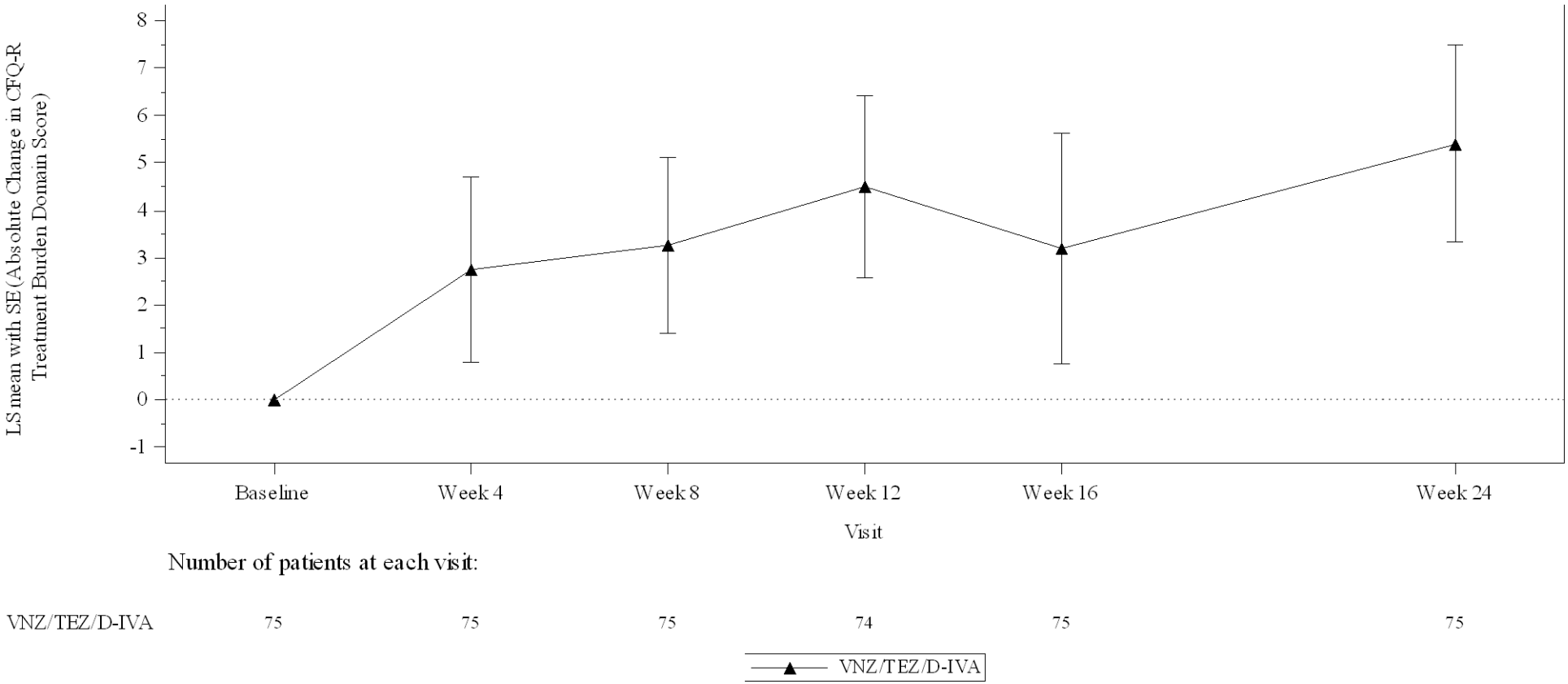
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Social



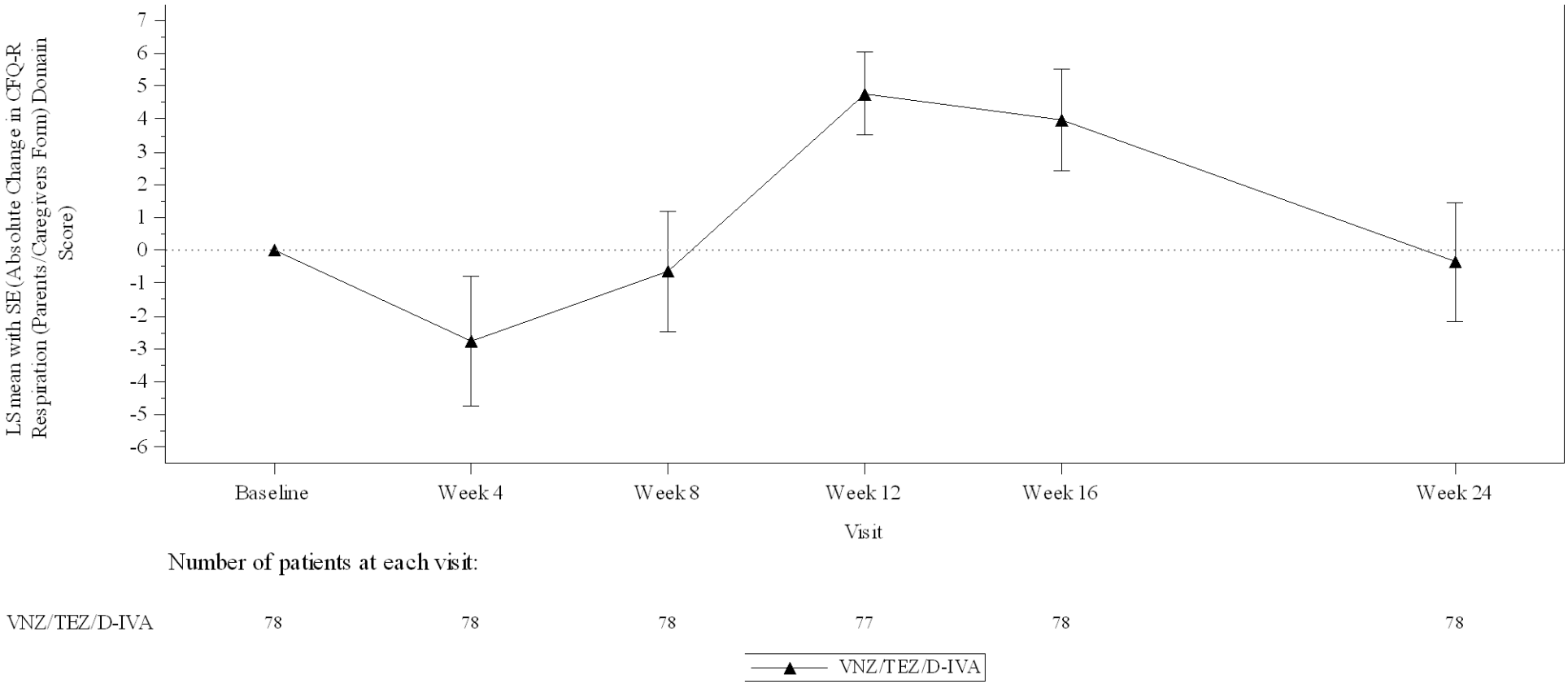
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Treatment Burden



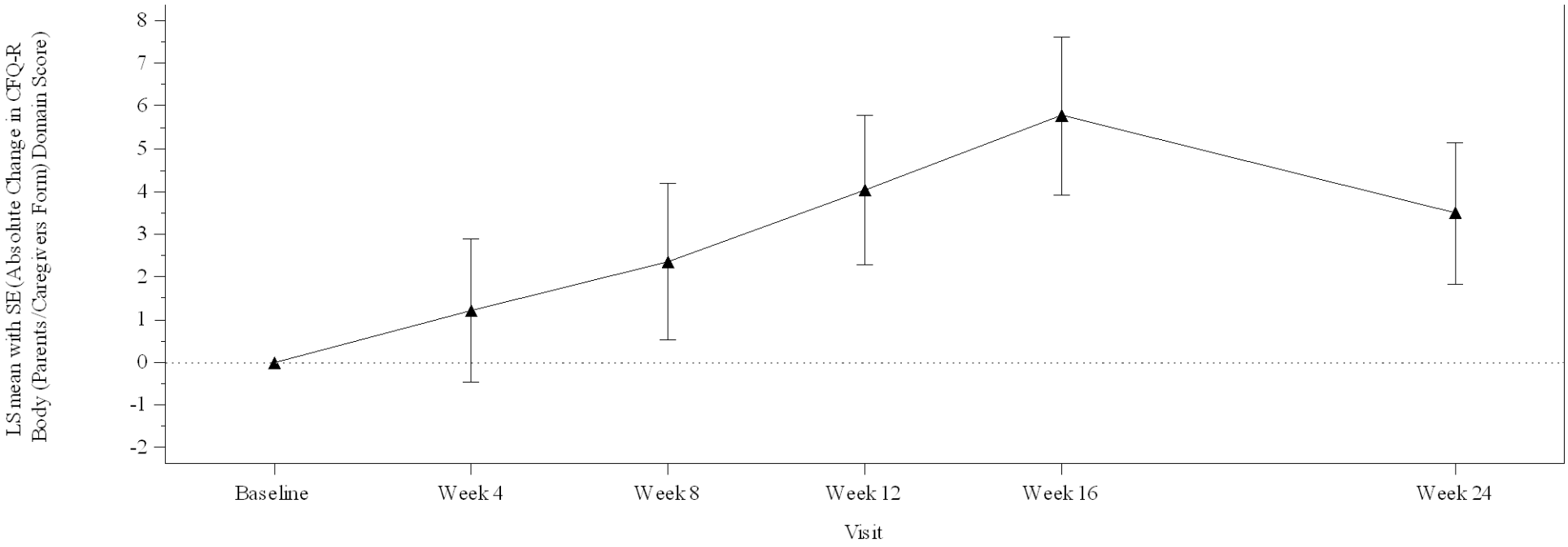
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)



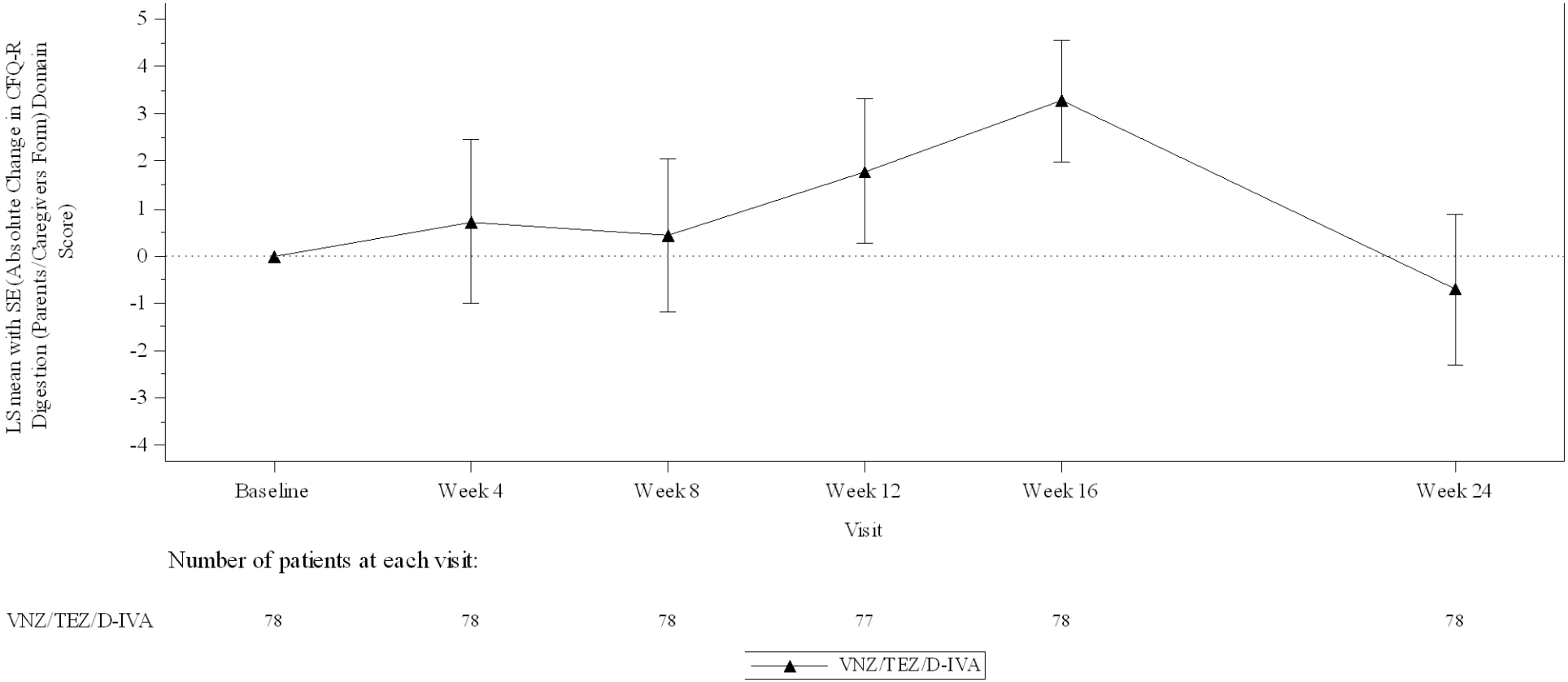
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Body (Parents/Caregivers Form)



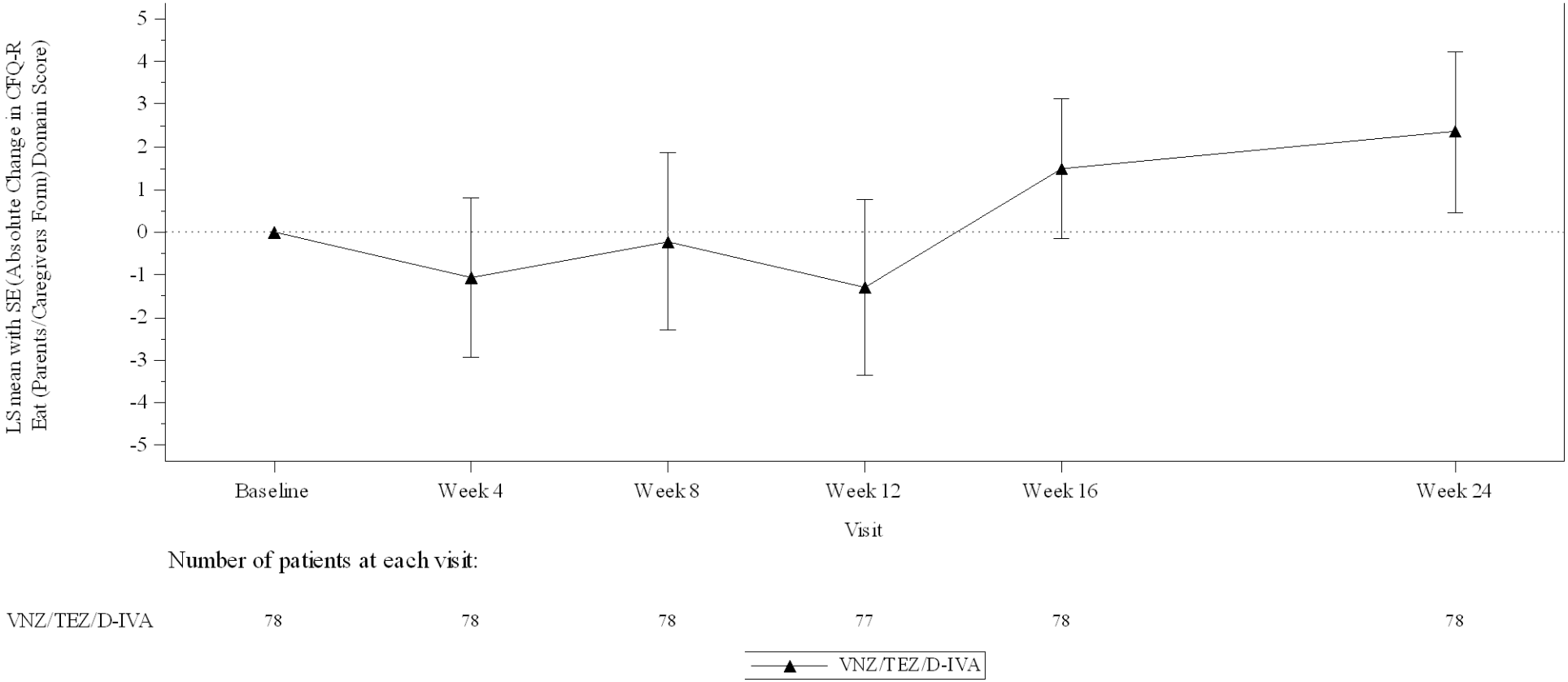
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)



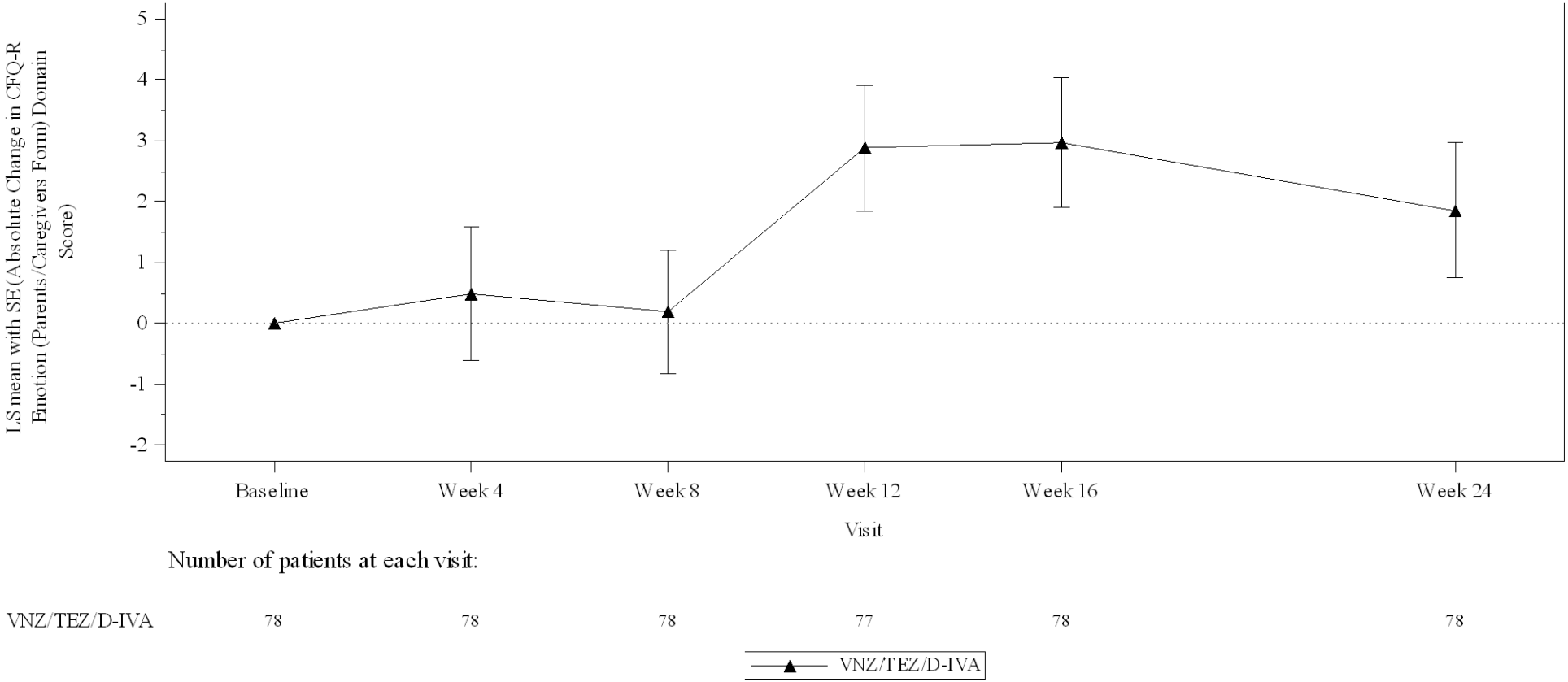
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)



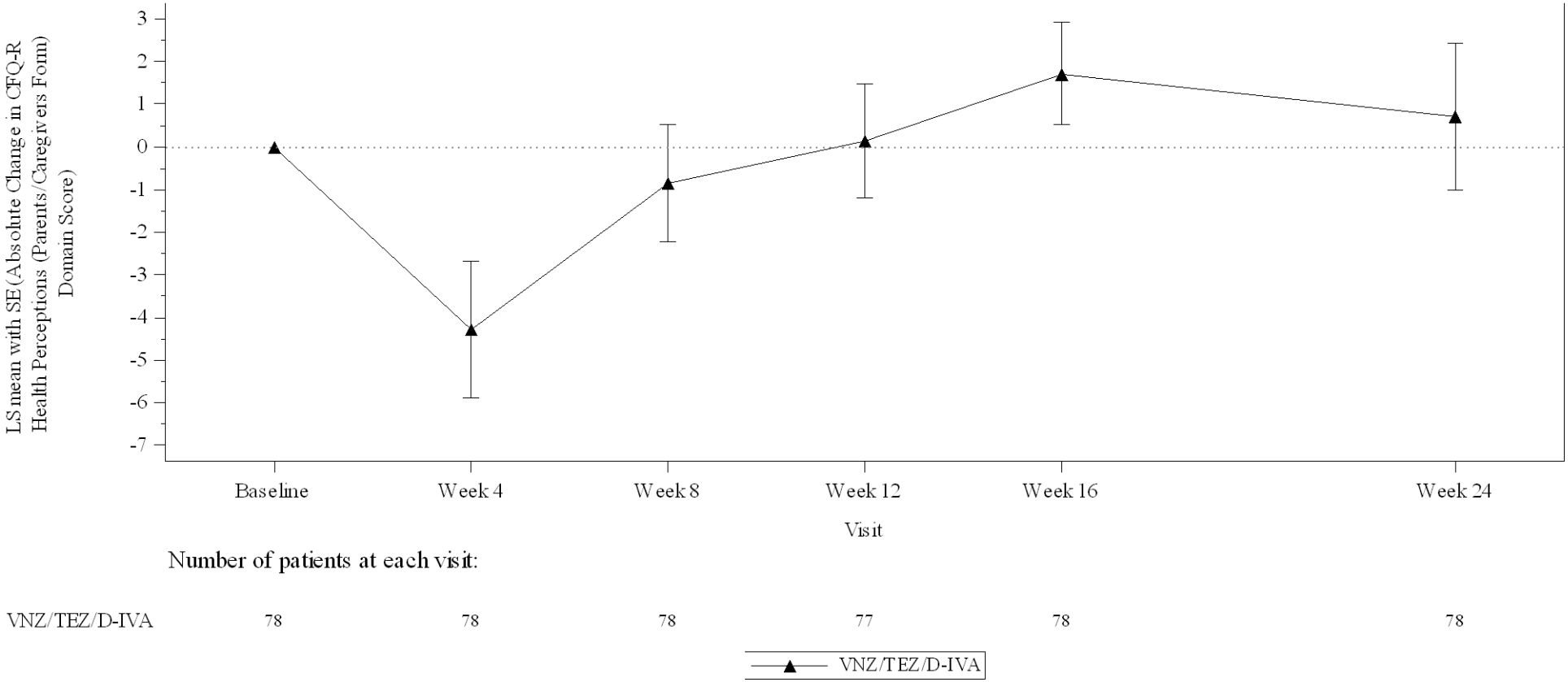
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)



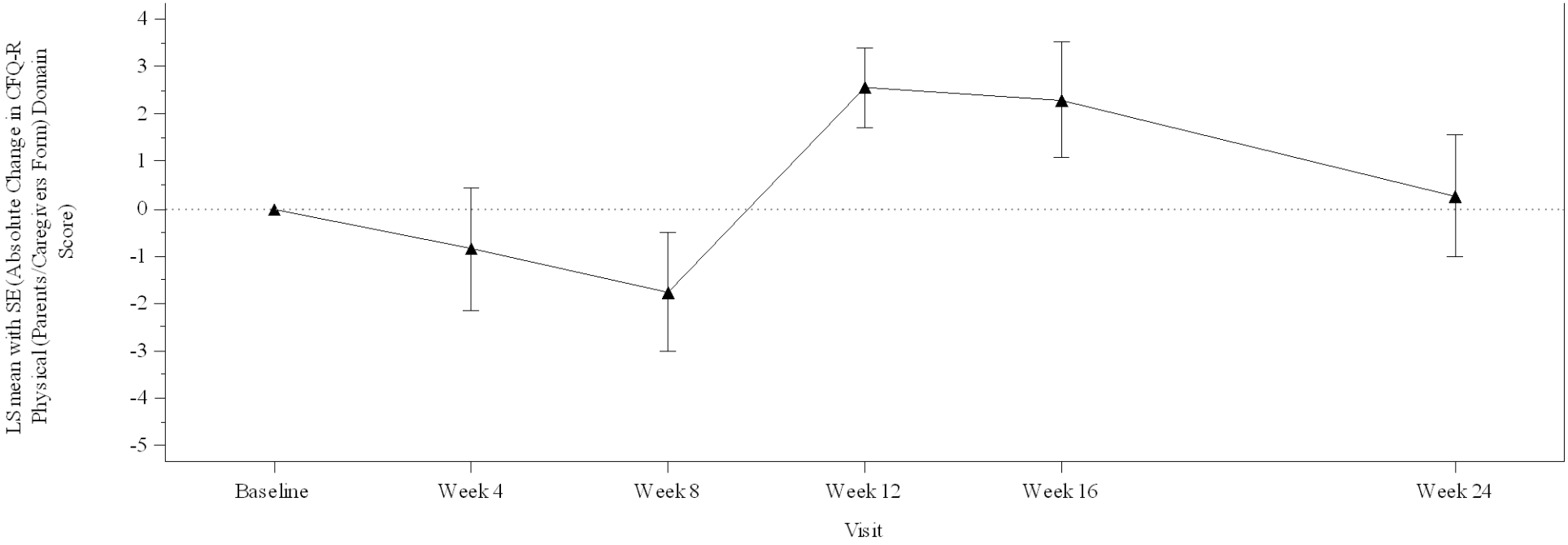
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)



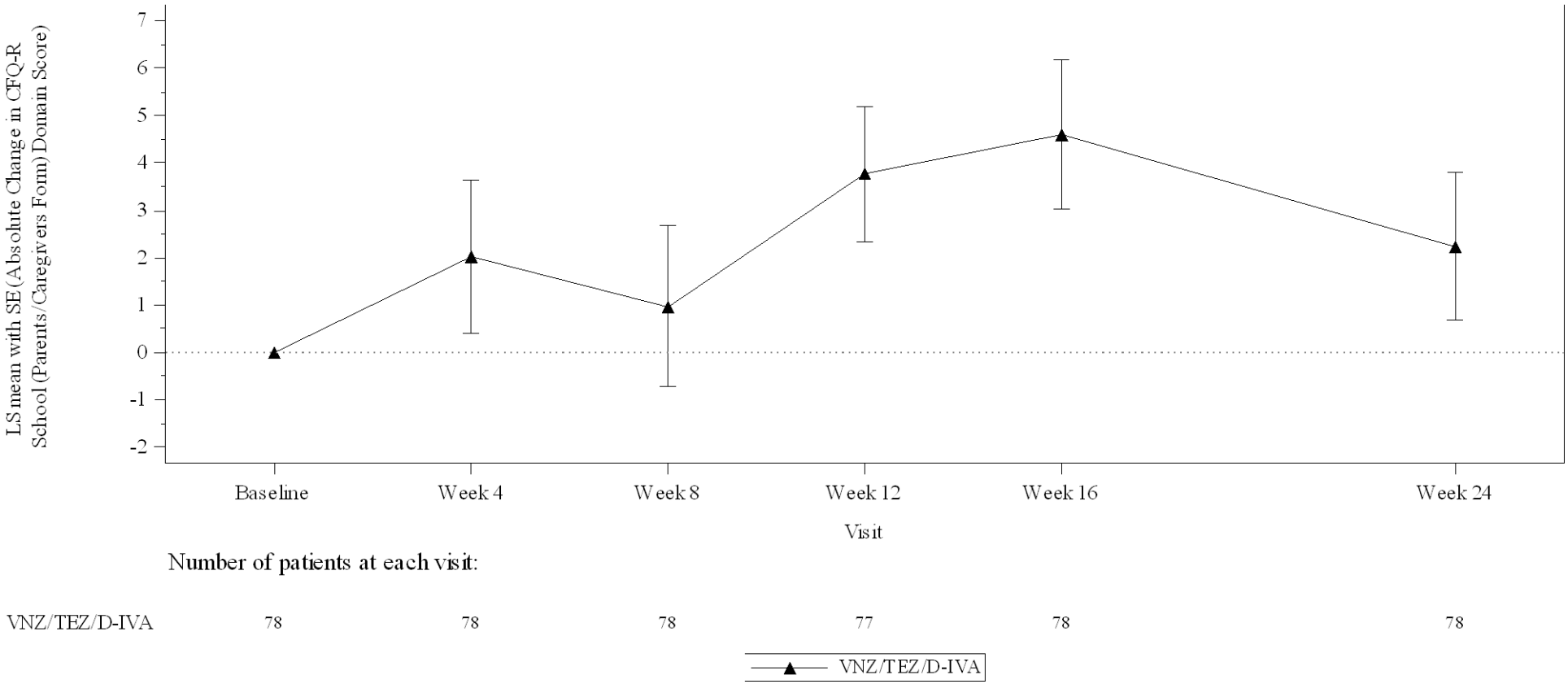
Number of patients at each visit:

	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	78	78	78	77	78	78

VNZ/TEZ/D-IVA

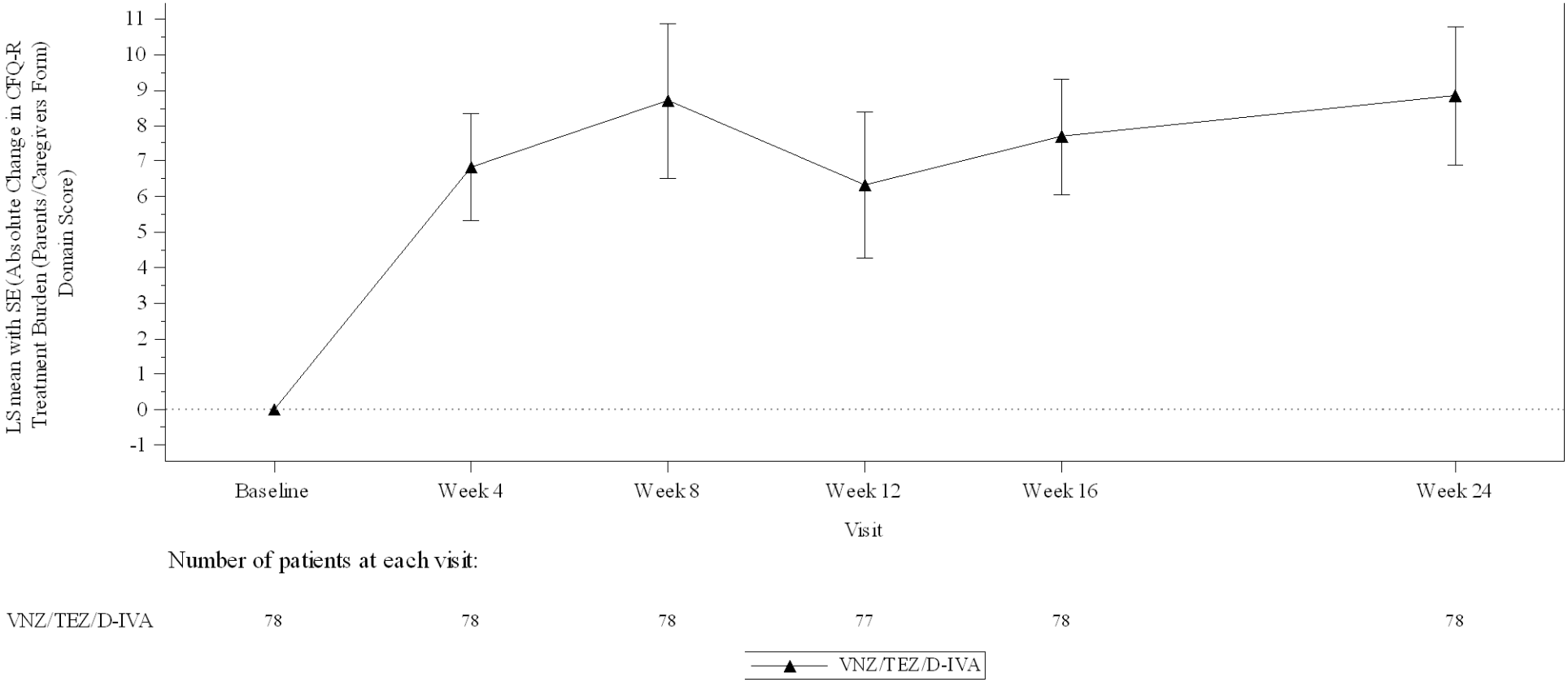
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: School (Parents/Caregivers Form)



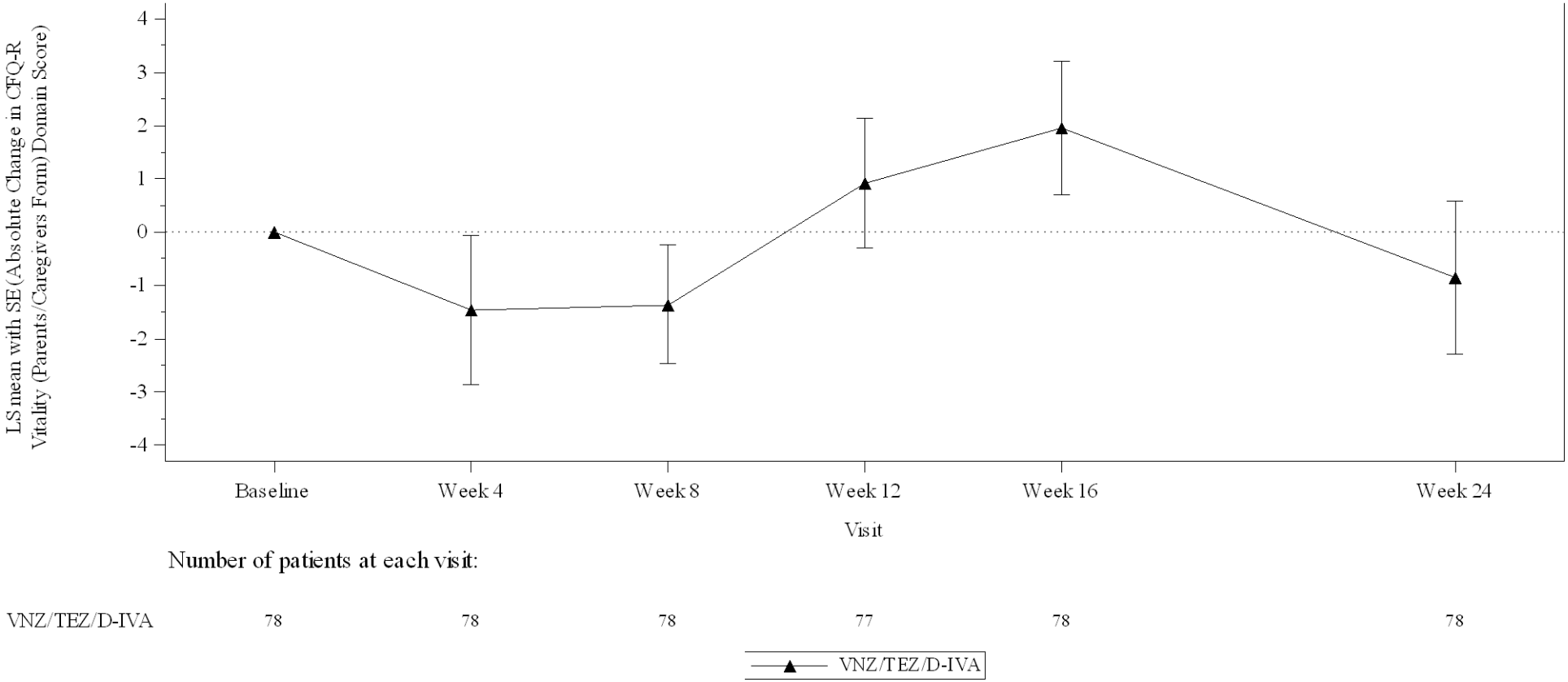
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)



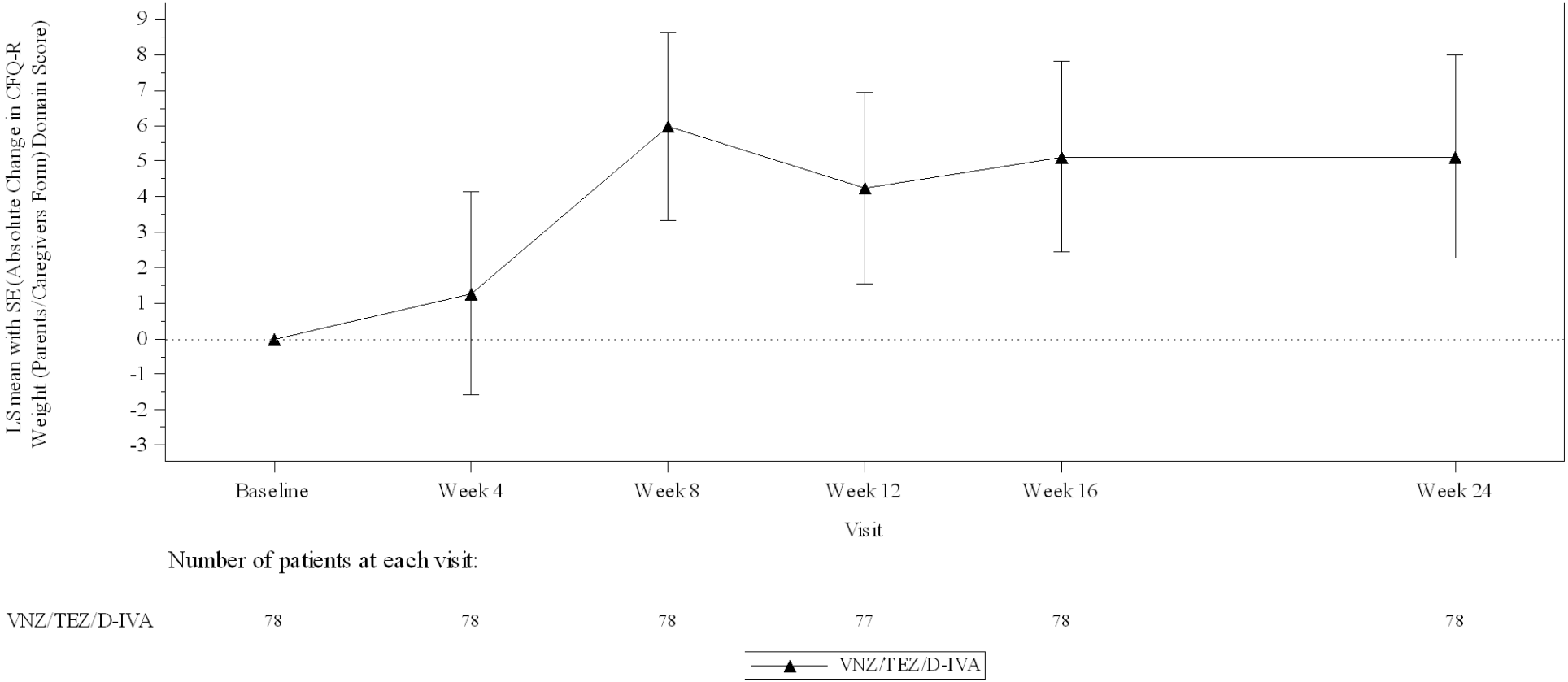
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)



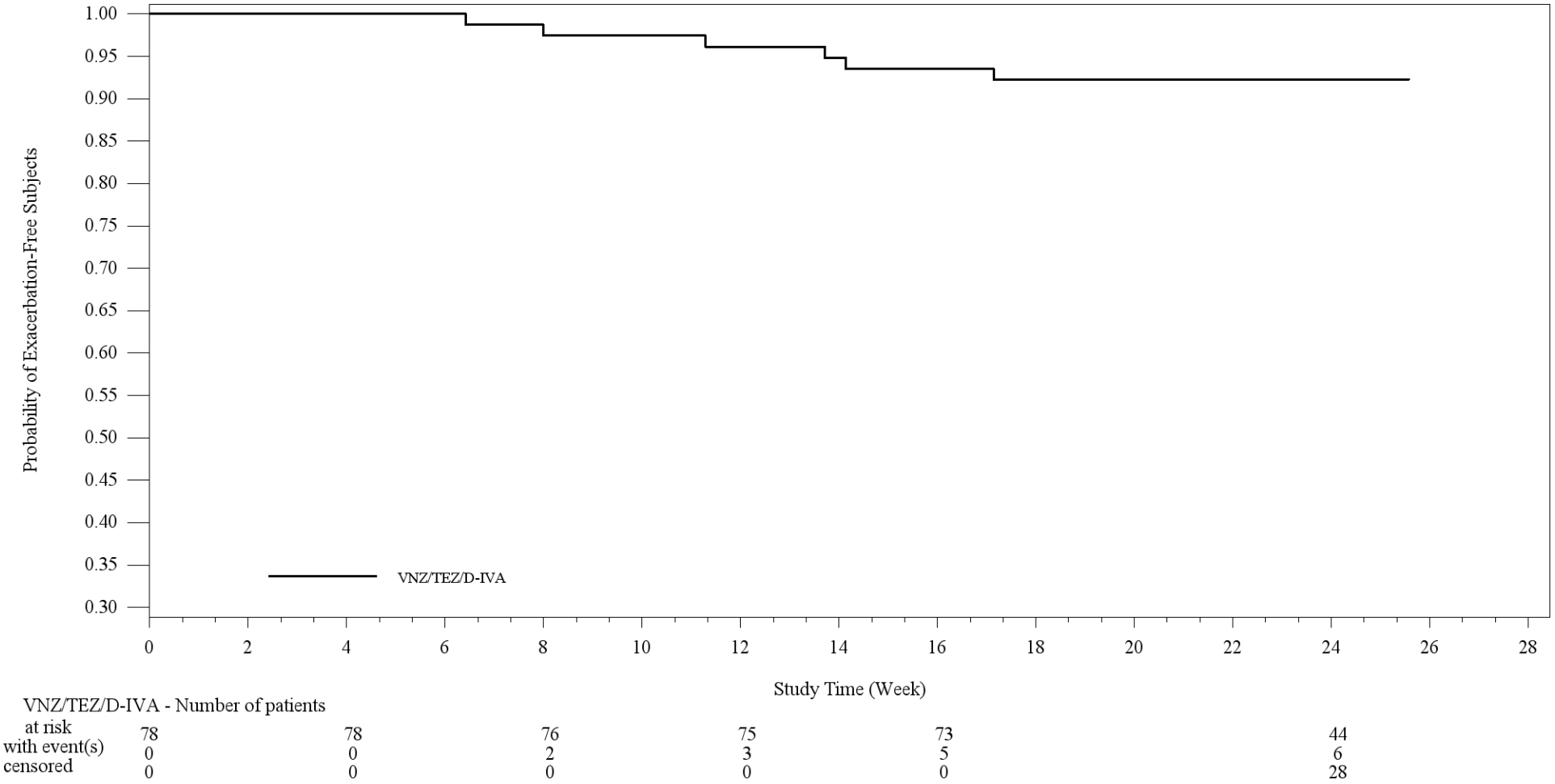
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Vitality (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.1.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)



- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

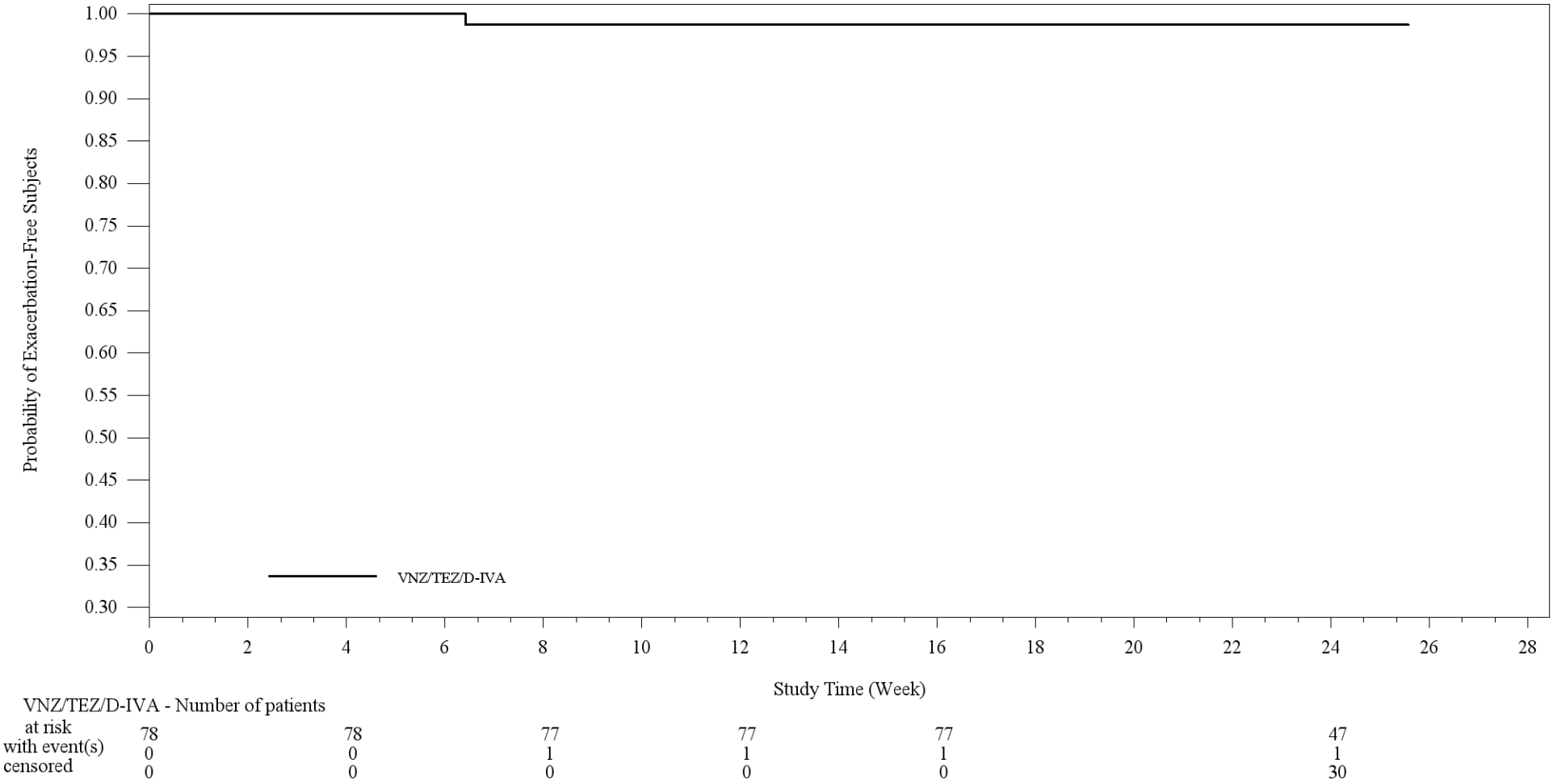
Figure 3.2.1.14.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation through Week 24
Full Analysis Set



VNZ/TEZ/D-IVA - Number of patients						
at risk	78	78	76	75	73	44
with event(s)	0	0	2	3	5	6
censored	0	0	0	0	0	28

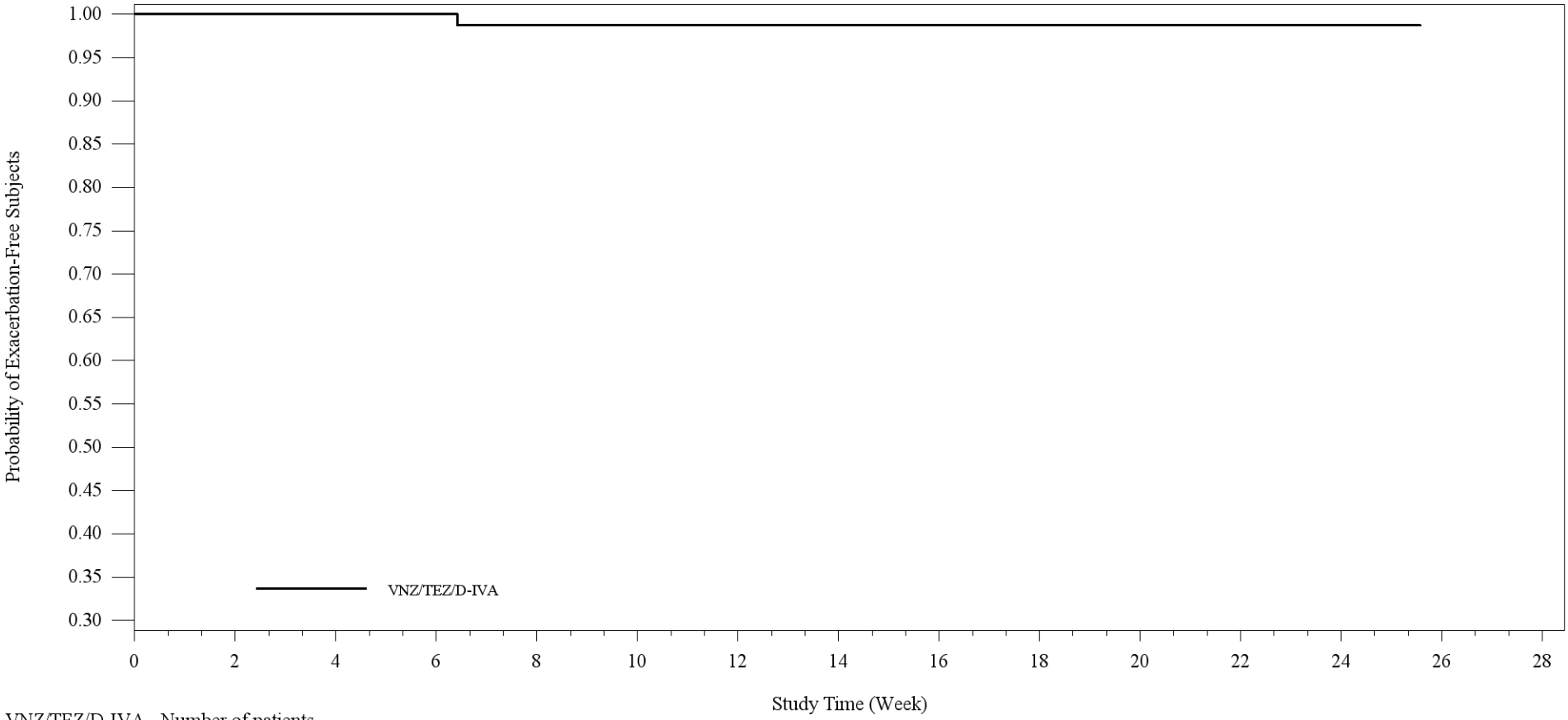
Zusatzanalysen zur Studie VX21-121-105

Figure 3.2.1.15.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring Hospitalization through Week 24
Full Analysis Set



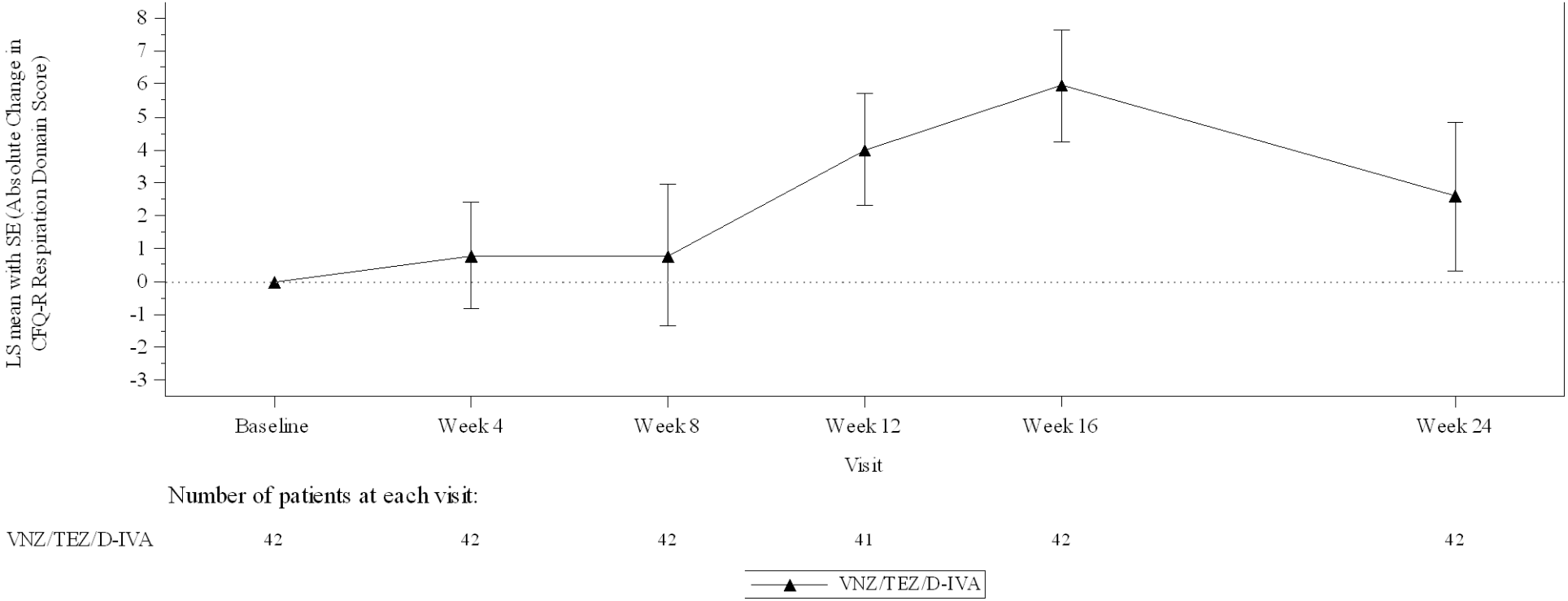
VNZ/TEZ/D-IVA - Number of patients						
at risk	78	78	77	77	77	47
with event(s)	0	0	1	1	1	1
censored	0	0	0	0	0	30

Figure 3.2.1.16.2
Study VX21-121-105: Kaplan-Meier Plot for Time-to-First Pulmonary Exacerbation Requiring IV Antibiotics through Week 24
Full Analysis Set



VNZ/TEZ/D-IVA - Number of patients						
at risk	78	78	77	77	77	47
with event(s)	0	0	1	1	1	1
censored	0	0	0	0	0	30

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration
Sex = Male



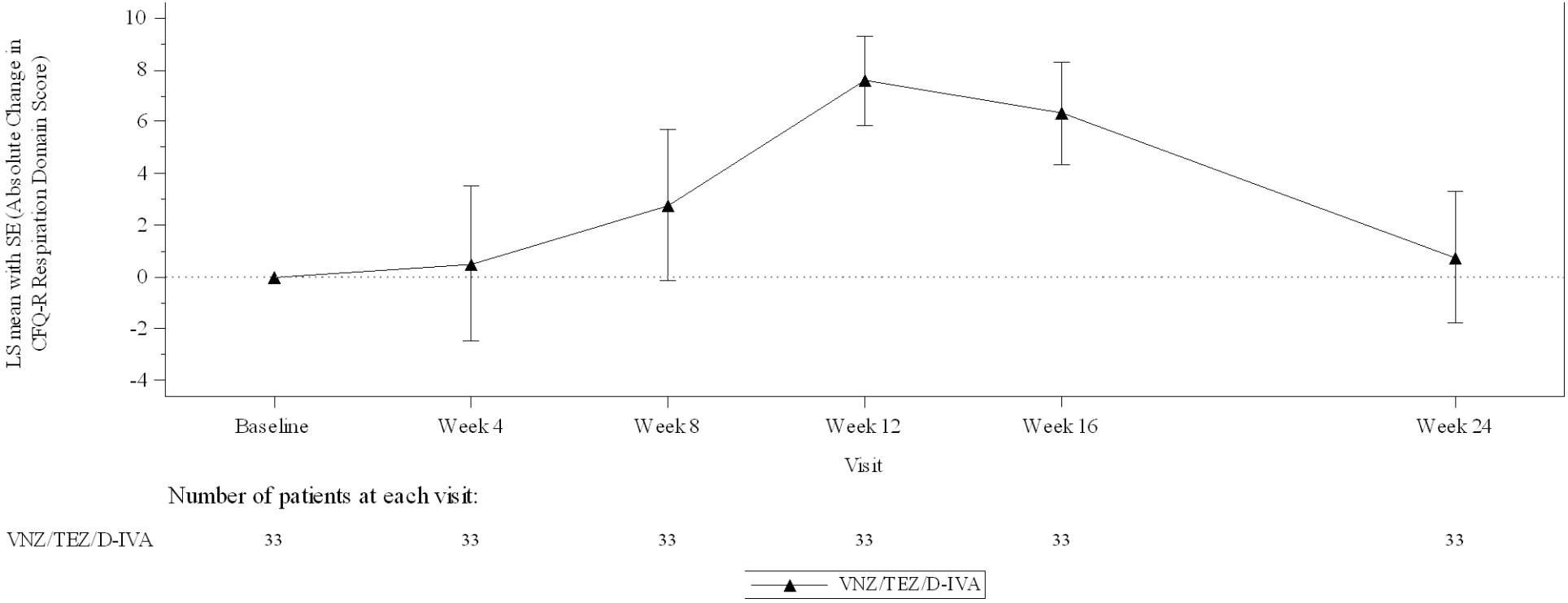
Number of patients at each visit:

	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	42	42	42	41	42	42

VNZ/TEZ/D-IVA

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration
Sex = Female



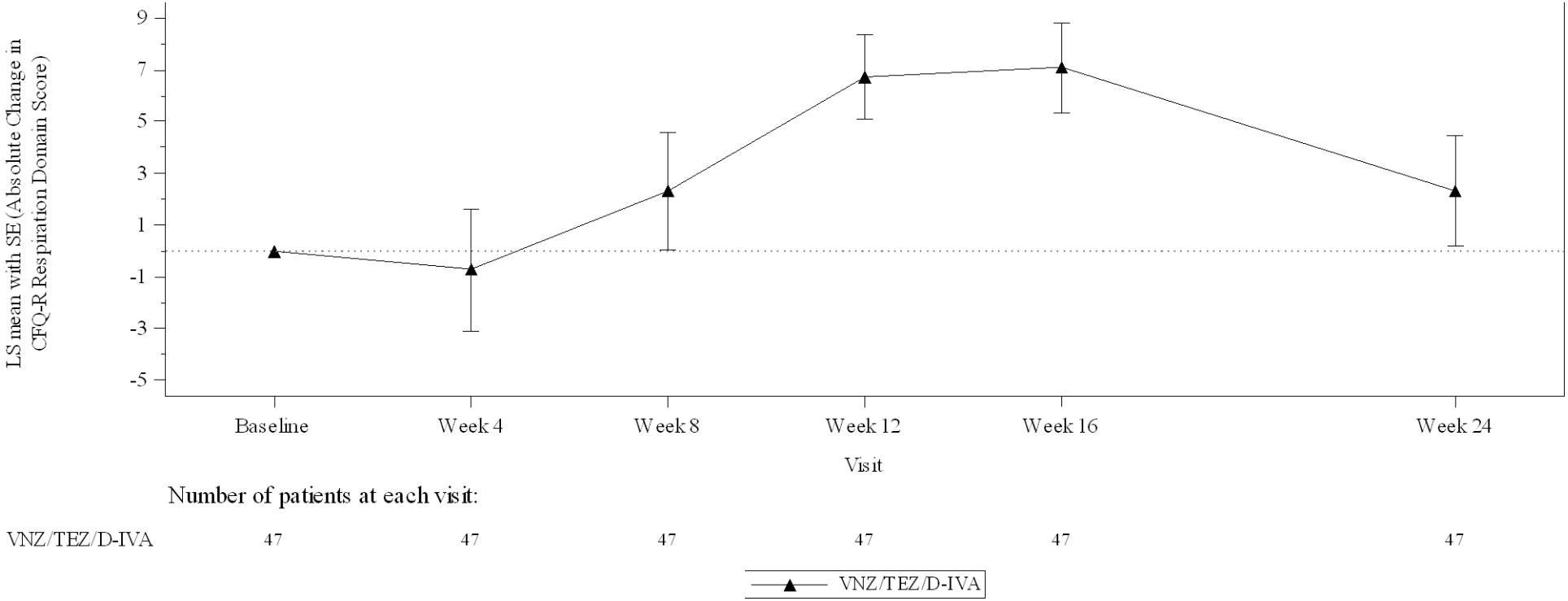
Number of patients at each visit:

	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	33	33	33	33	33	33

VNZ/TEZ/D-IVA

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration
Region = North America



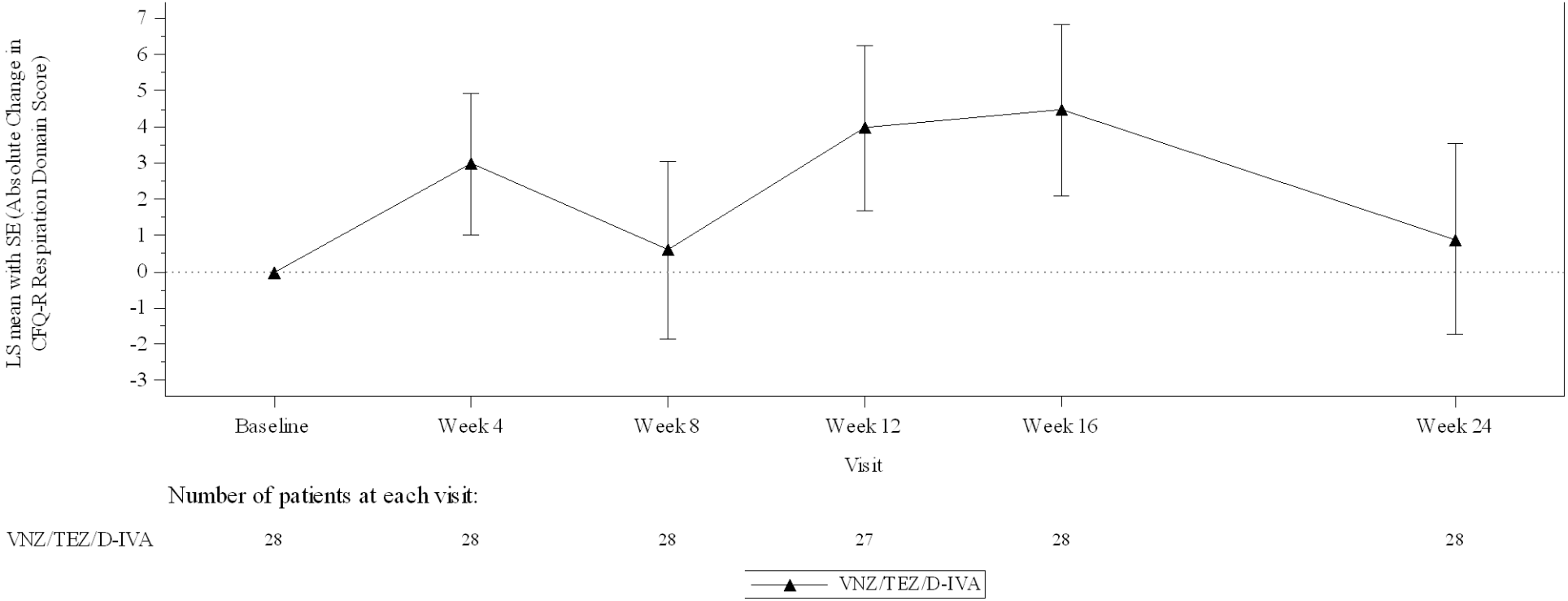
Number of patients at each visit:

	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	47	47	47	47	47	47

VNZ/TEZ/D-IVA

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration
Region = Rest of World



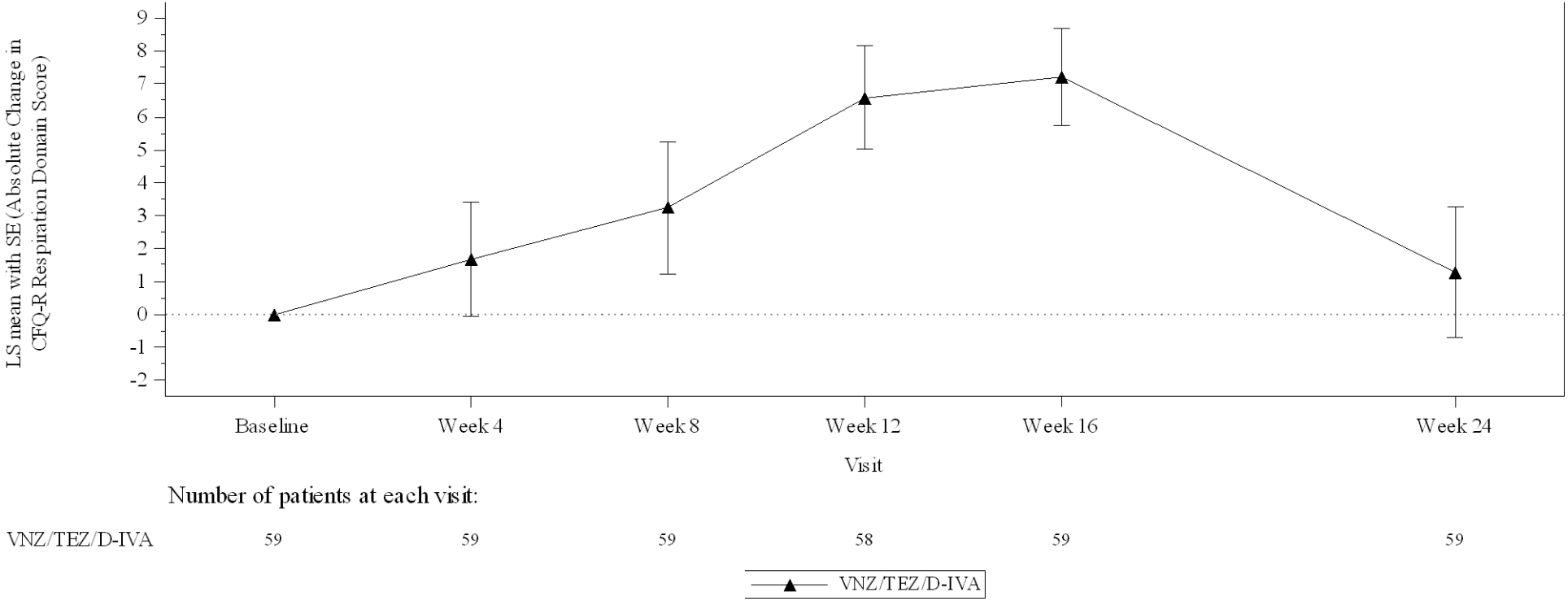
Number of patients at each visit:

VNZ/TEZ/D-IVA	28	28	28	27	28	28

VNZ/TEZ/D-IVA

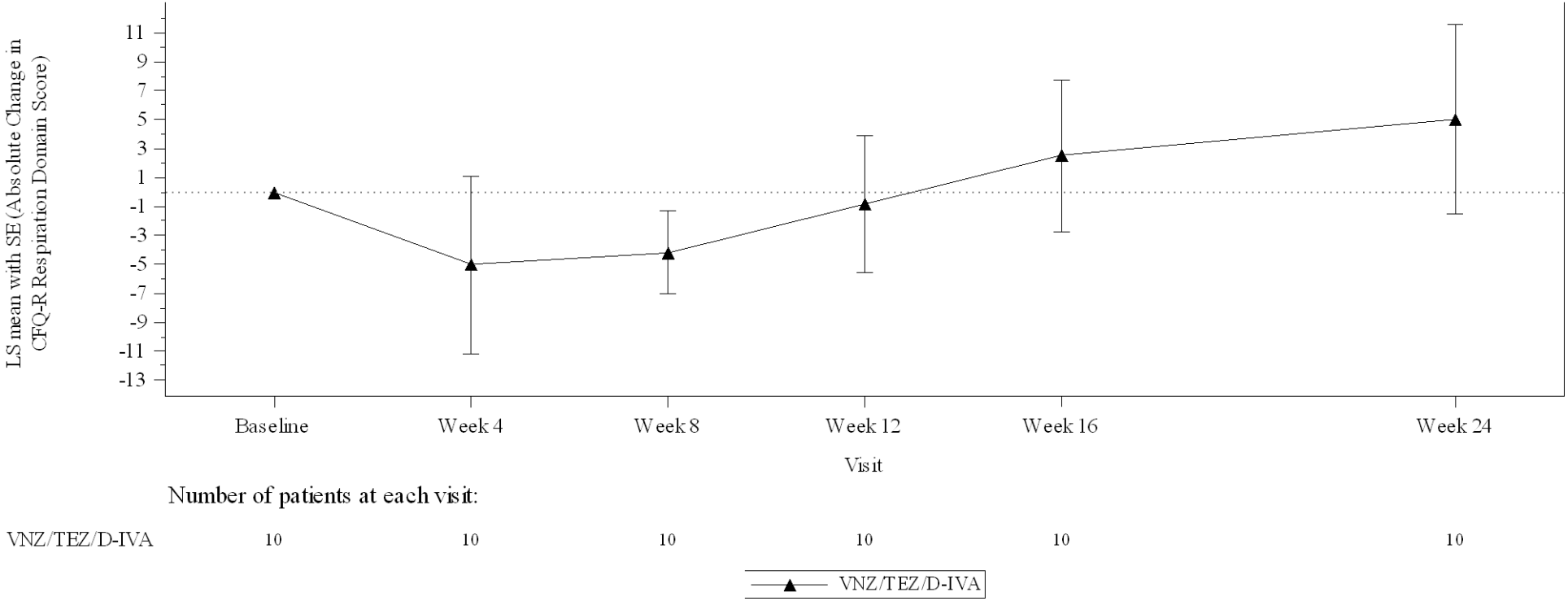
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration
$LCI_{2.5}$ at baseline <7.5



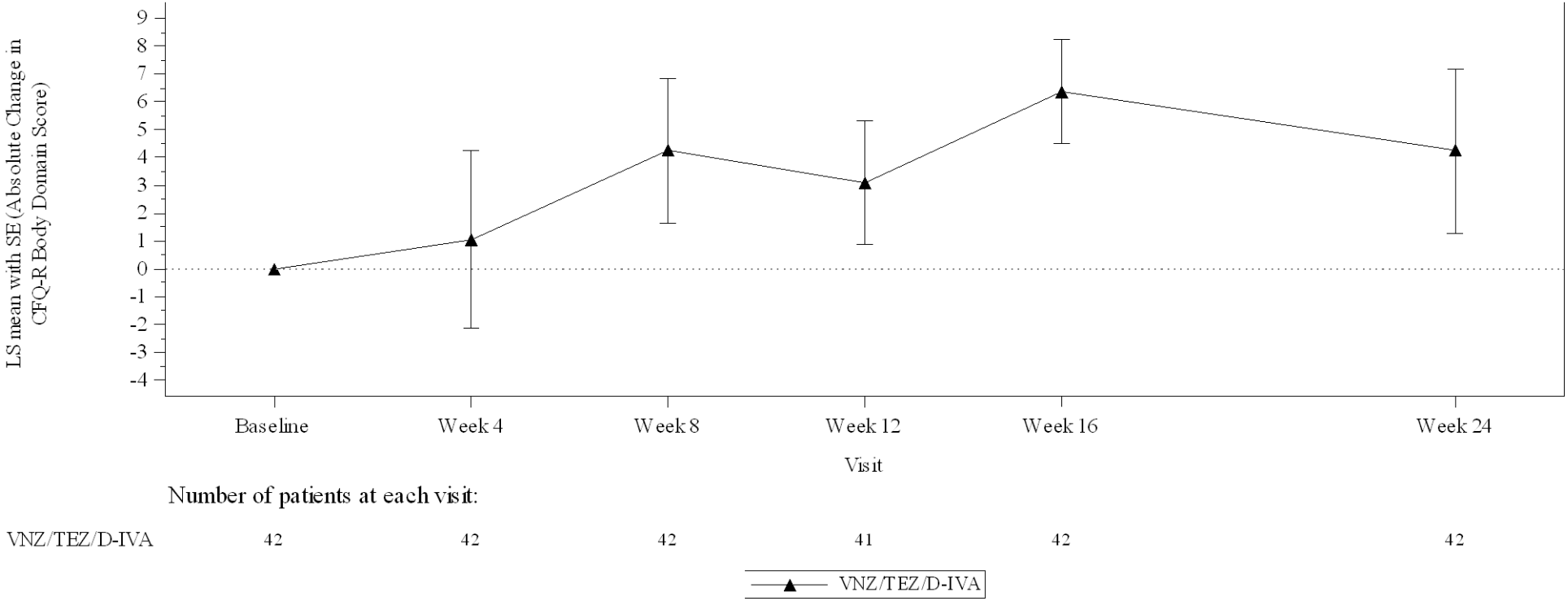
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration
$LCI_{2.5}$ at baseline ≥7.5



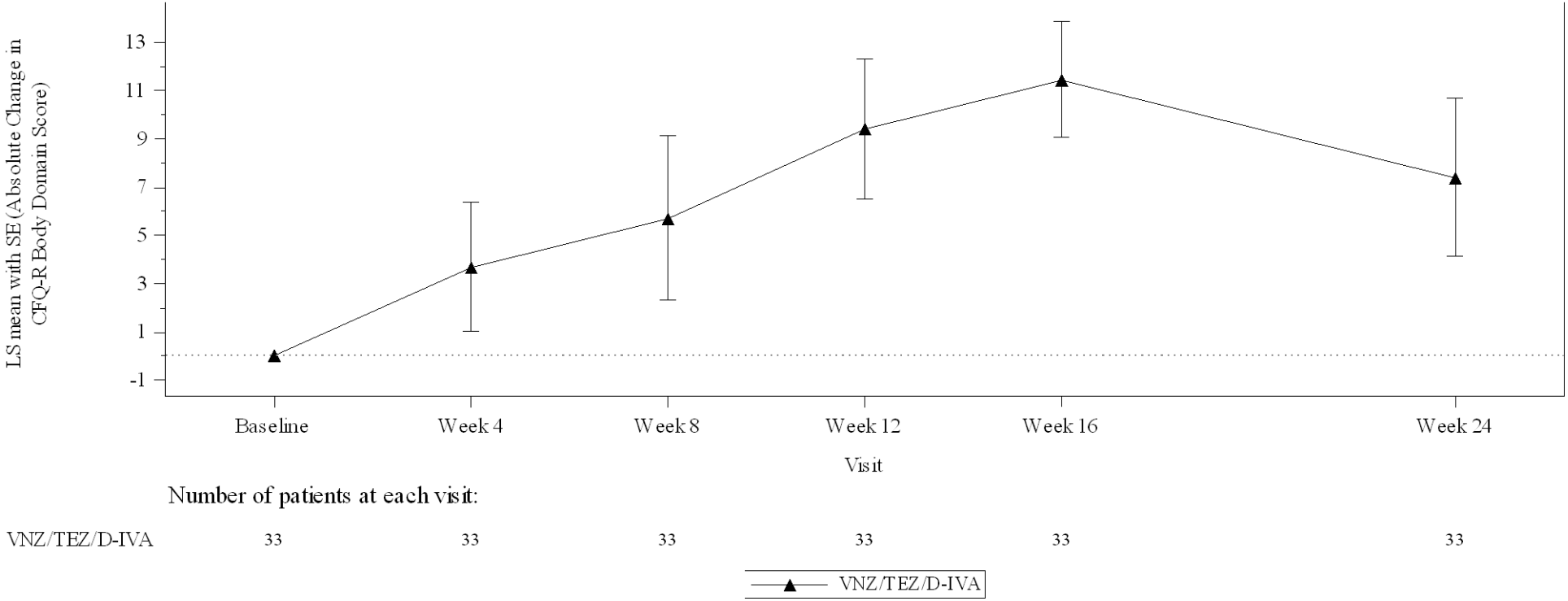
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Respiration Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body
Sex = Male



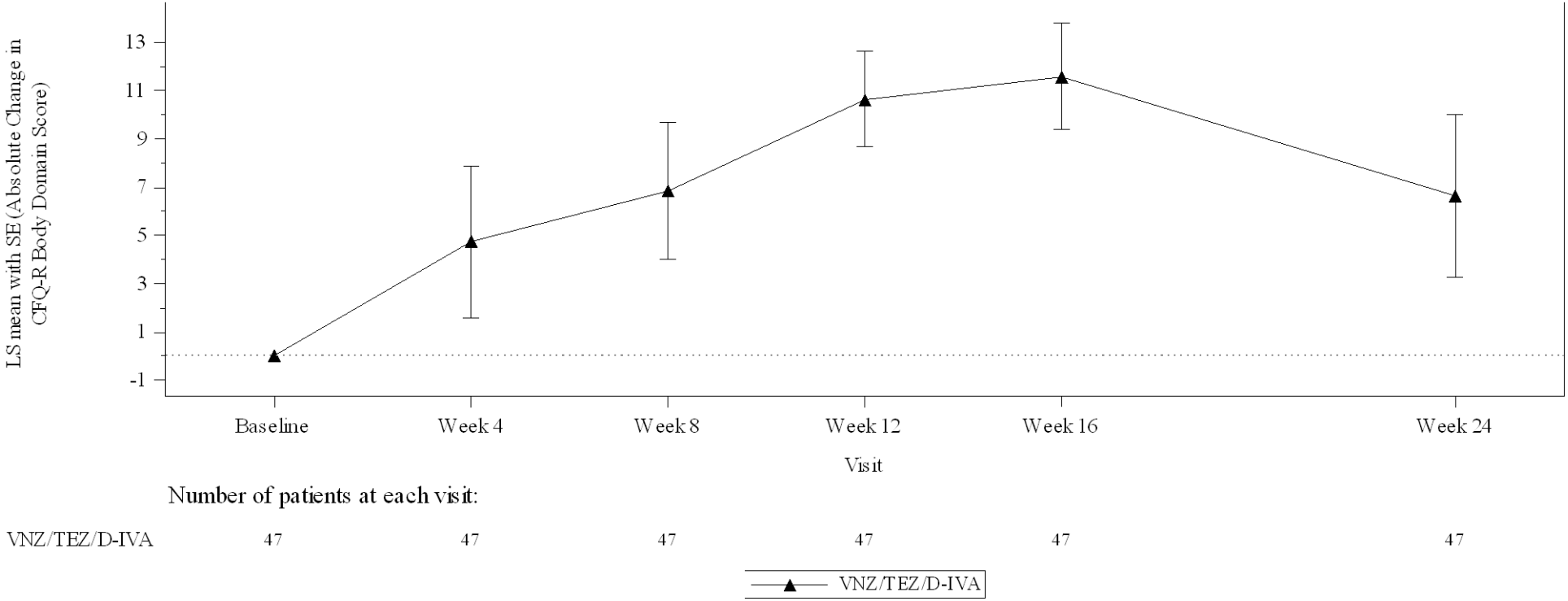
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body
Sex = Female



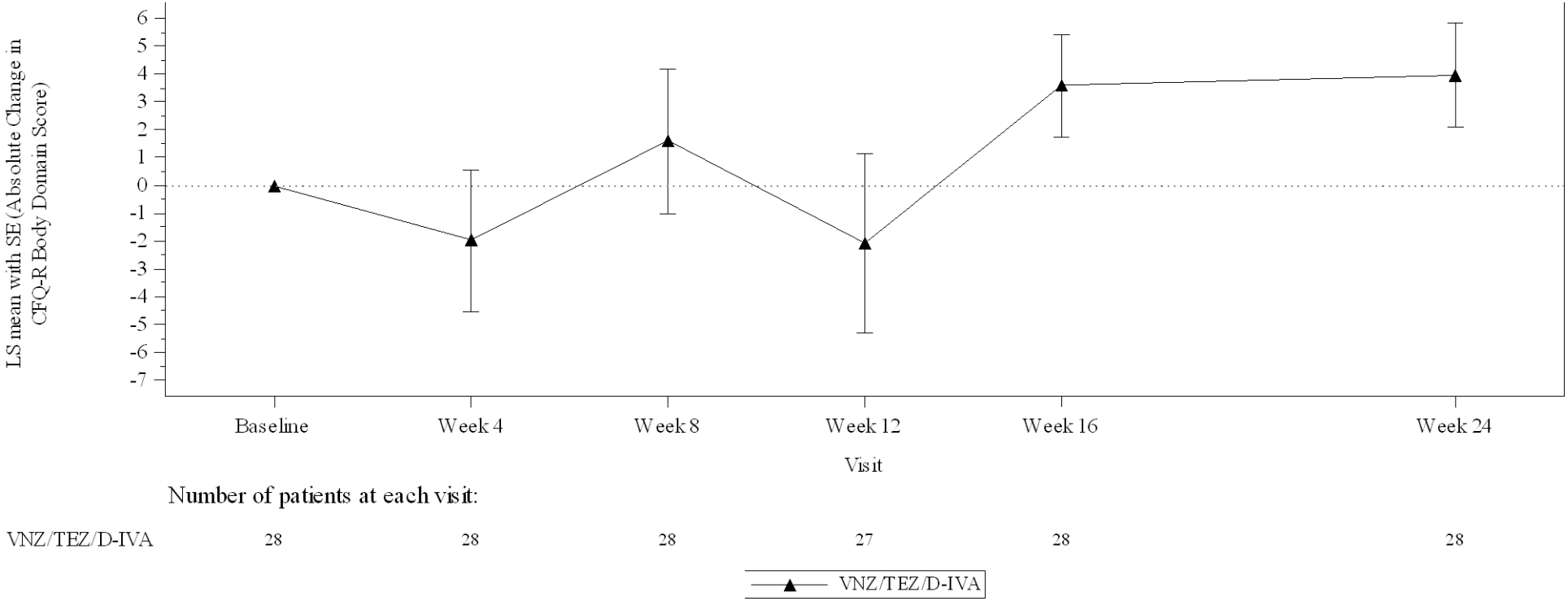
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body
Region = North America



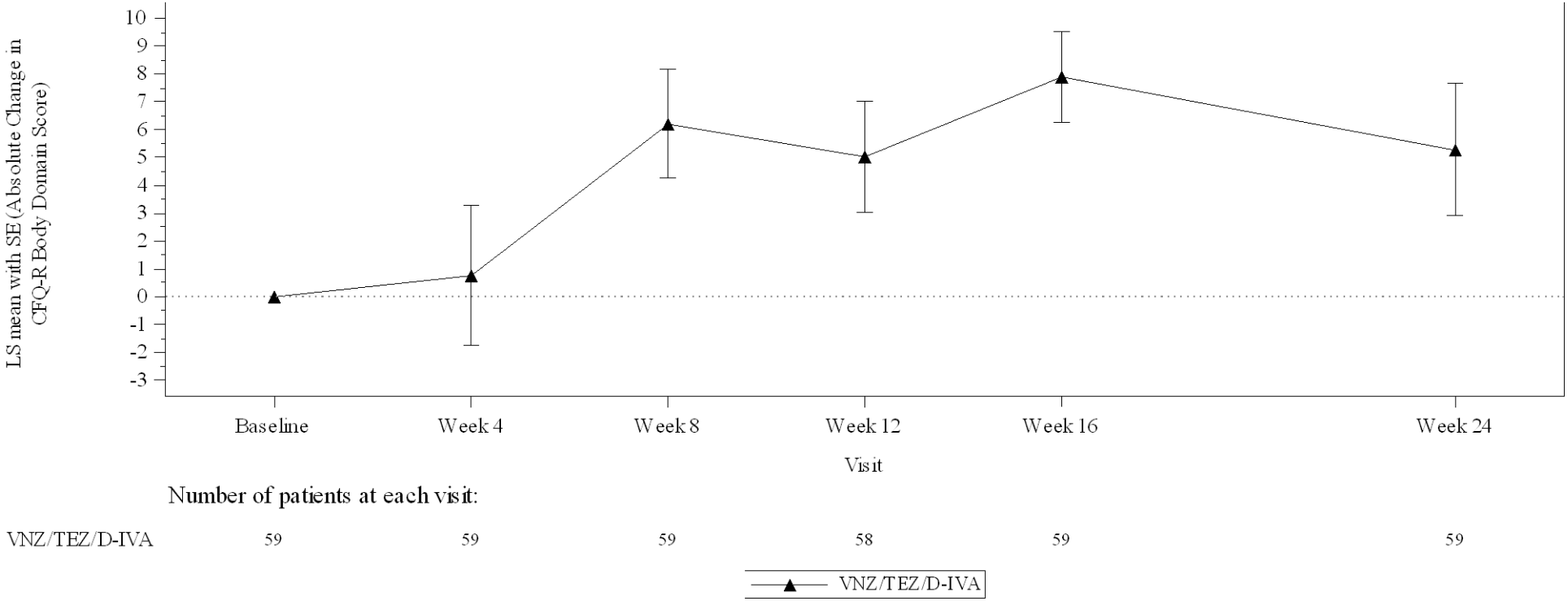
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body
Region = Rest of World



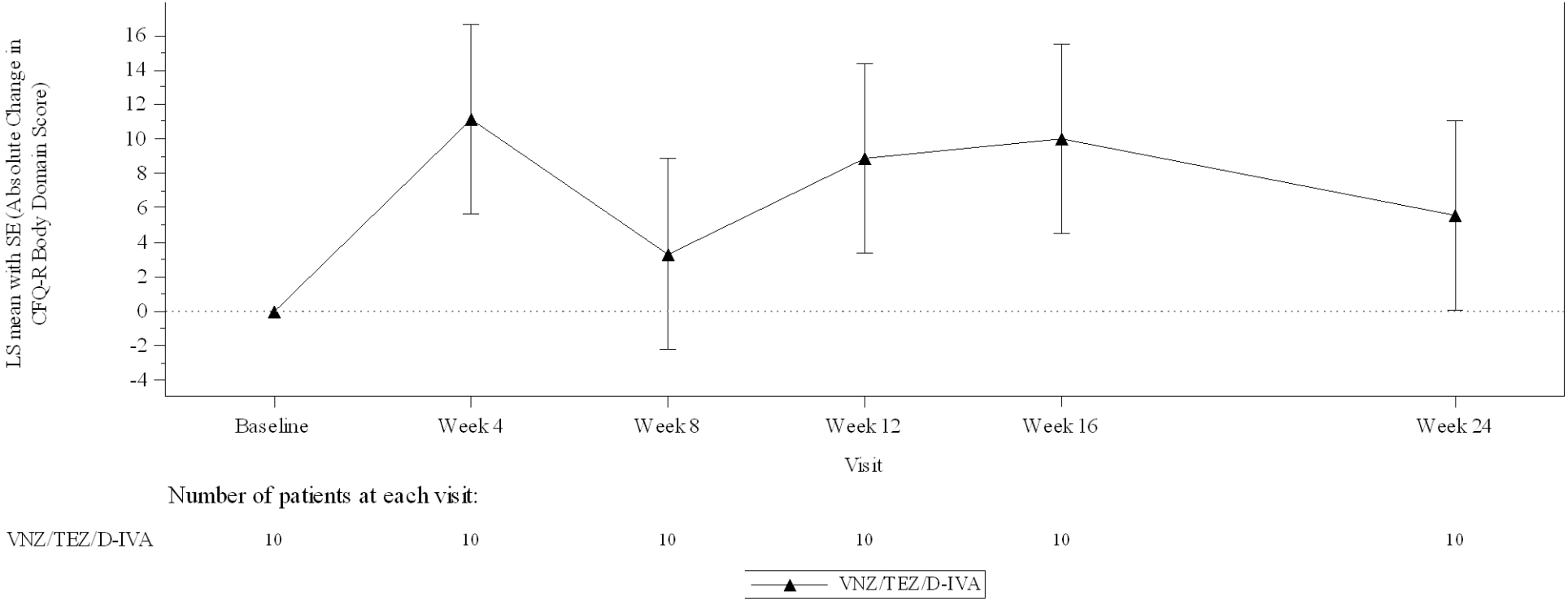
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body
$LCI_{2.5}$ at baseline <7.5



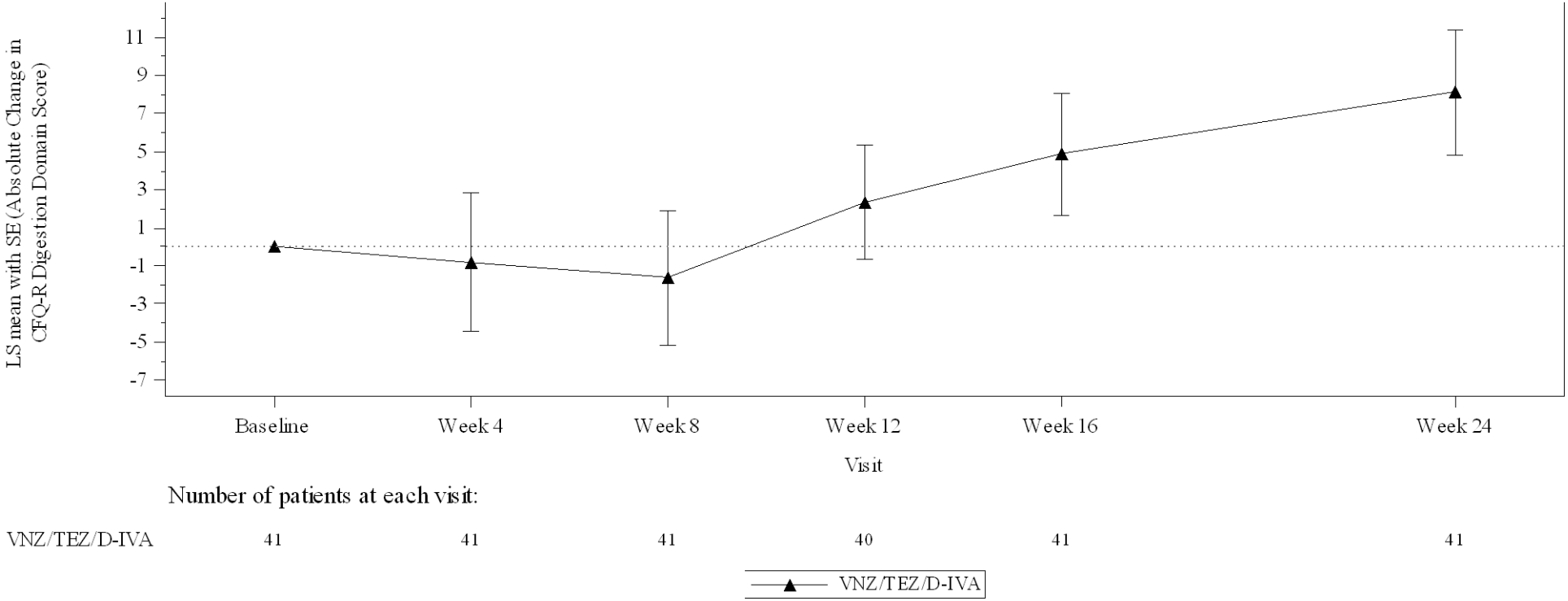
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body
$LCI_{2.5}$ at baseline ≥7.5



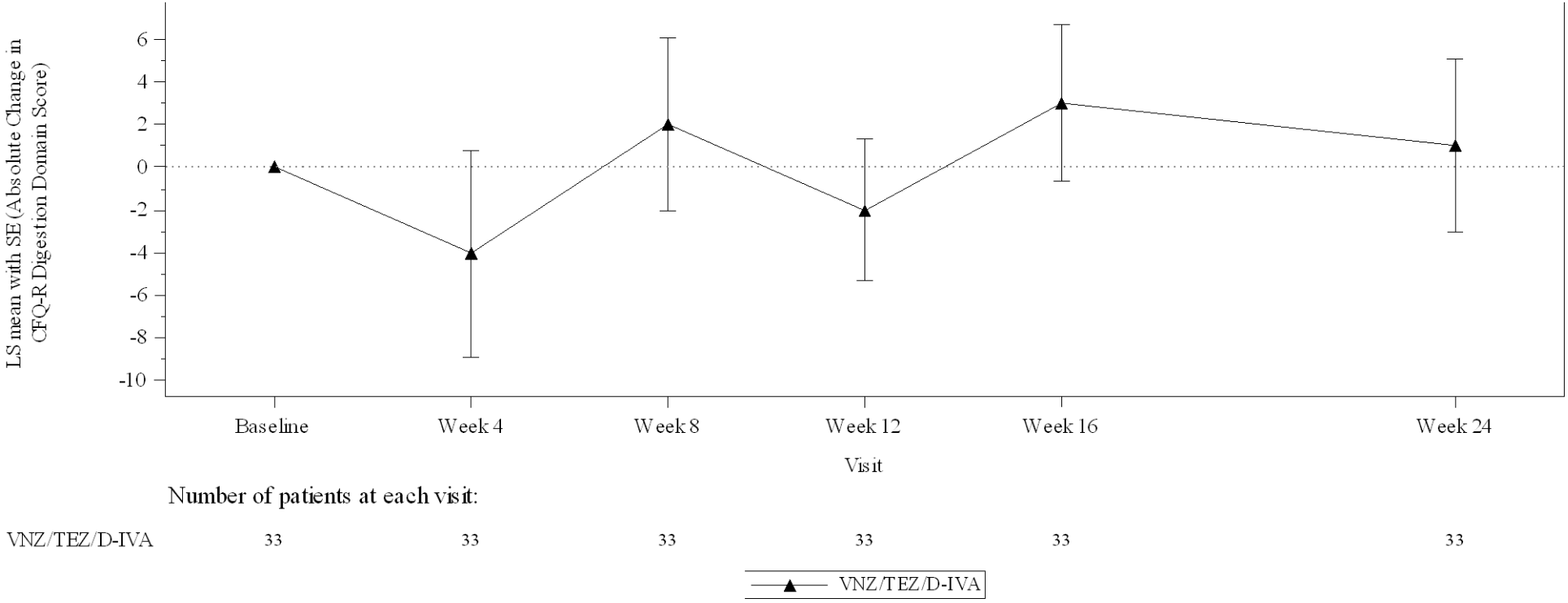
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Body Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion
Sex = Male



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion
Sex = Female



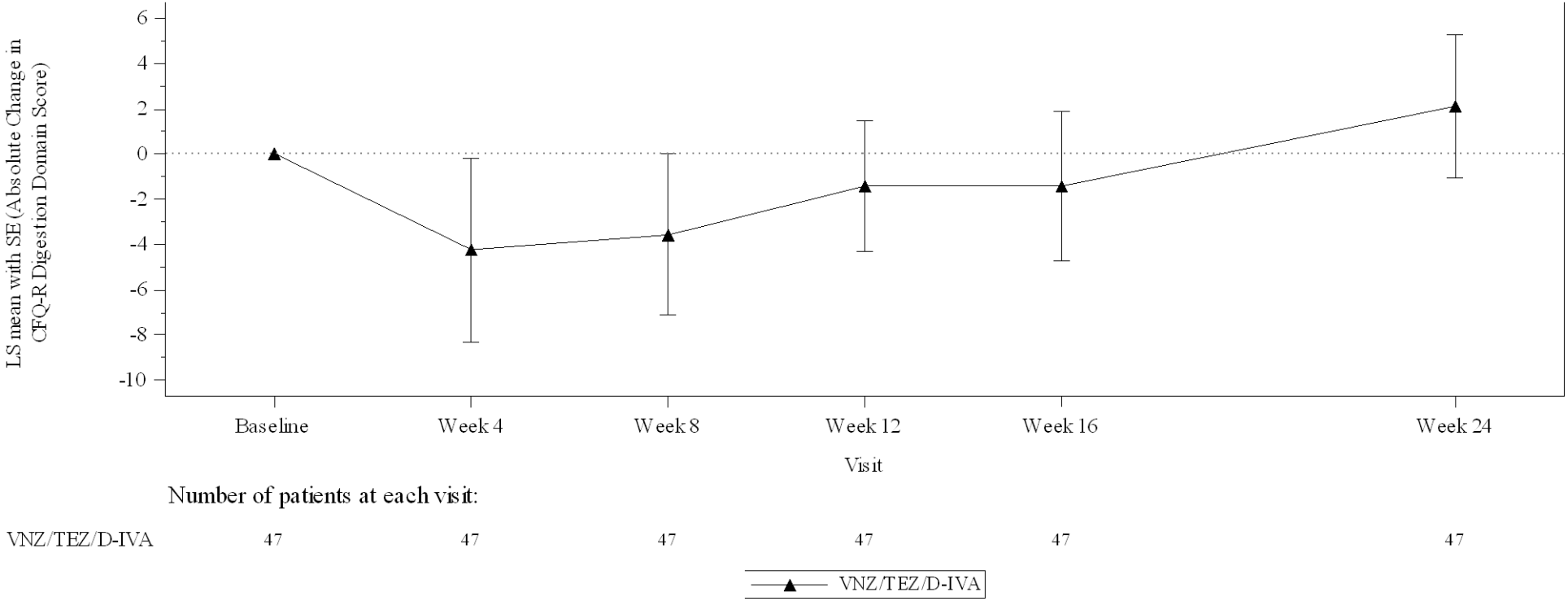
Number of patients at each visit:

	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	33	33	33	33	33	33

VNZ/TEZ/D-IVA

- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Digestion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion
Region = North America



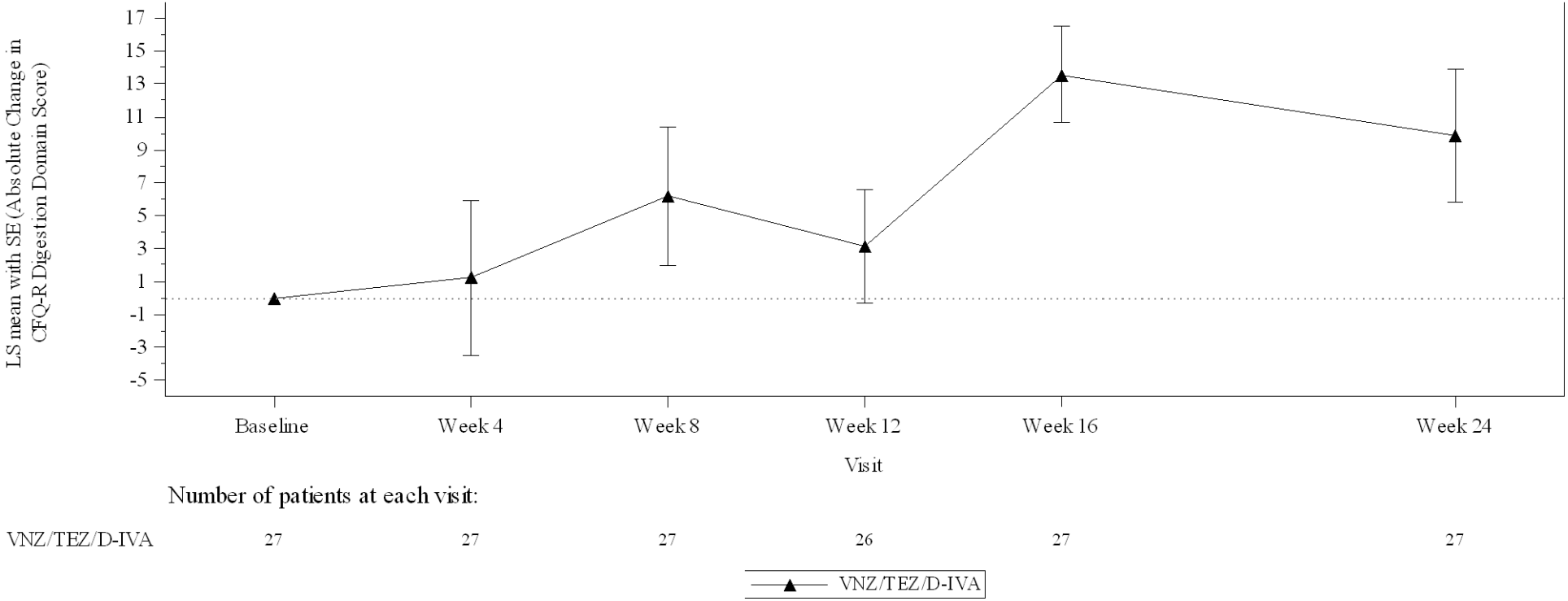
Number of patients at each visit:

VNZ/TEZ/D-IVA	47	47	47	47	47	47

VNZ/TEZ/D-IVA

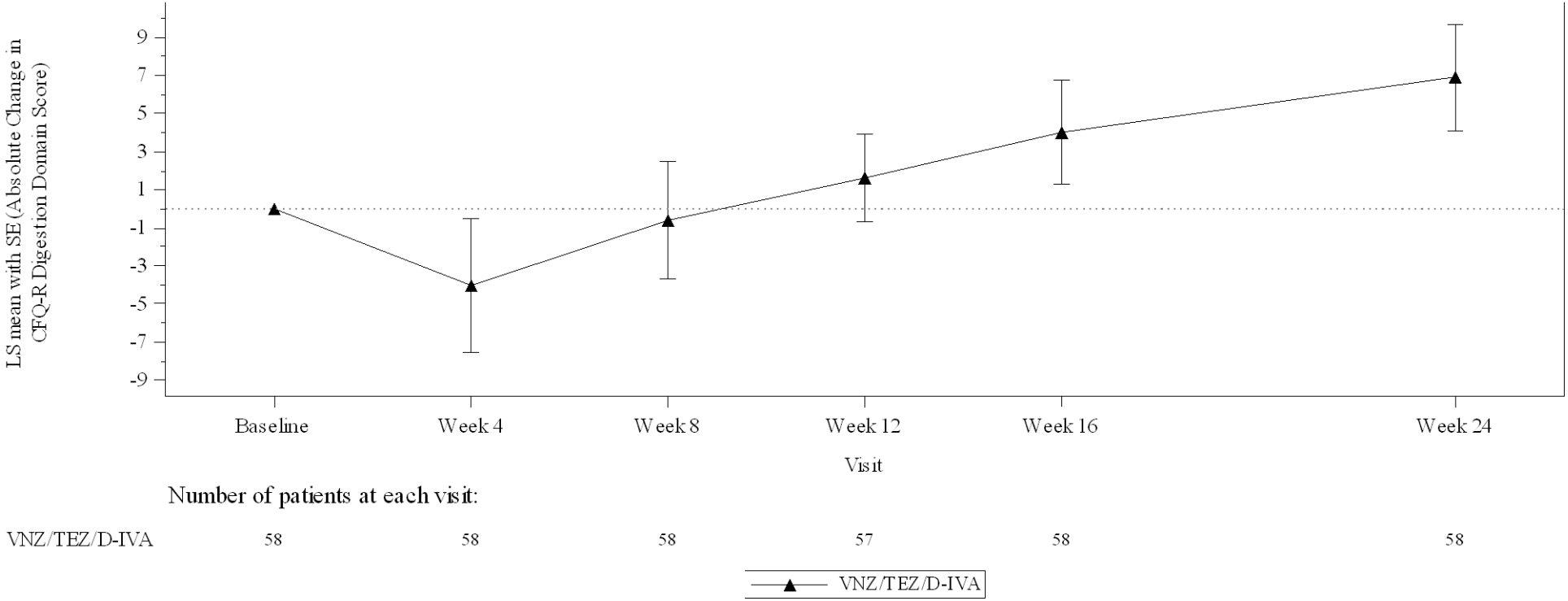
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion
Region = Rest of World



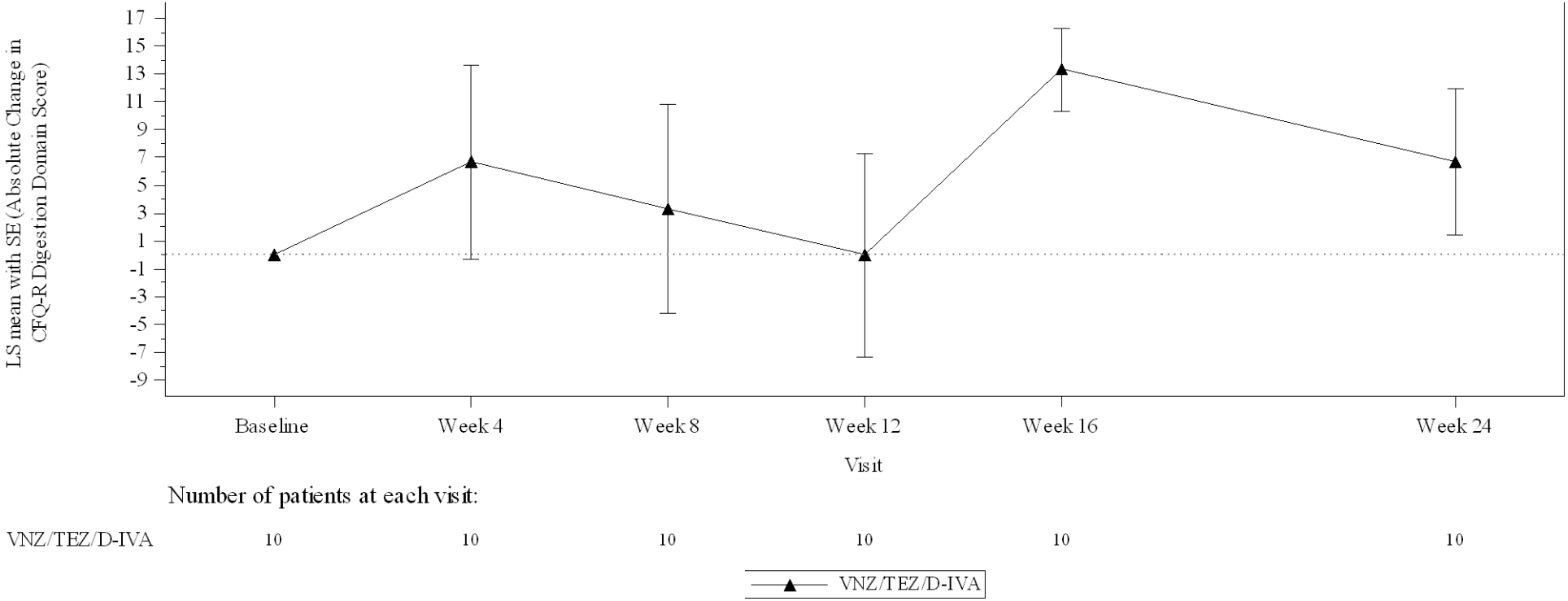
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion
$LCI_{2.5}$ at baseline <7.5



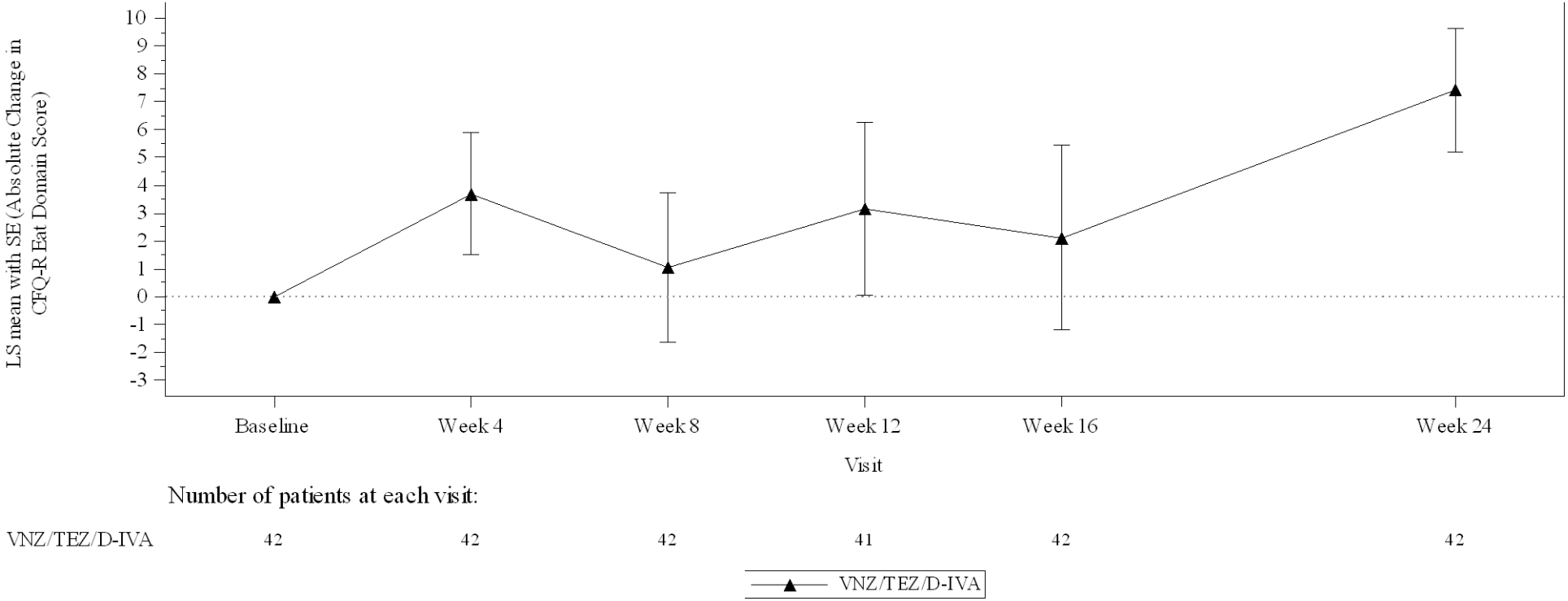
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Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion
$LCI_{2.5}$ at baseline ≥7.5



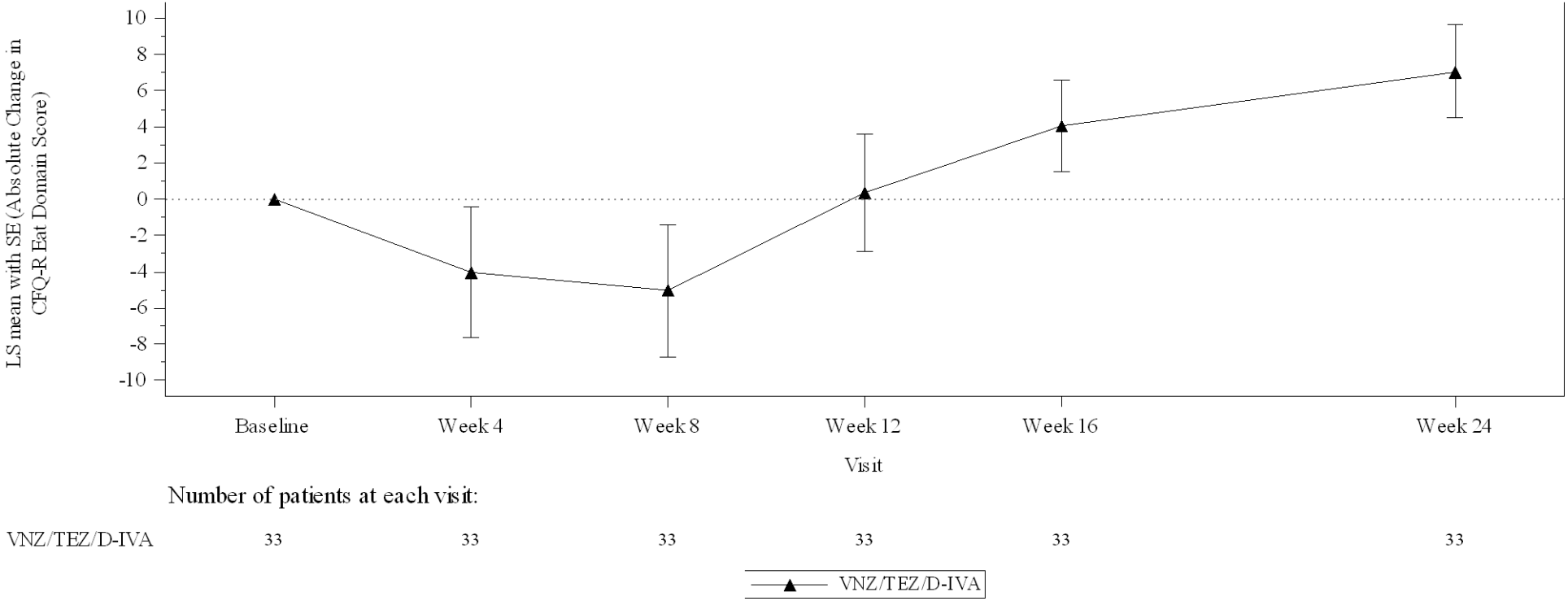
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Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat
Sex = Male



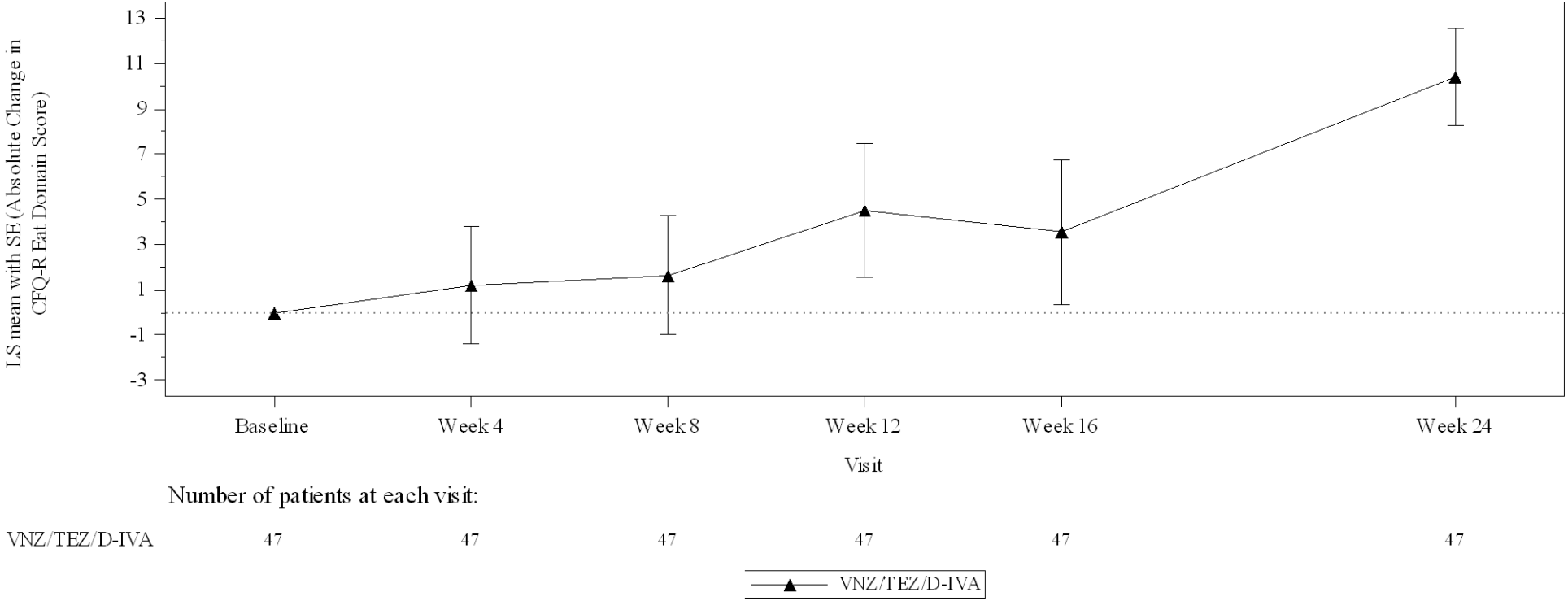
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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat
Sex = Female



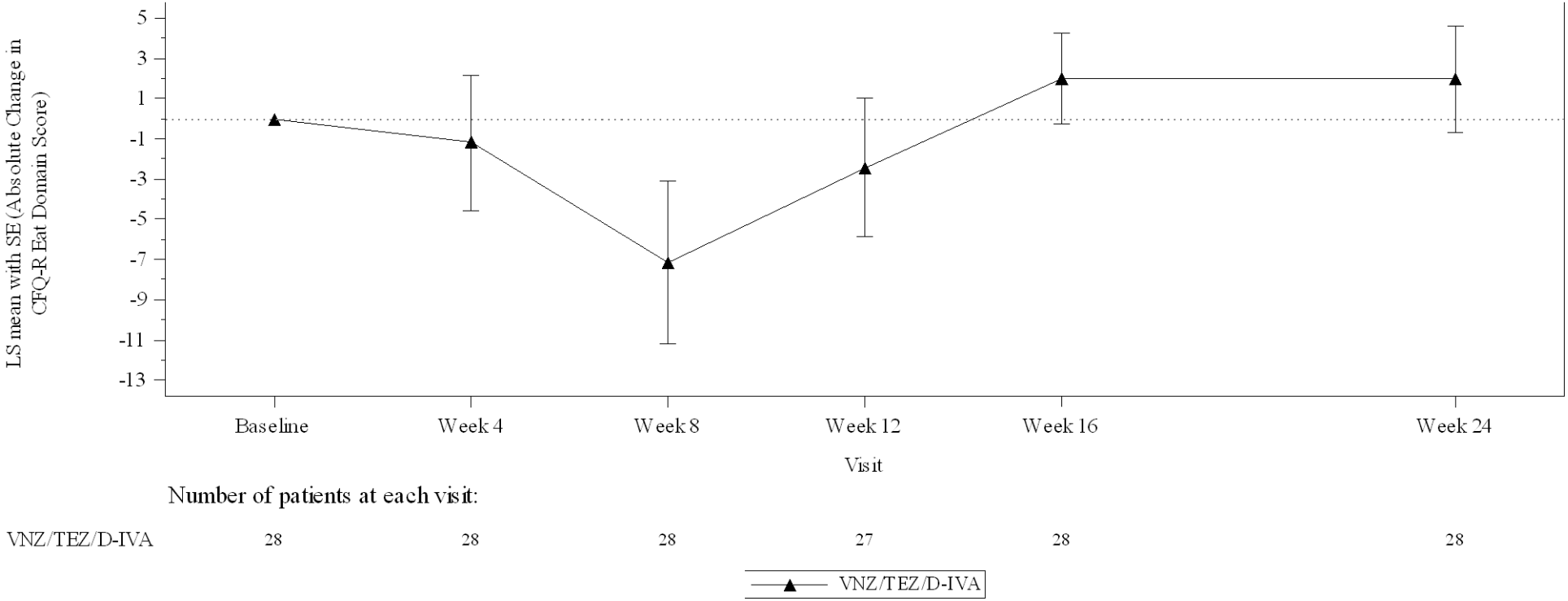
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat
Region = North America



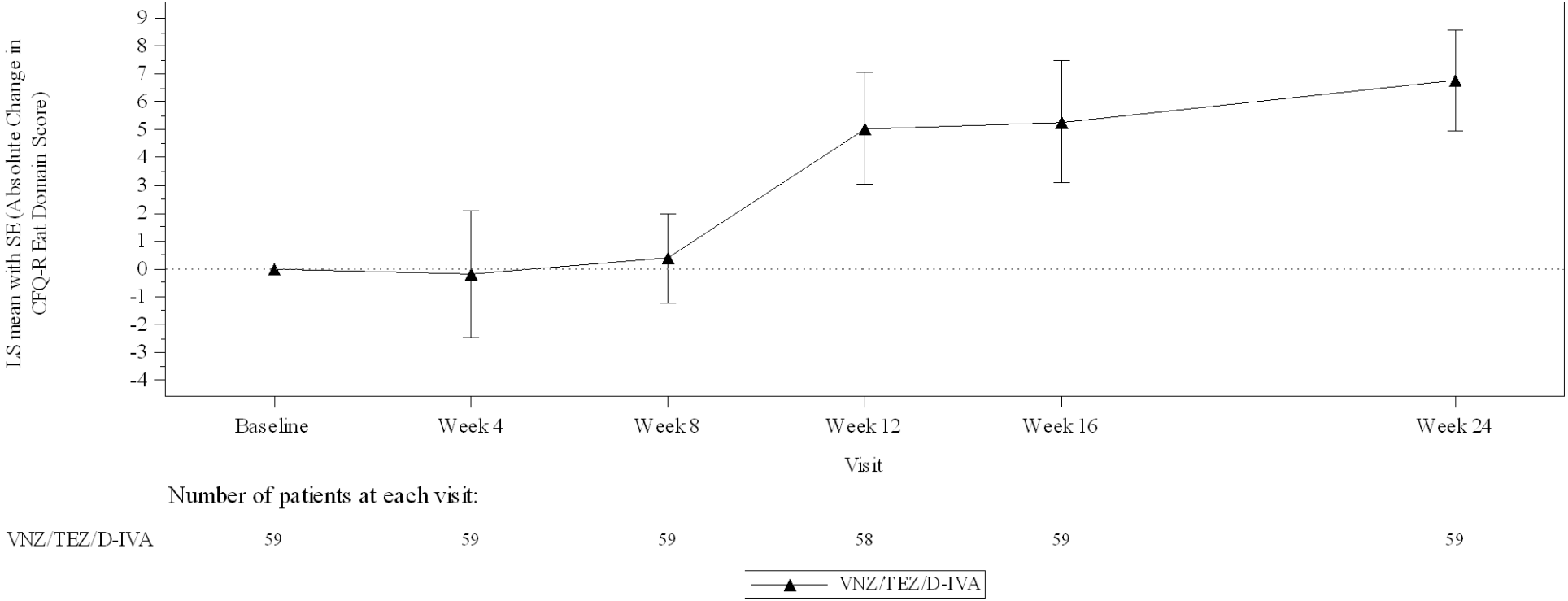
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat
Region = Rest of World



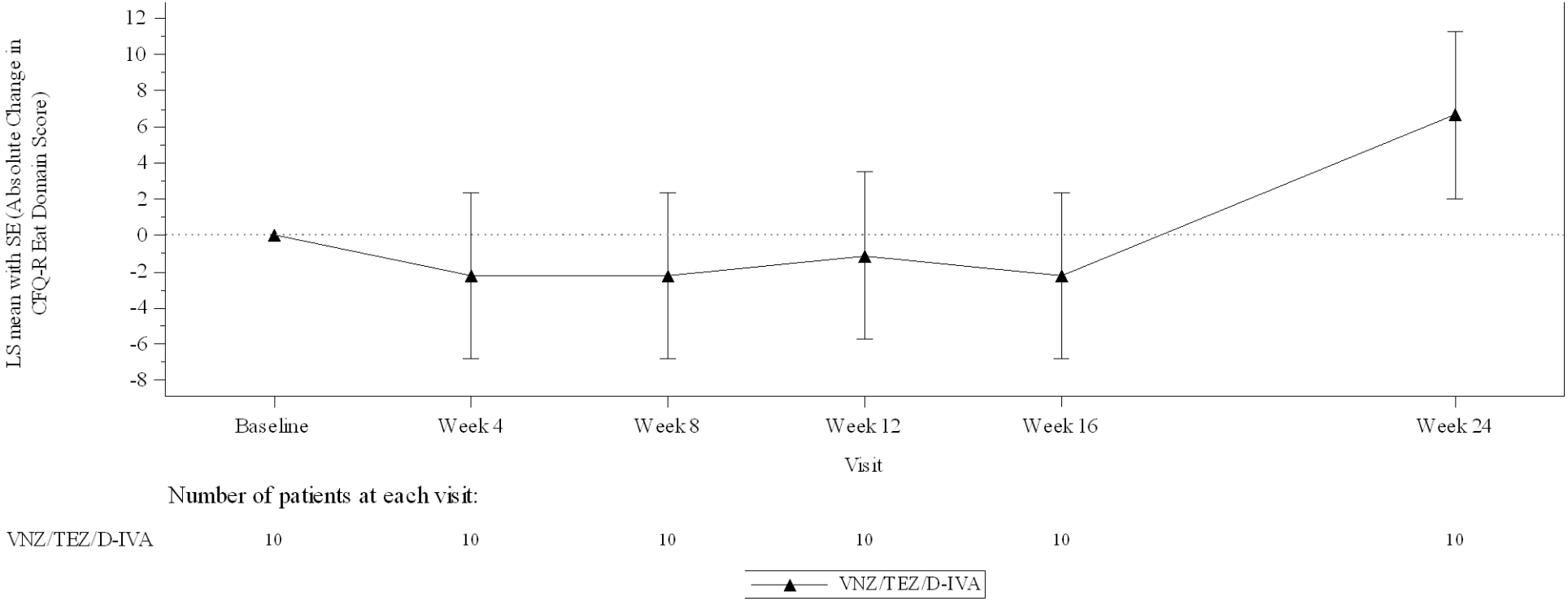
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat
$LCI_{2.5}$ at baseline <7.5



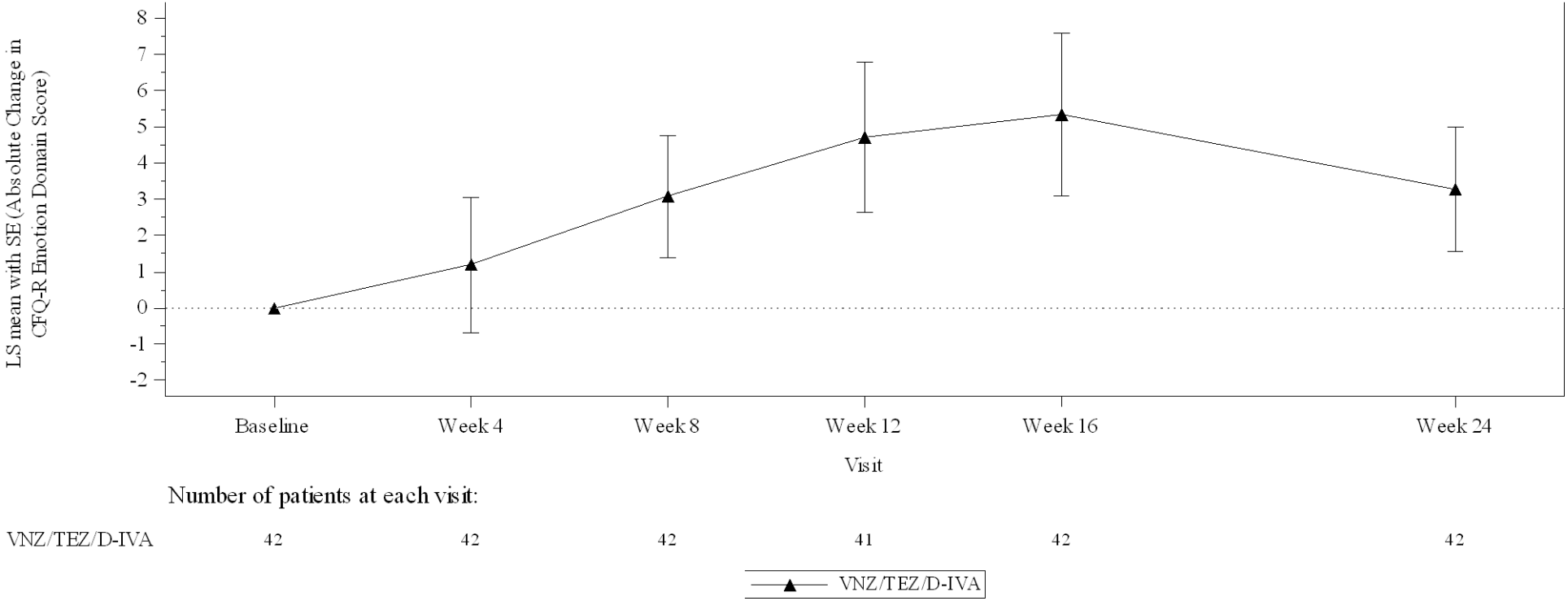
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat
$LCI_{2.5}$ at baseline ≥7.5



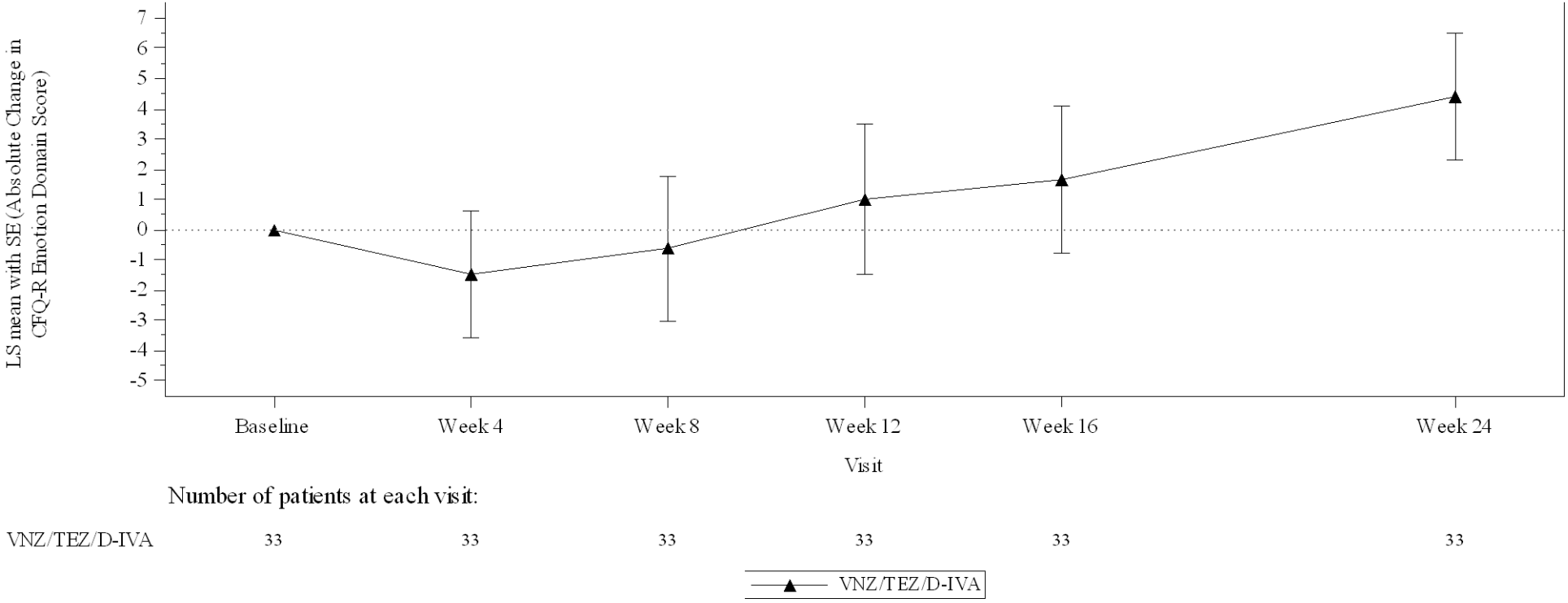
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion
Sex = Male



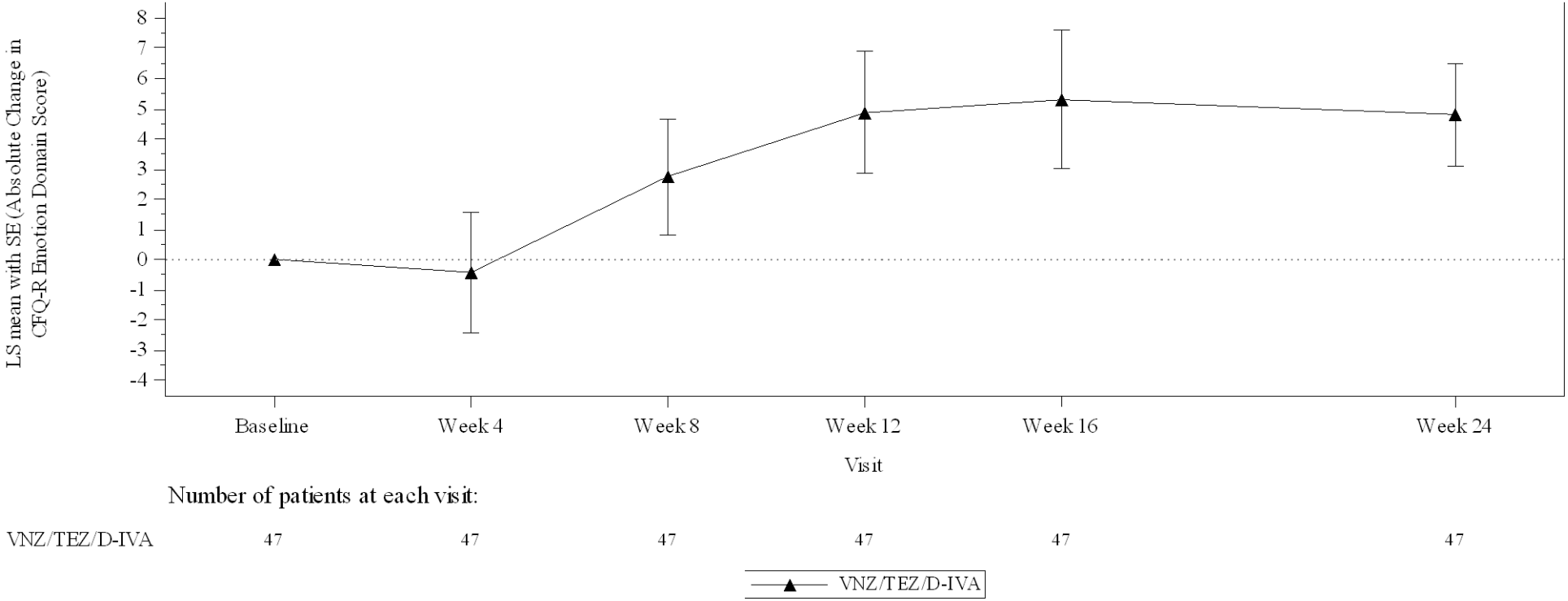
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion
Region = North America



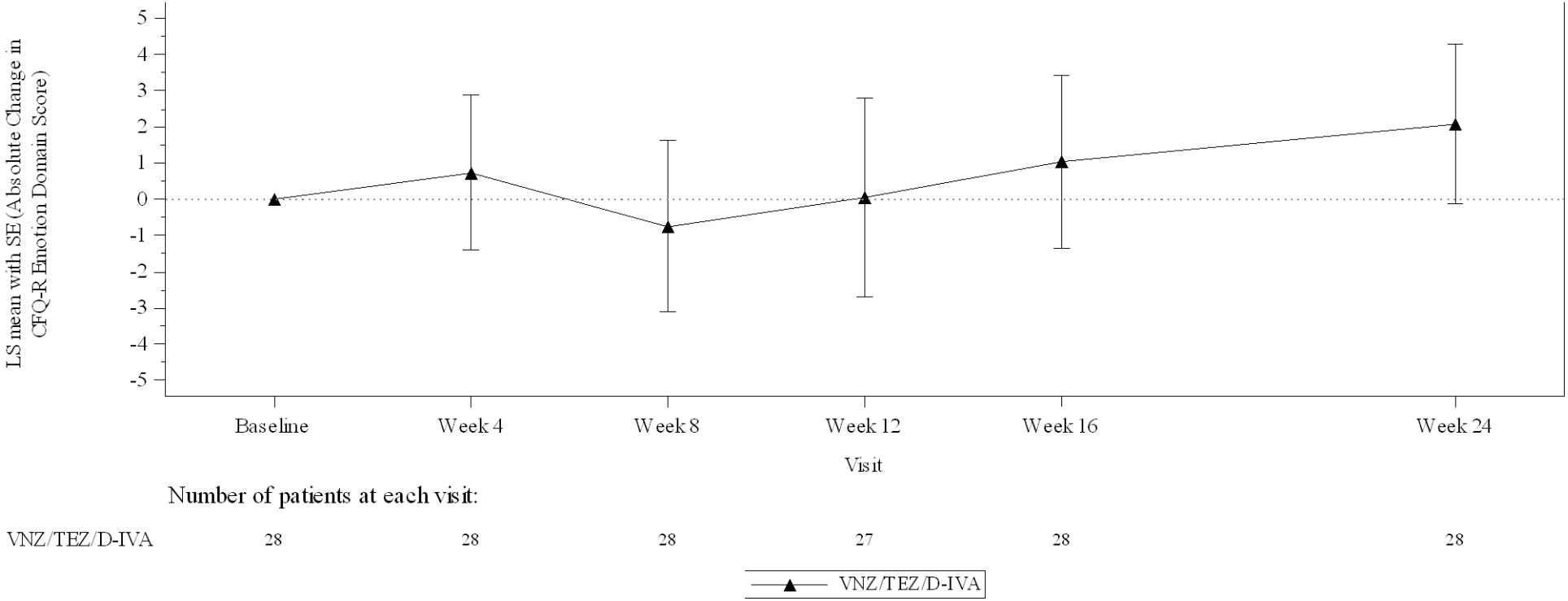
Number of patients at each visit:

VNZ/TEZ/D-IVA	47	47	47	47	47	47

VNZ/TEZ/D-IVA

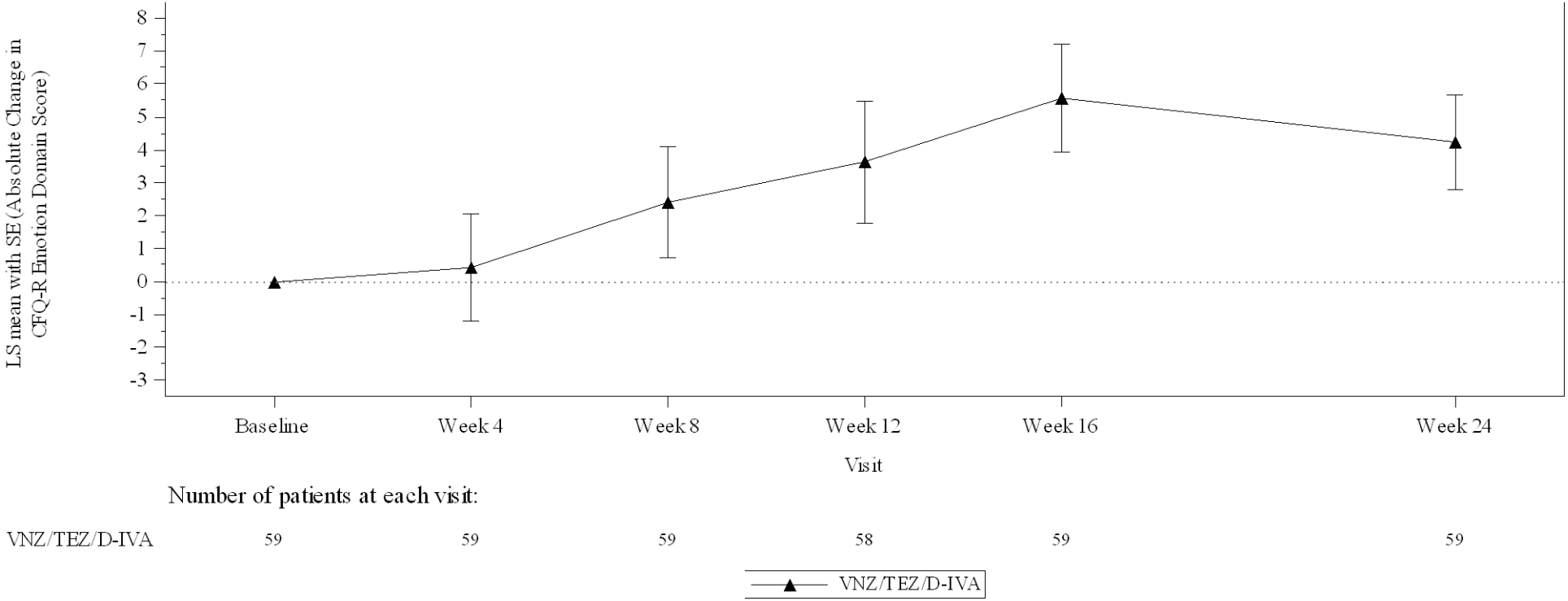
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion
Region = Rest of World



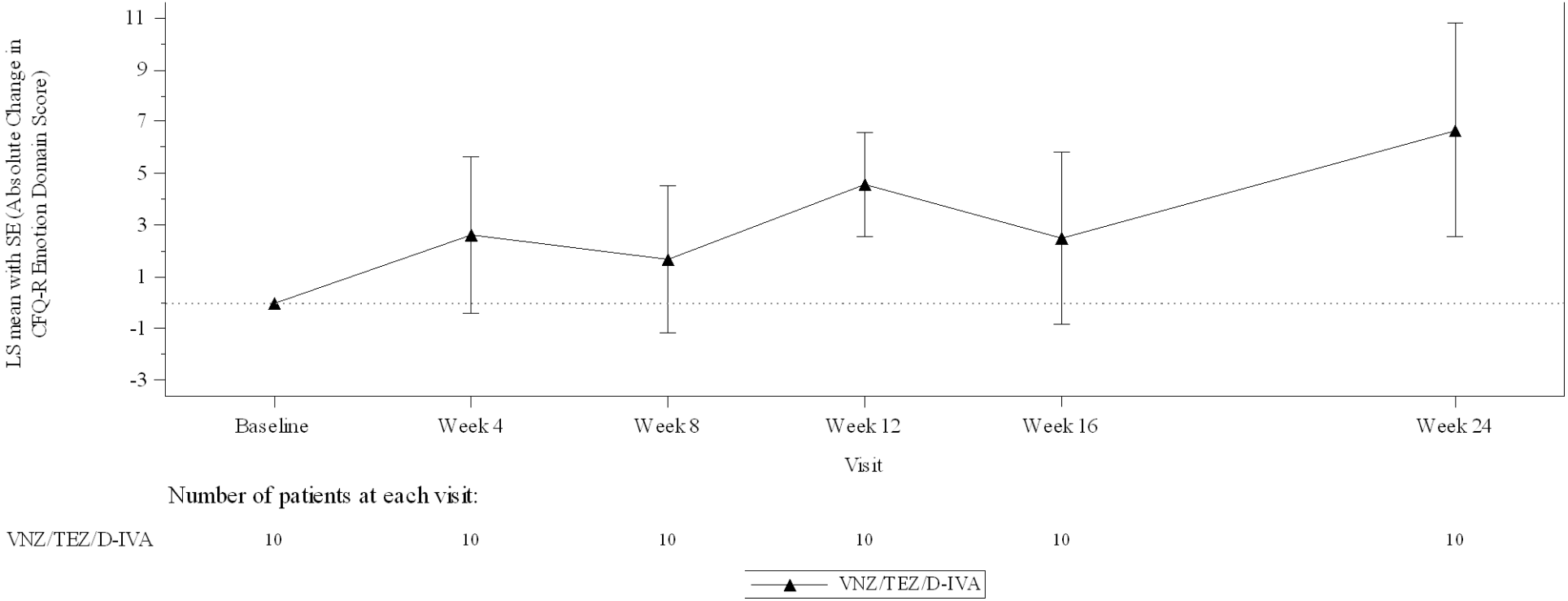
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion
$LCI_{2.5}$ at baseline <7.5



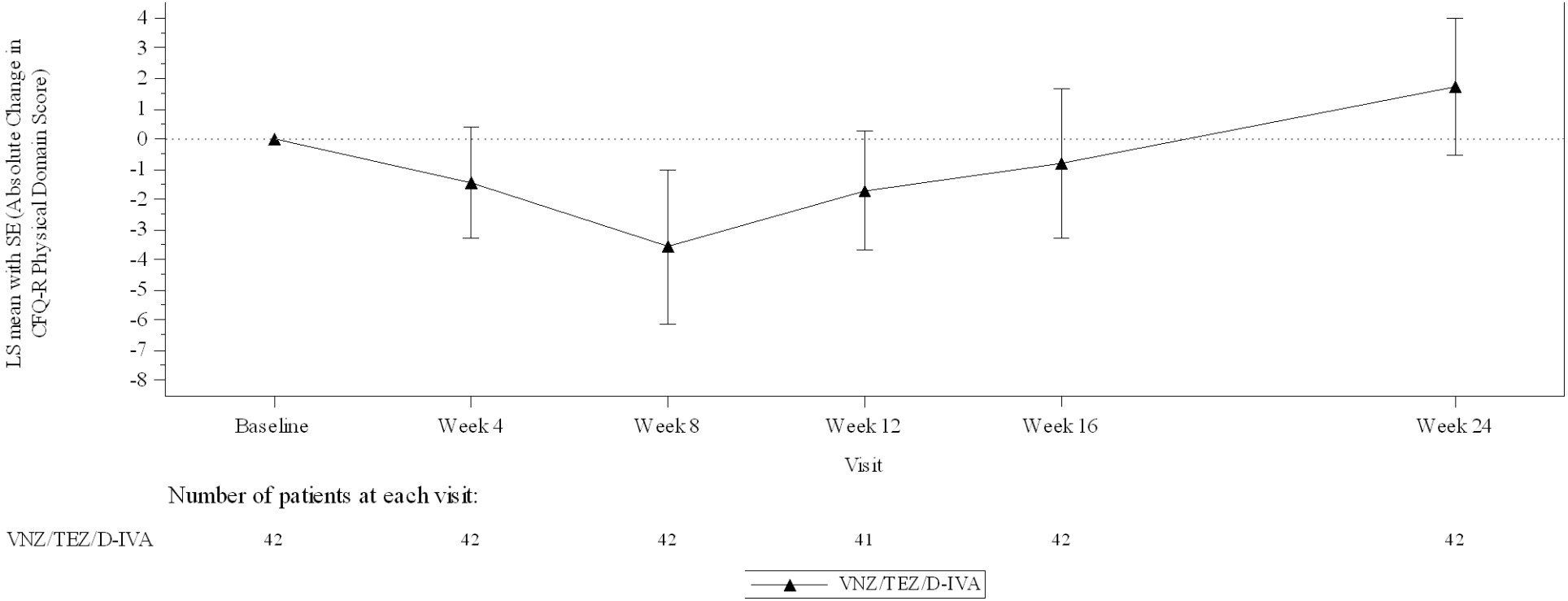
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion
$LCI_{2.5}$ at baseline ≥7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Emotion Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical
Sex = Male



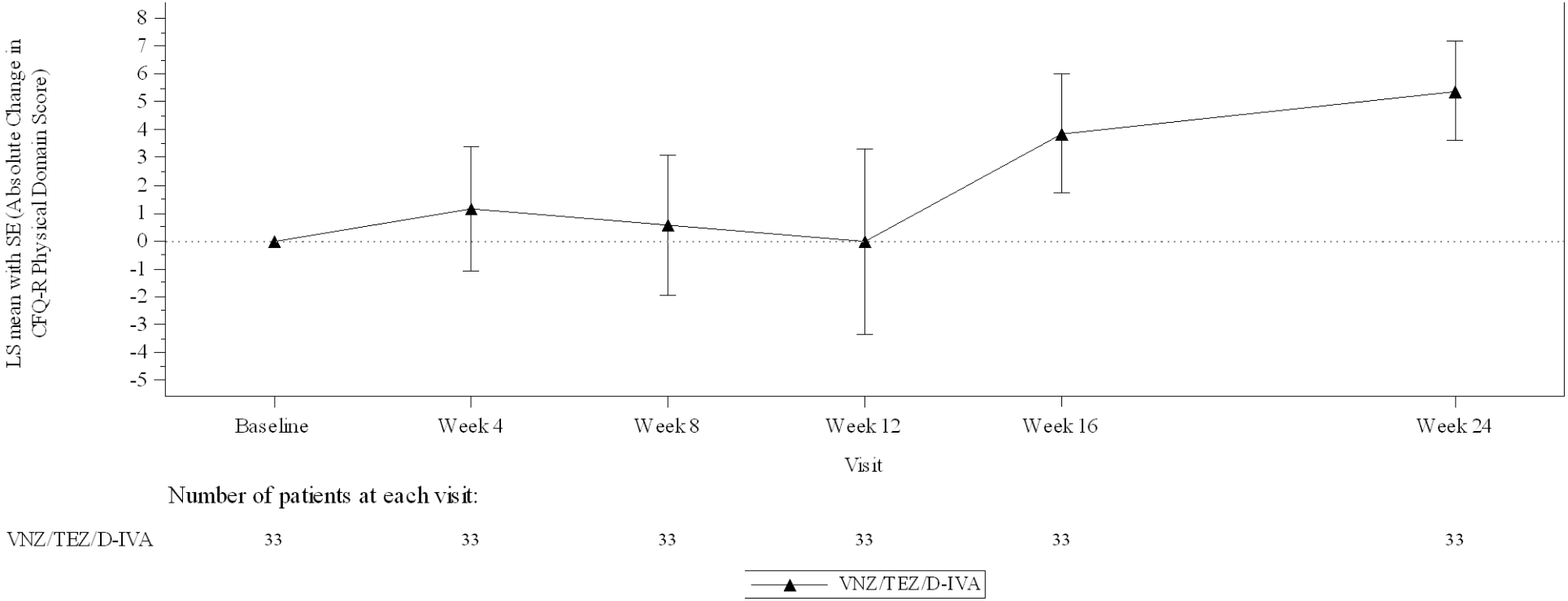
Number of patients at each visit:

VNZ/TEZ/D-IVA	42	42	42	41	42	42

VNZ/TEZ/D-IVA

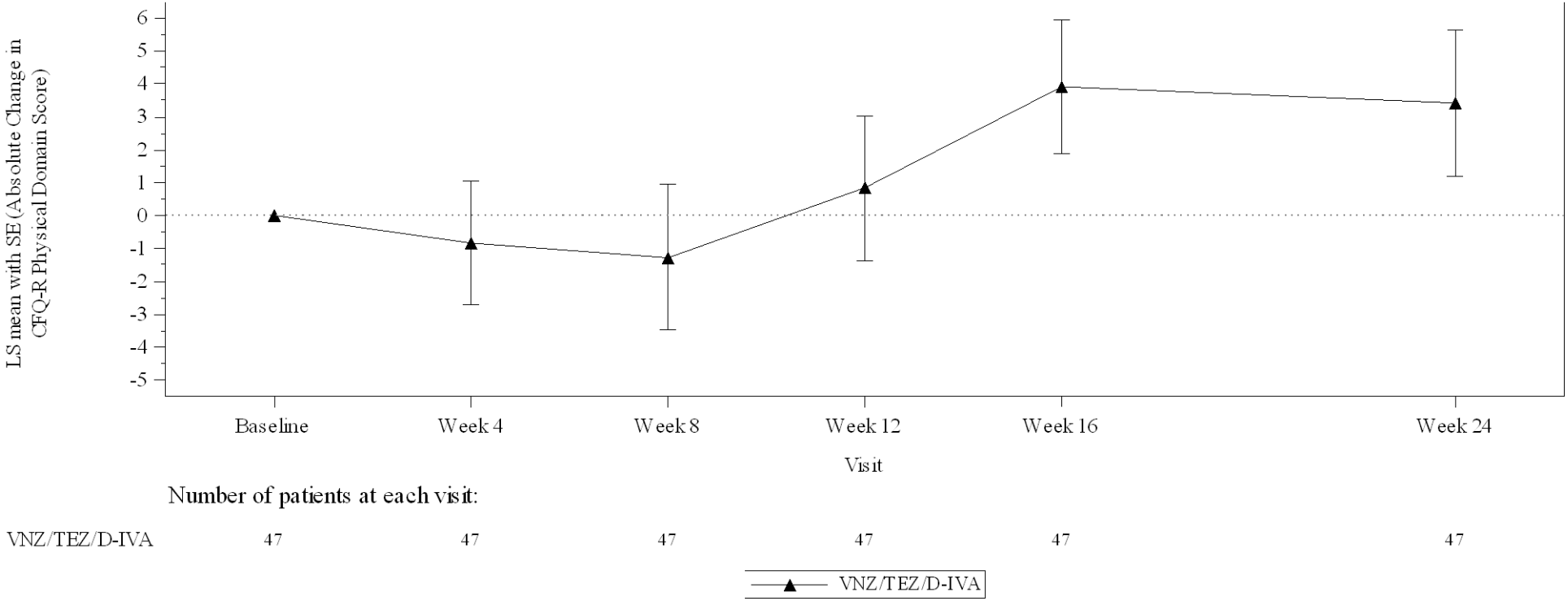
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical
Sex = Female



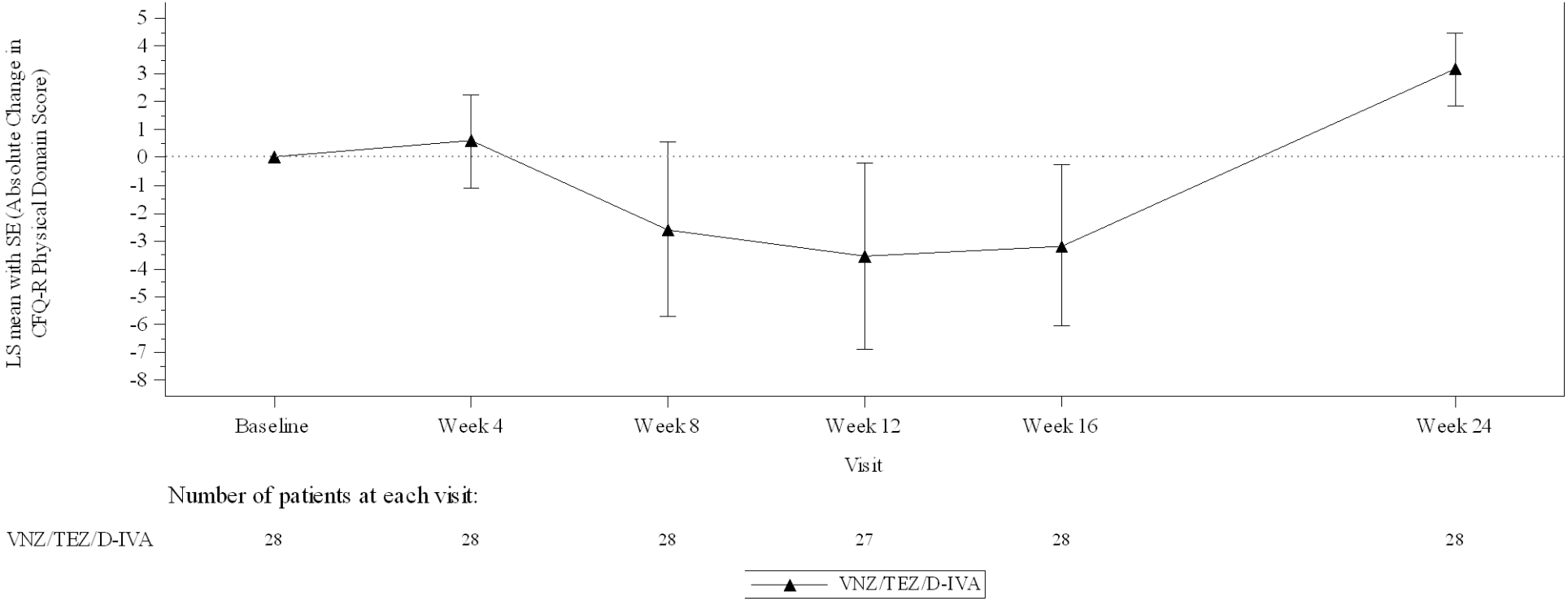
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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical
Region = North America



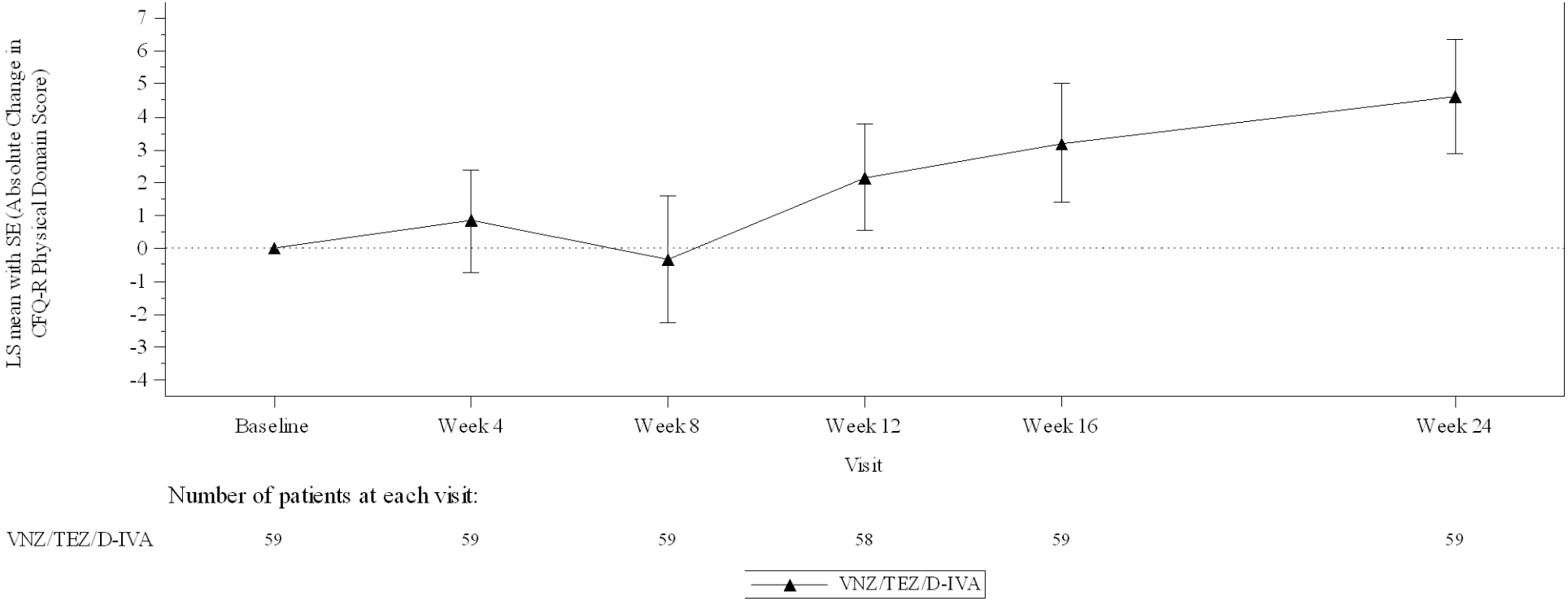
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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical
Region = Rest of World



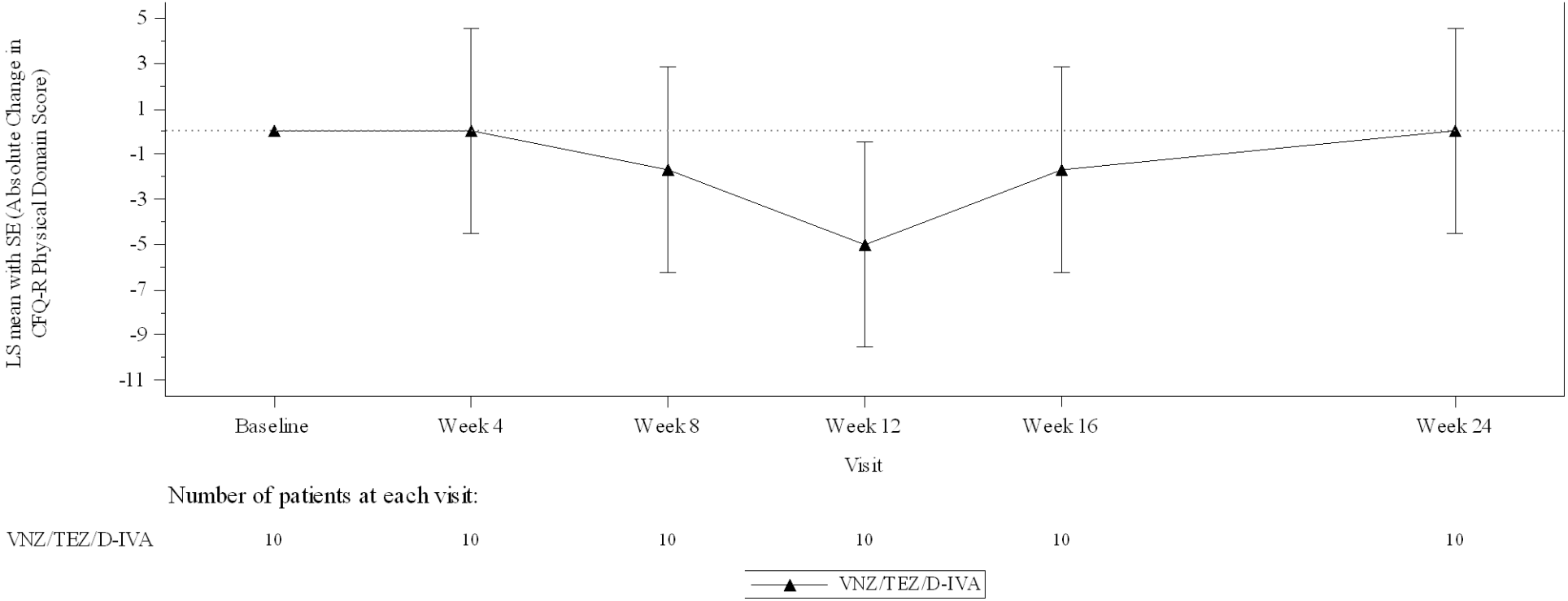
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical
$LCI_{2.5}$ at baseline <7.5



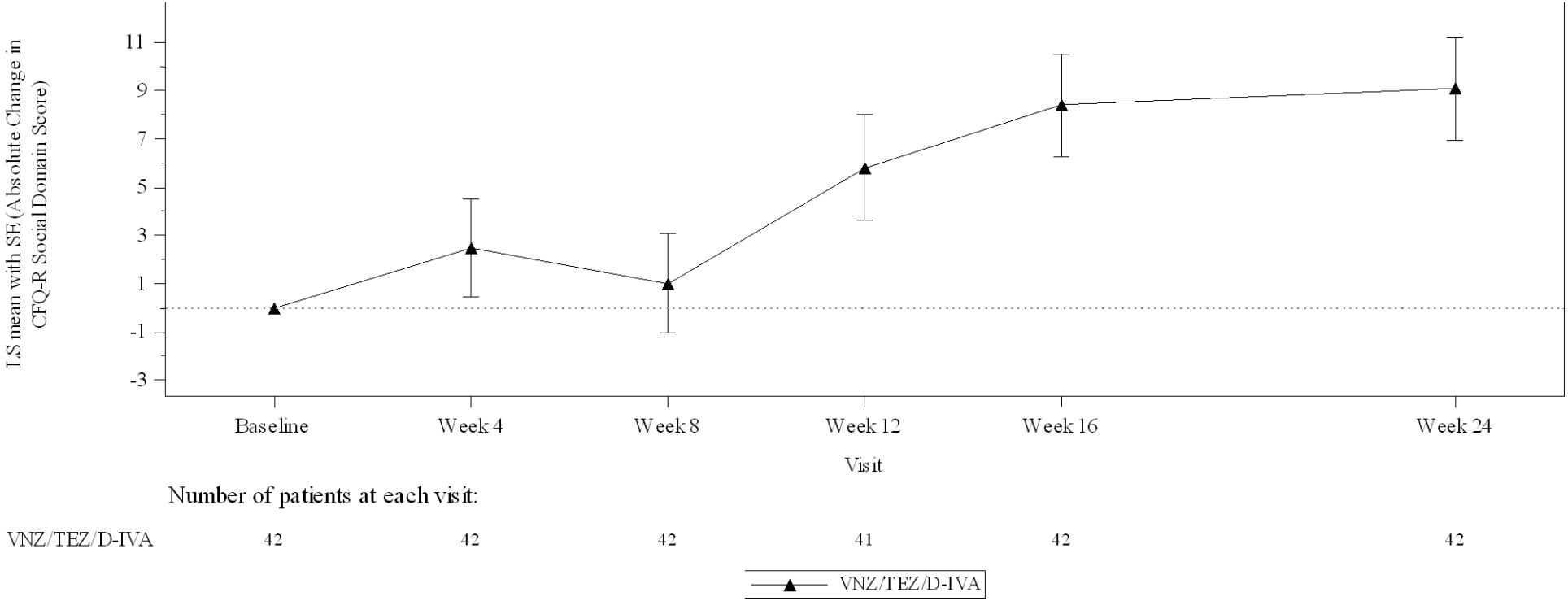
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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical
$LCI_{2.5}$ at baseline ≥7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Social
Sex = Male



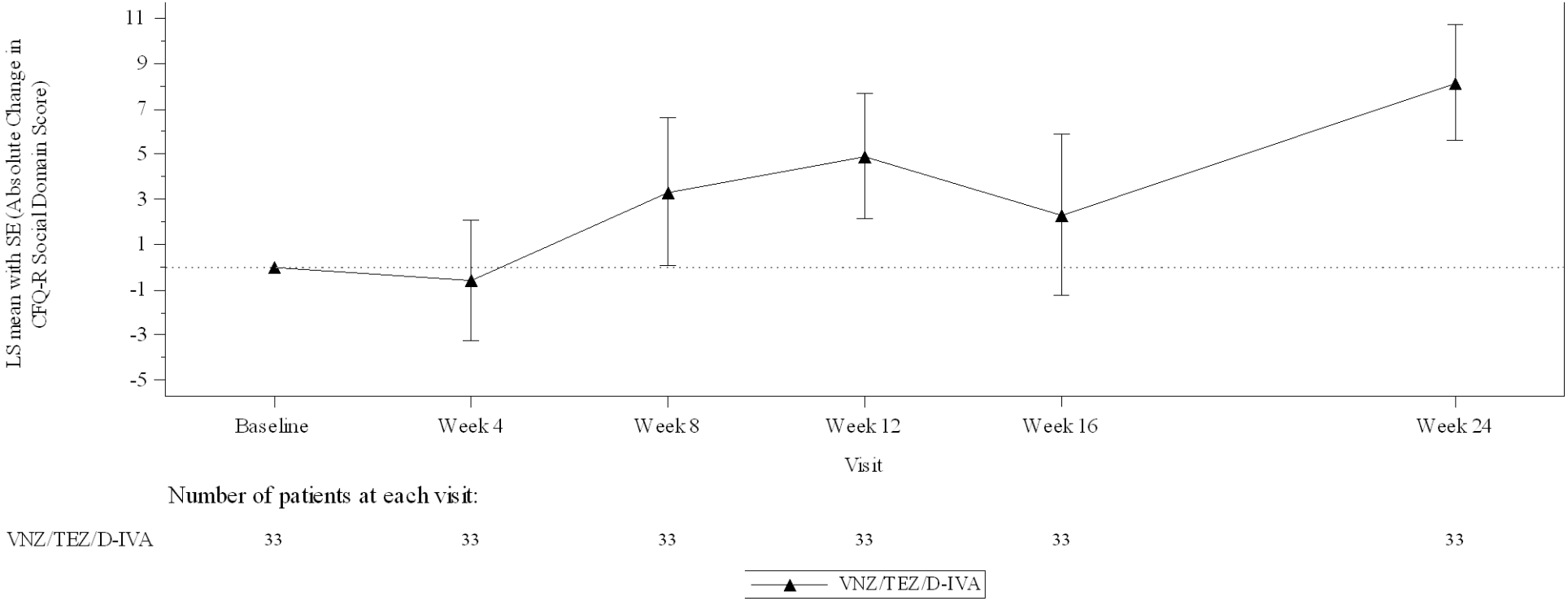
Number of patients at each visit:

	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	42	42	42	41	42	42

VNZ/TEZ/D-IVA

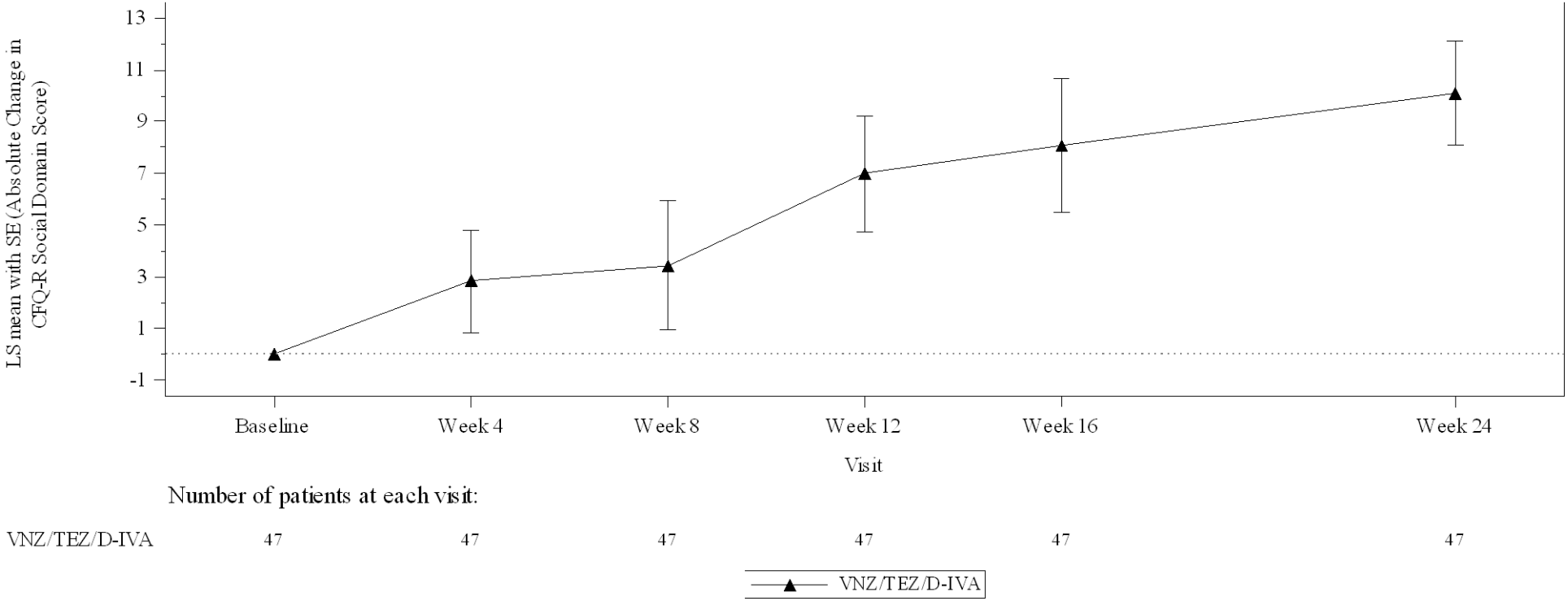
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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Social
Sex = Female



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Social
Region = North America



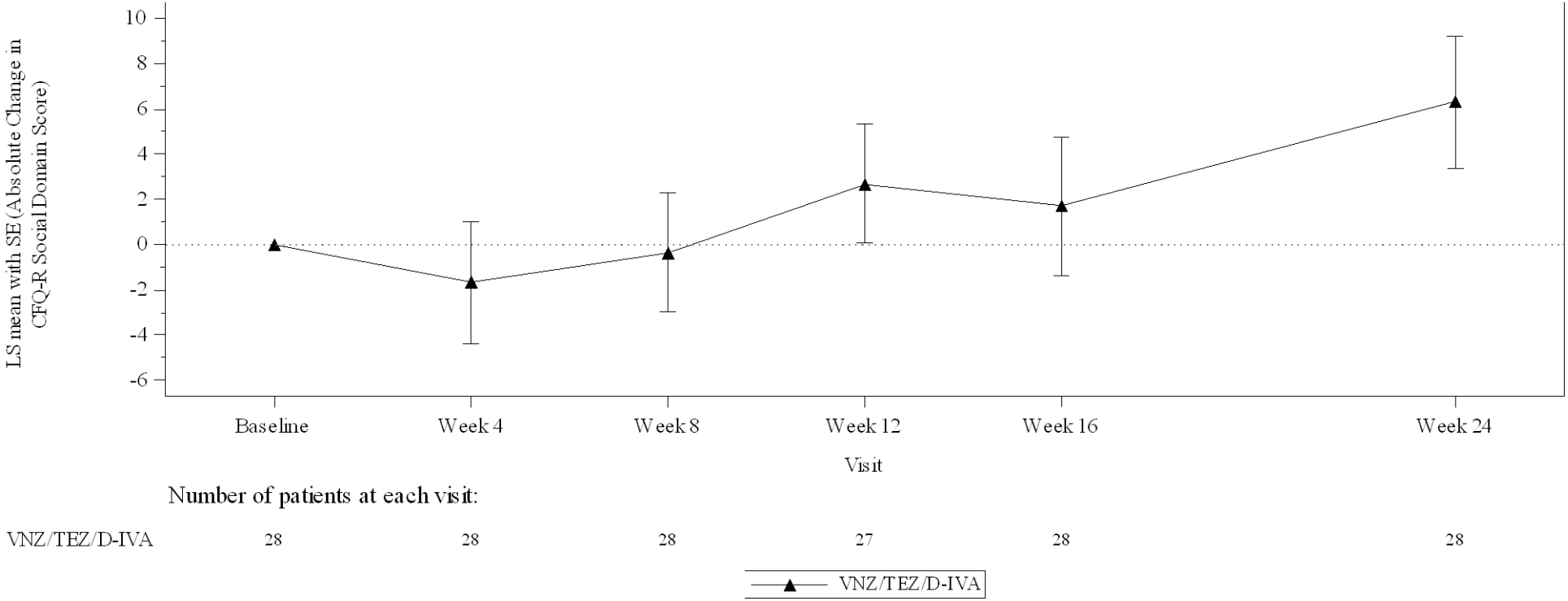
Number of patients at each visit:

	Baseline	Week 4	Week 8	Week 12	Week 16	Week 24
VNZ/TEZ/D-IVA	47	47	47	47	47	47

VNZ/TEZ/D-IVA

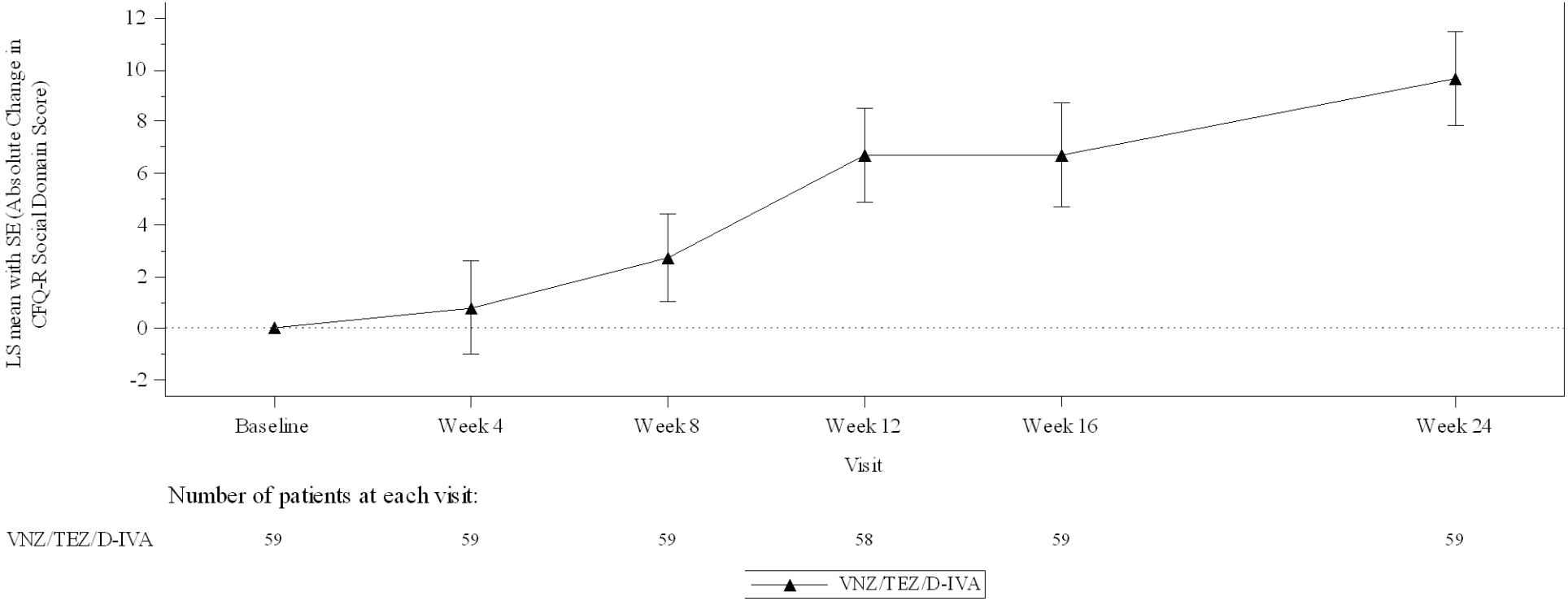
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Social
Region = Rest of World



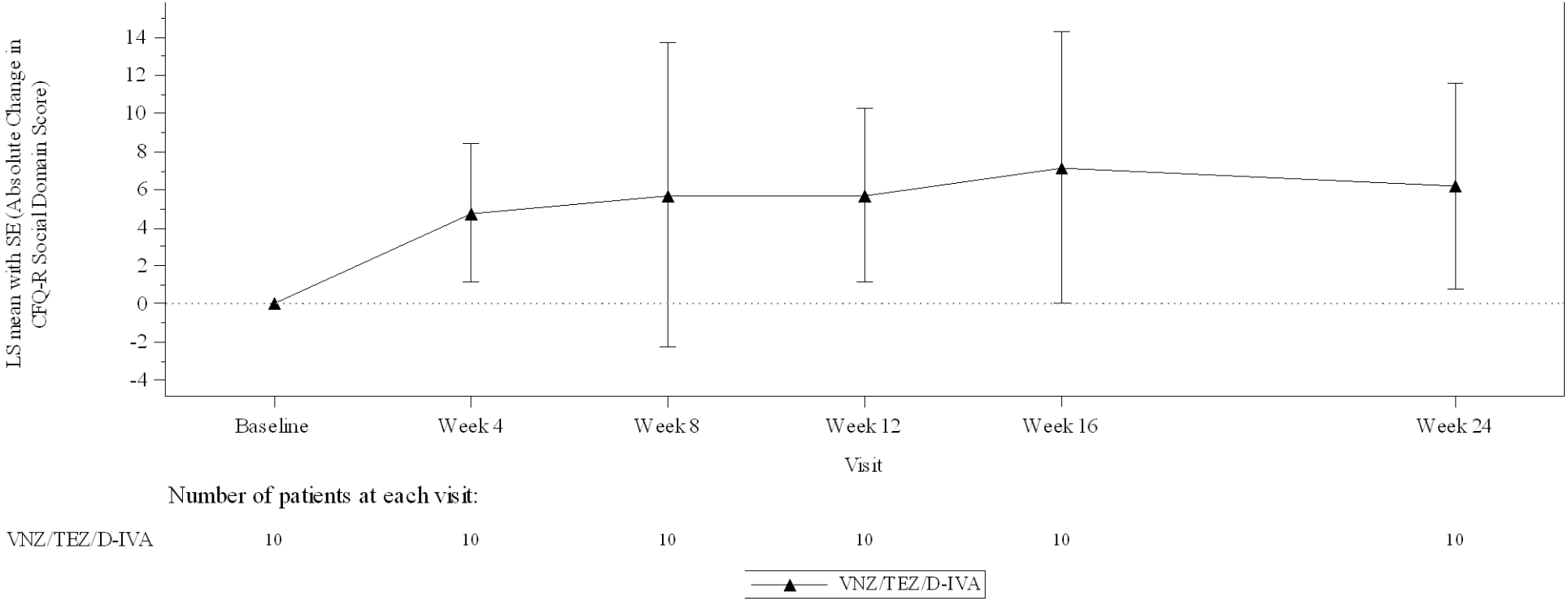
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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Social
$LCI_{2.5}$ at baseline <7.5



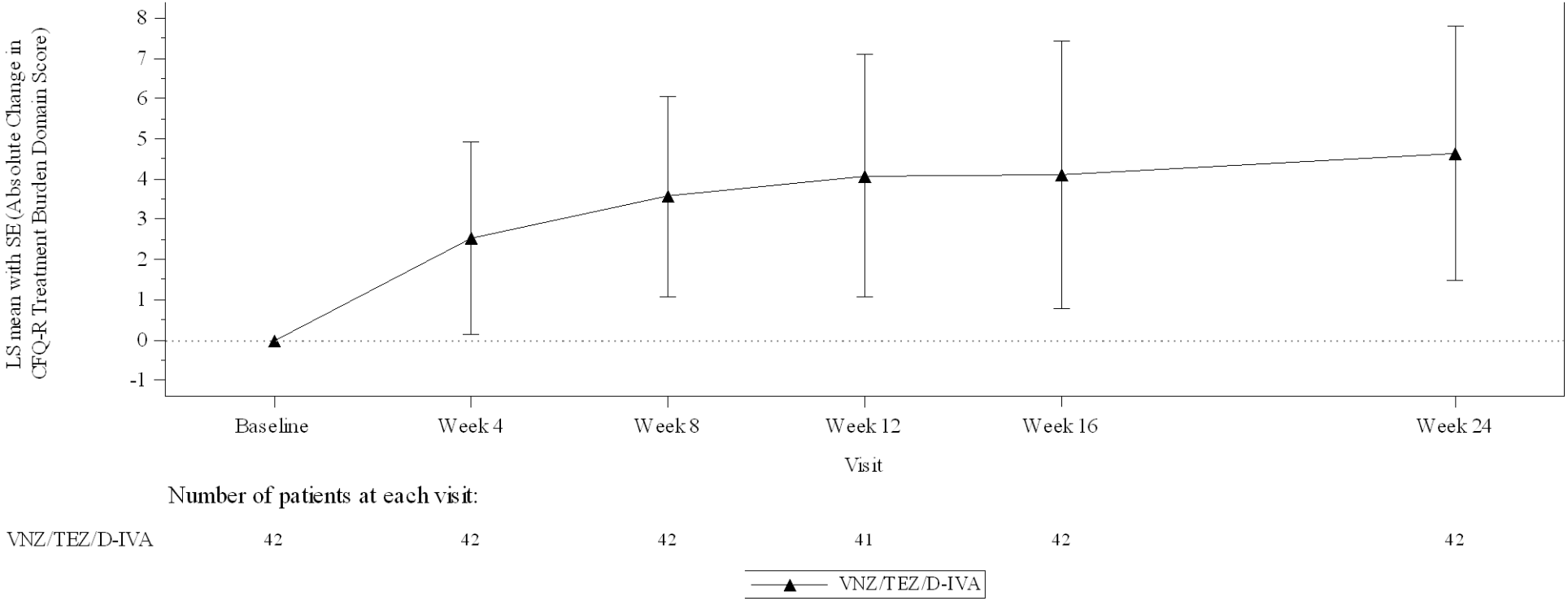
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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Social
$LCI_{2.5}$ at baseline ≥7.5



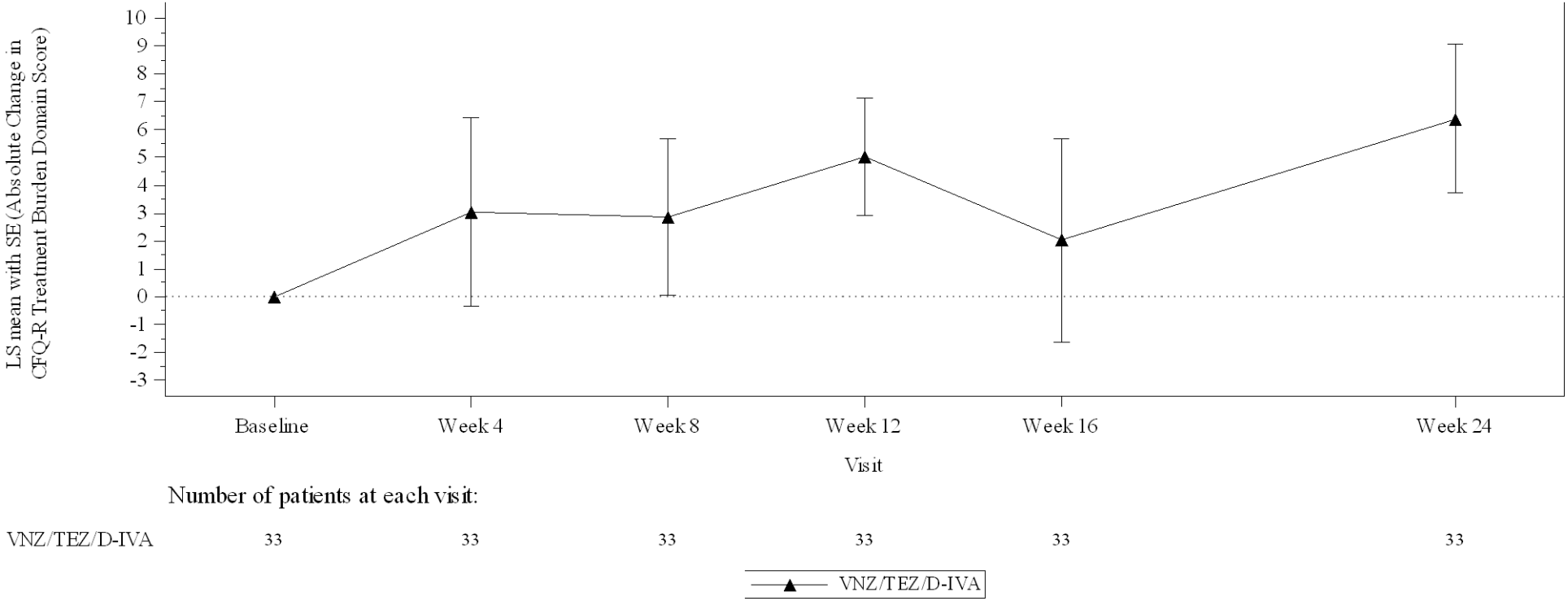
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Social Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden
Sex = Male



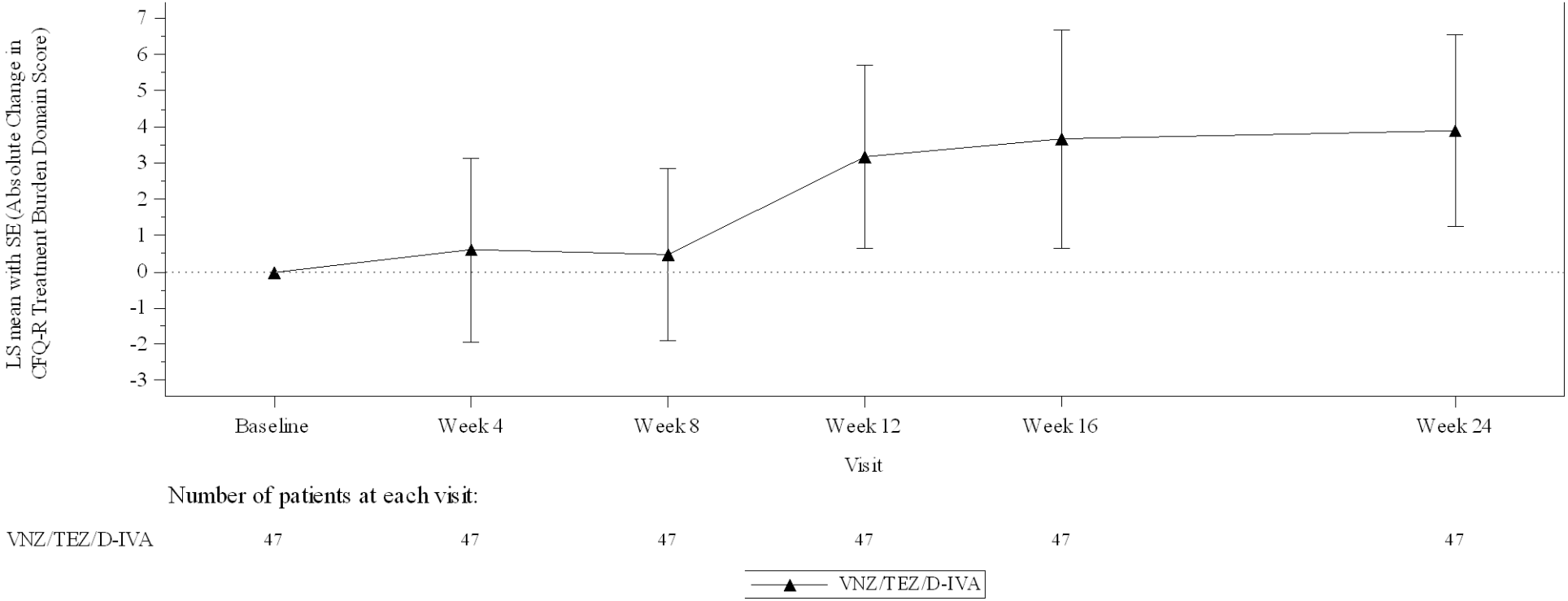
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden
Sex = Female



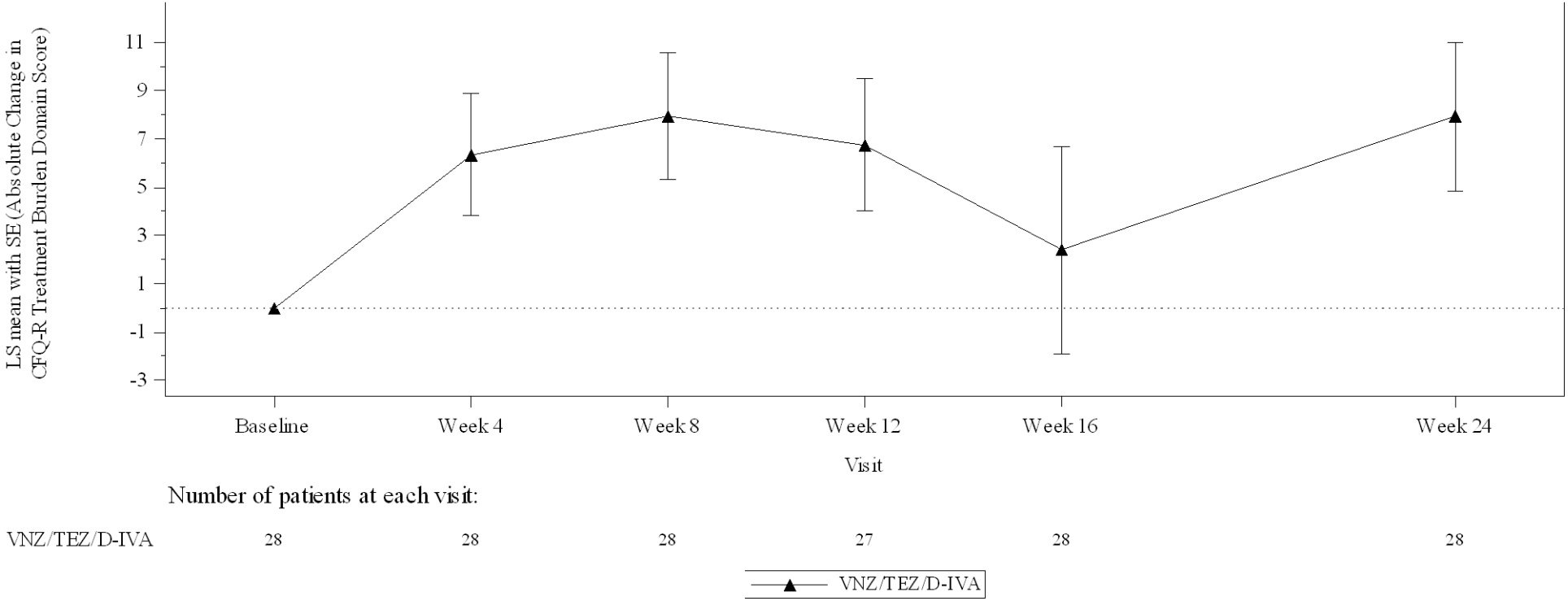
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden
Region = North America



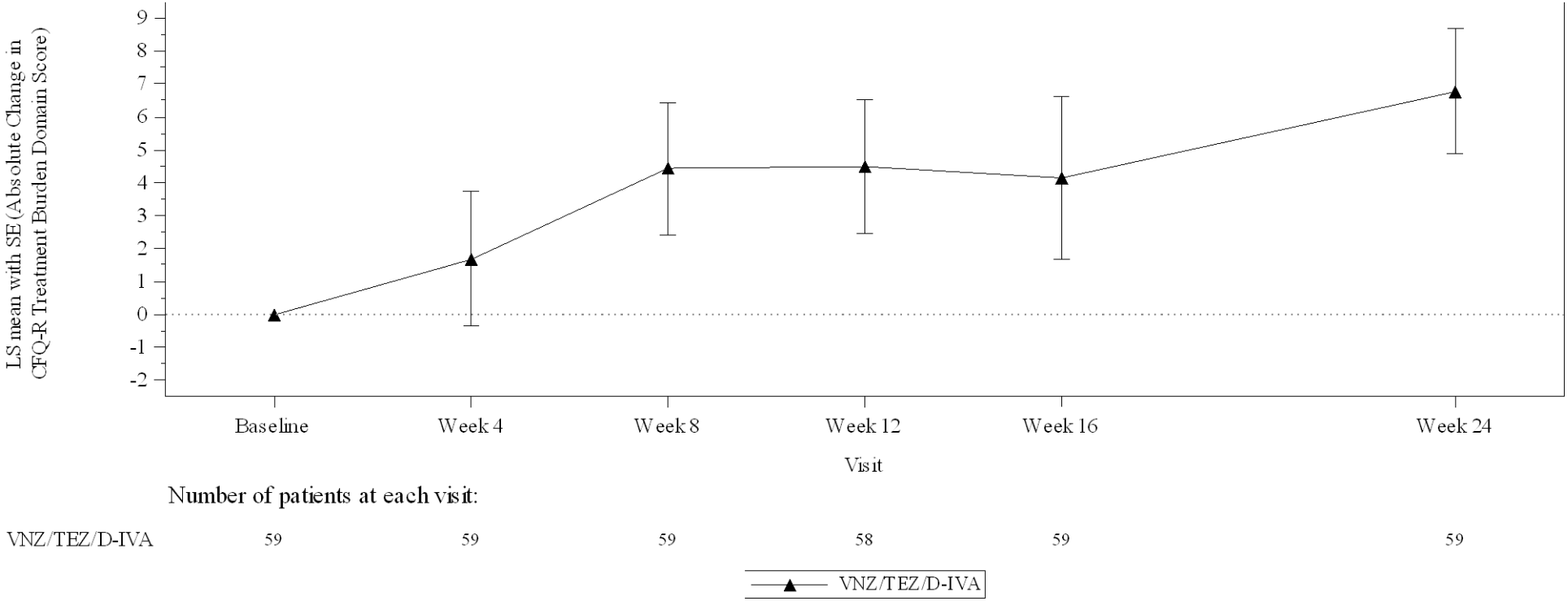
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden
Region = Rest of World



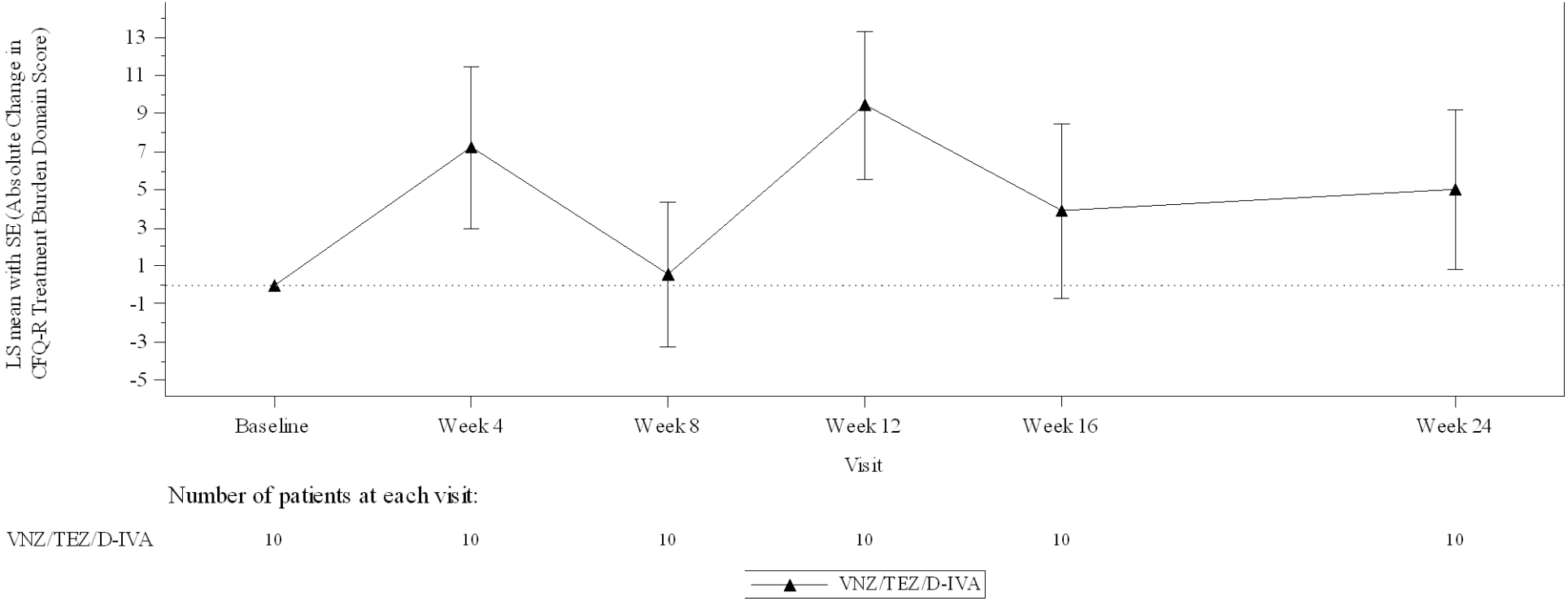
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden
$LCI_{2.5}$ at baseline <7.5



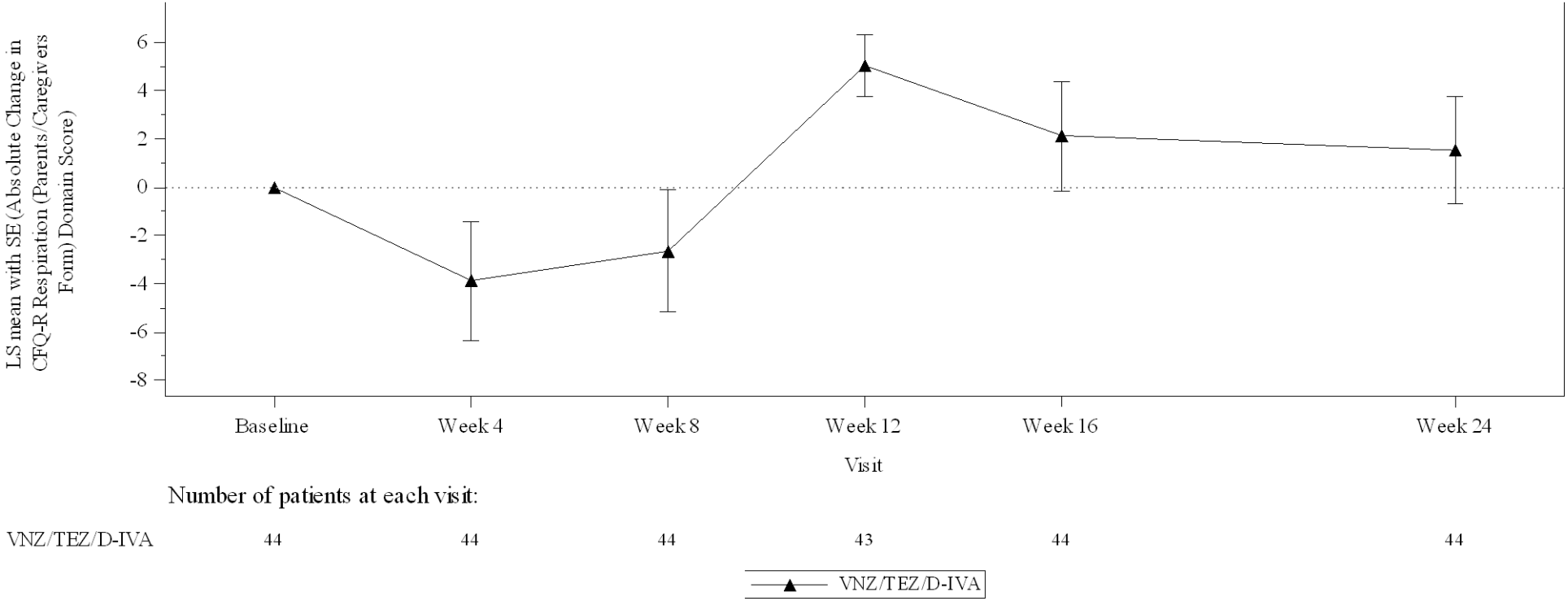
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- Baseline is defined as the pre-dose Day 1 value.
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Figure 3.2.2.10.5
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Child's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden
$LCI_{2.5}$ at baseline ≥7.5



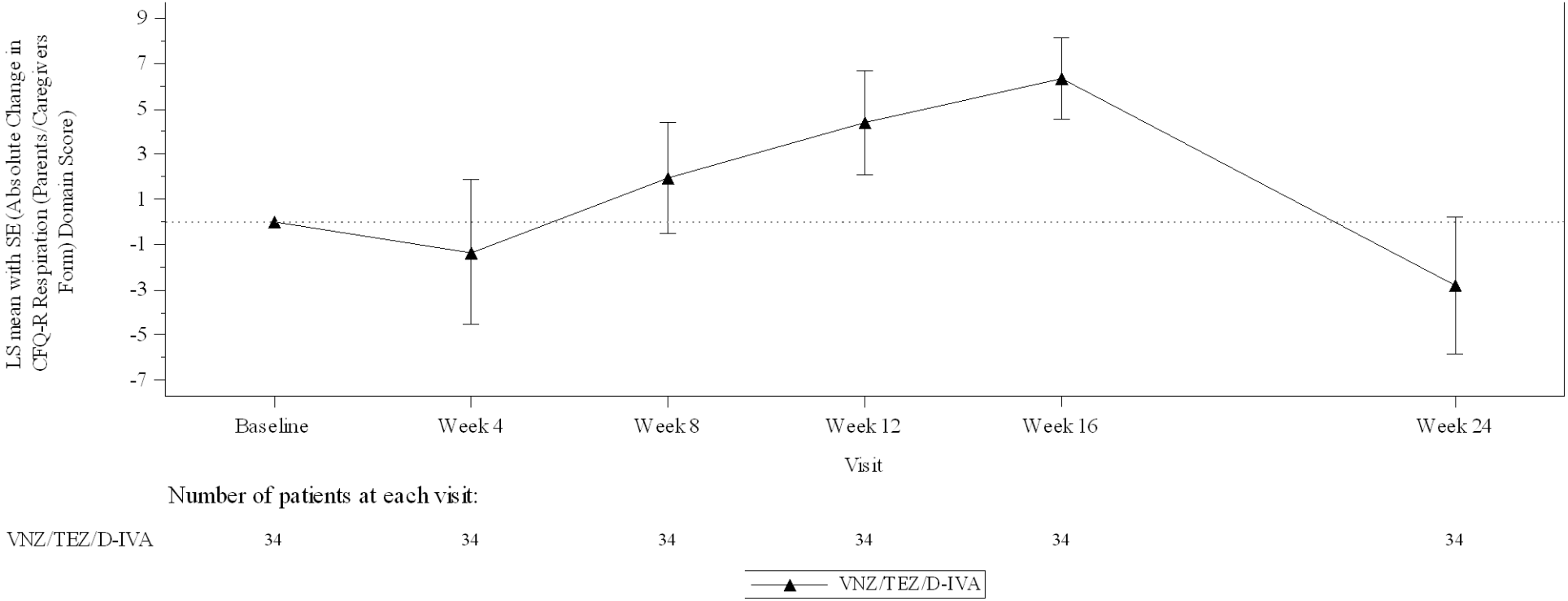
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Sex = Male



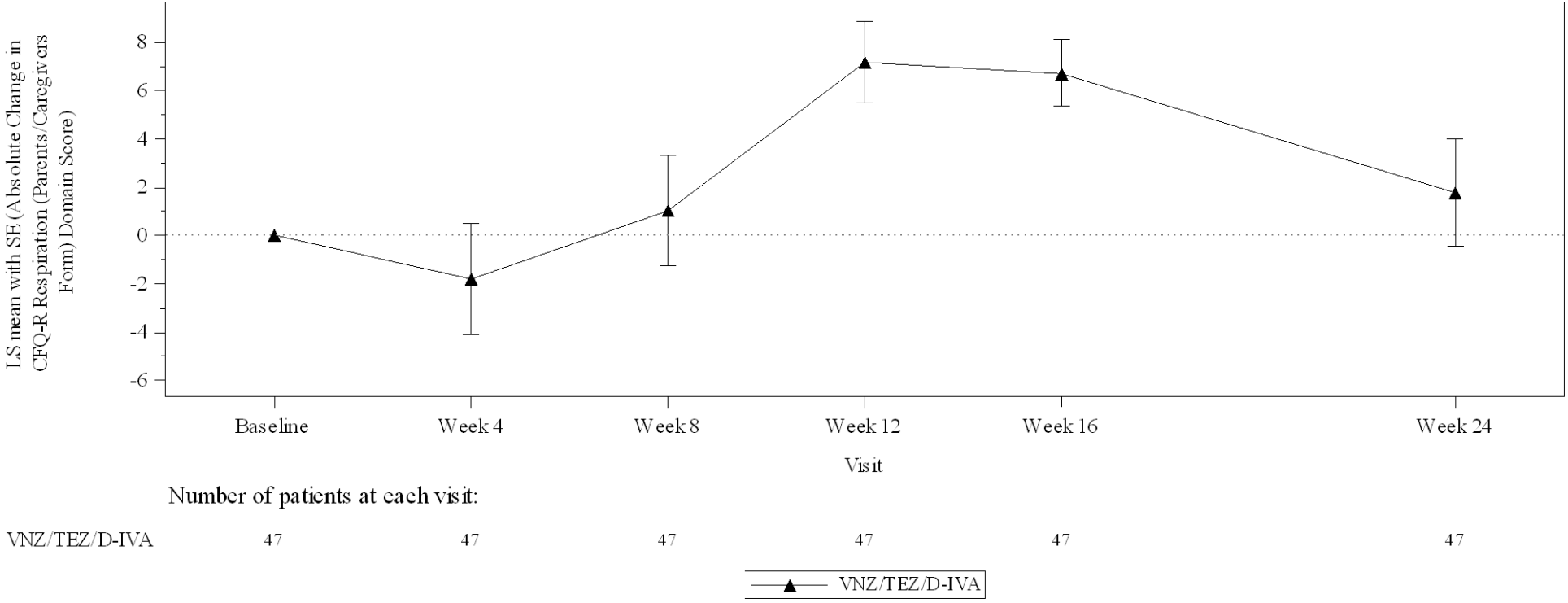
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Sex = Female



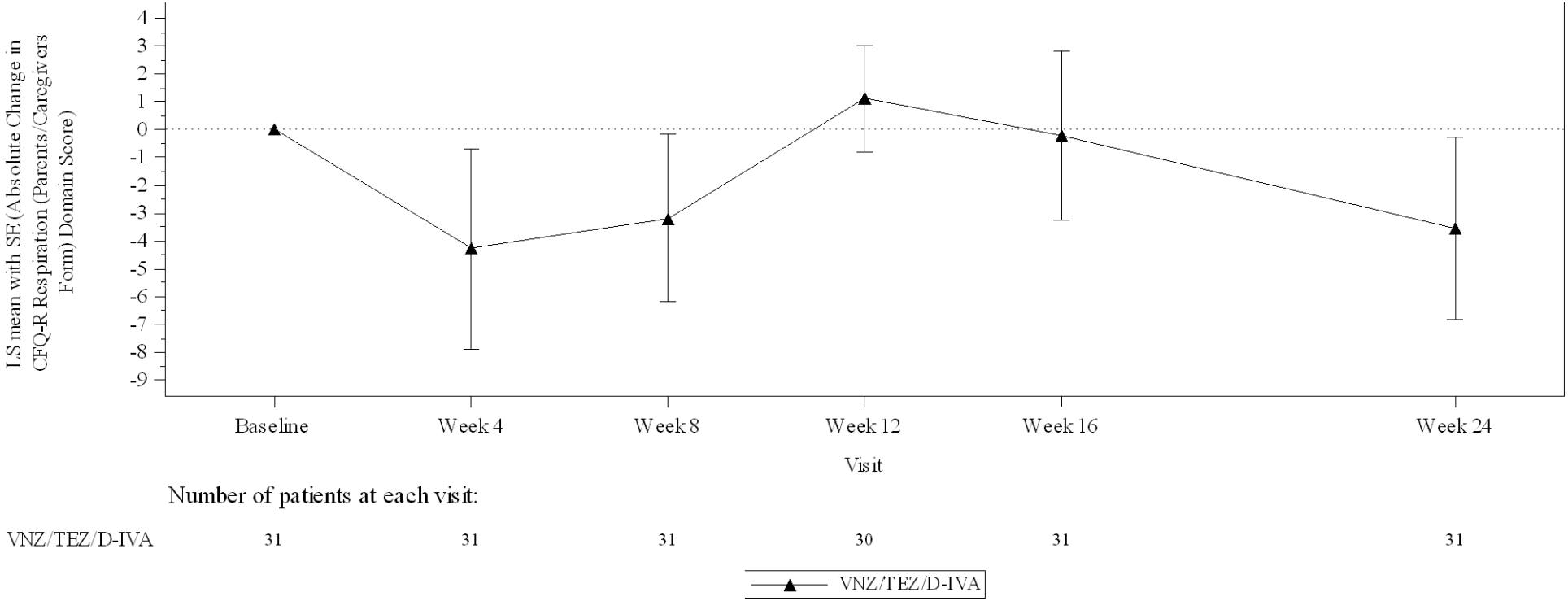
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Region = North America



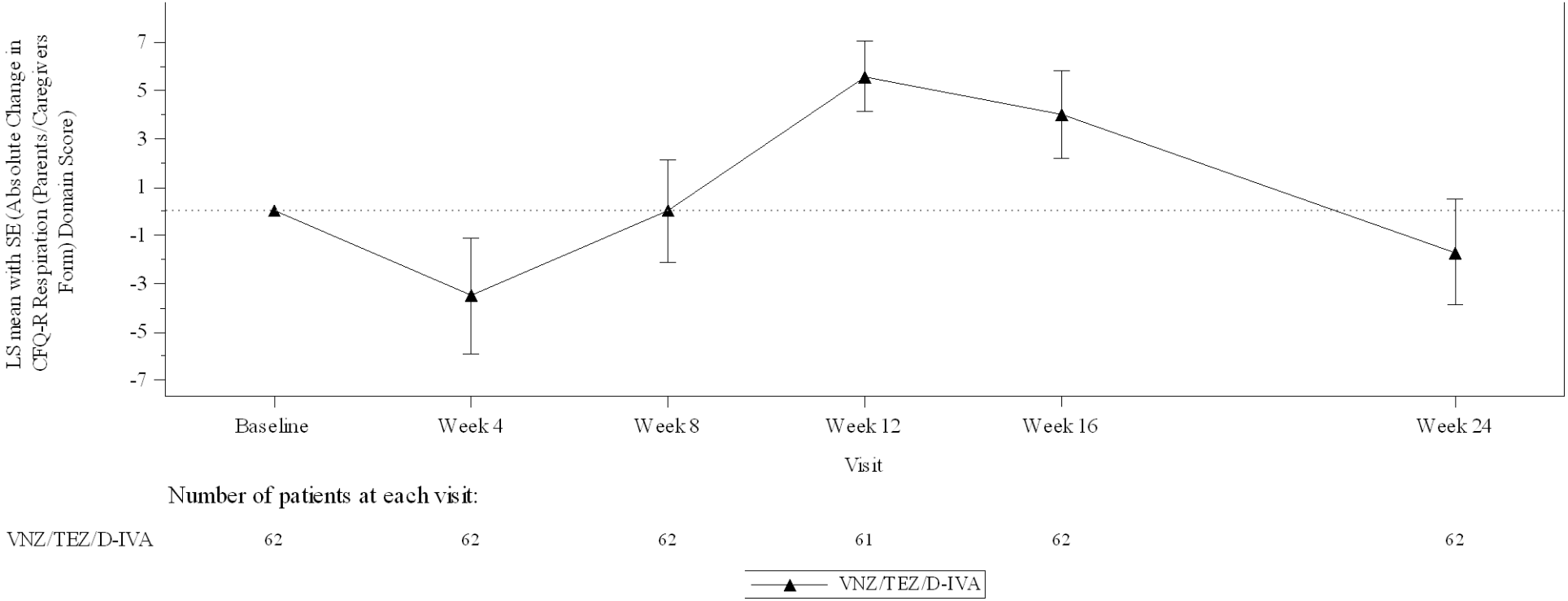
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
Region = Rest of World



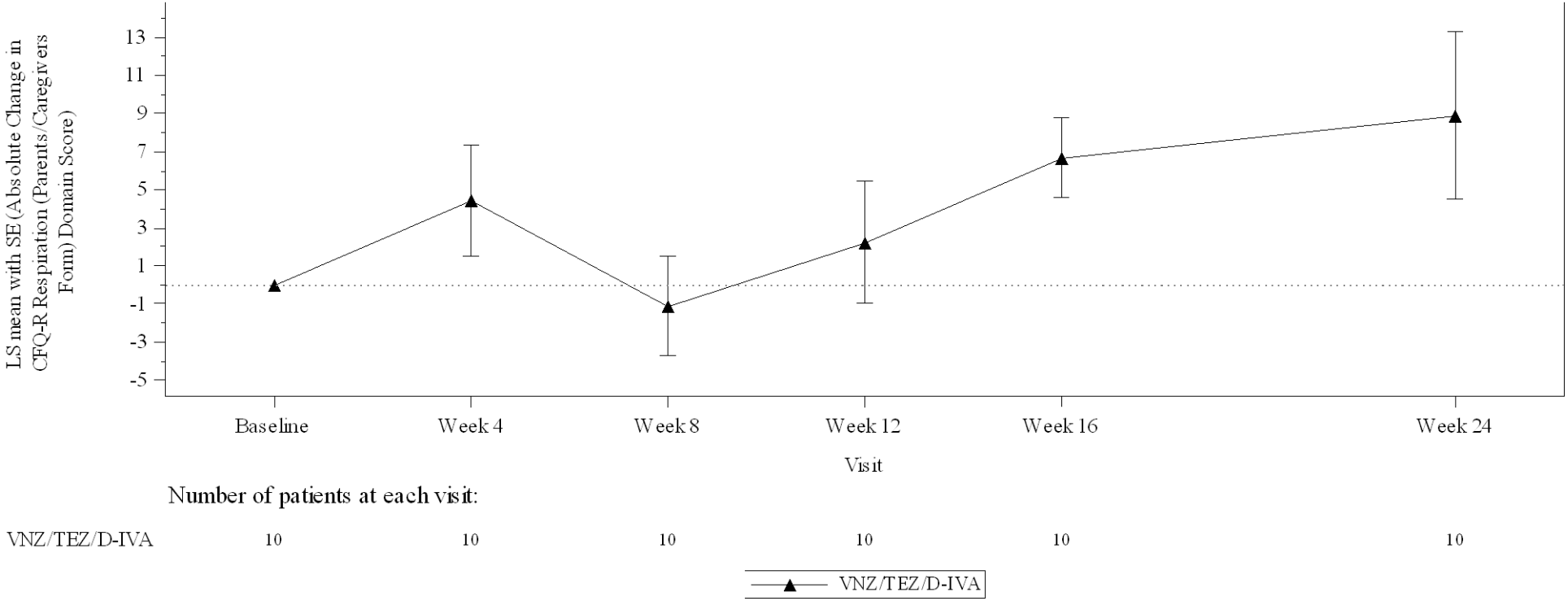
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



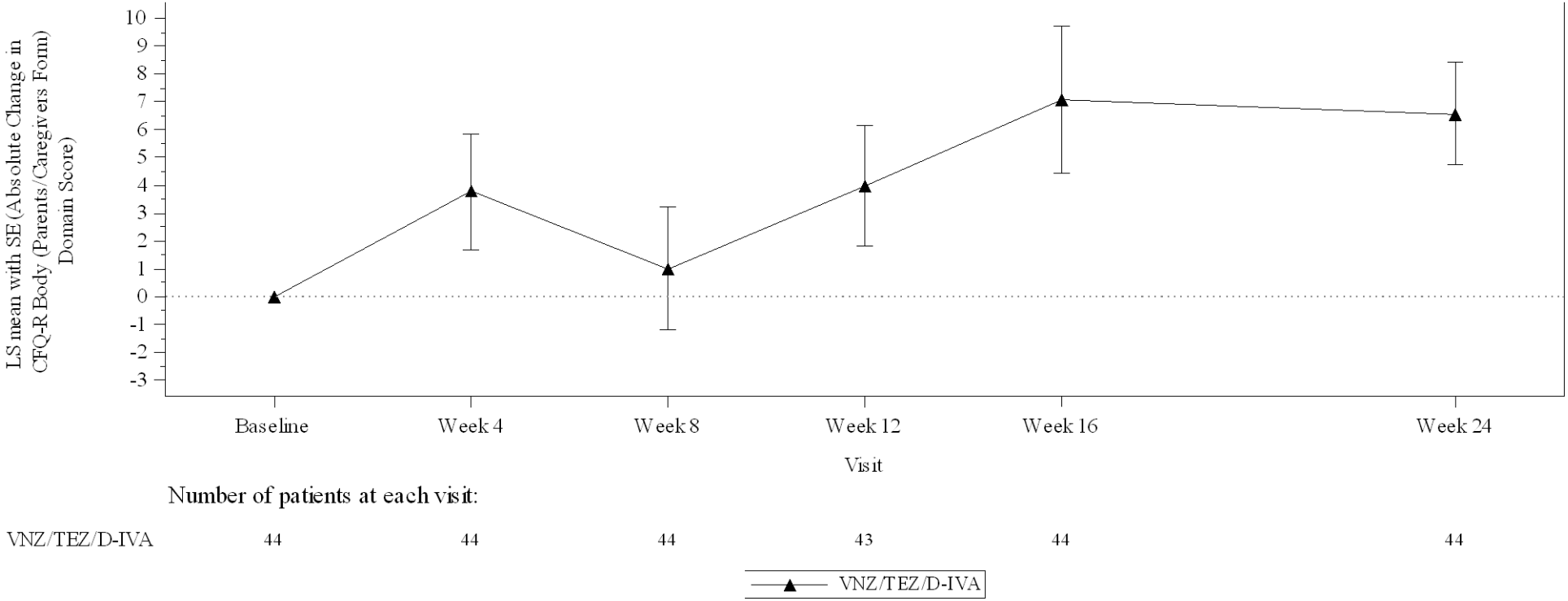
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Respiration (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



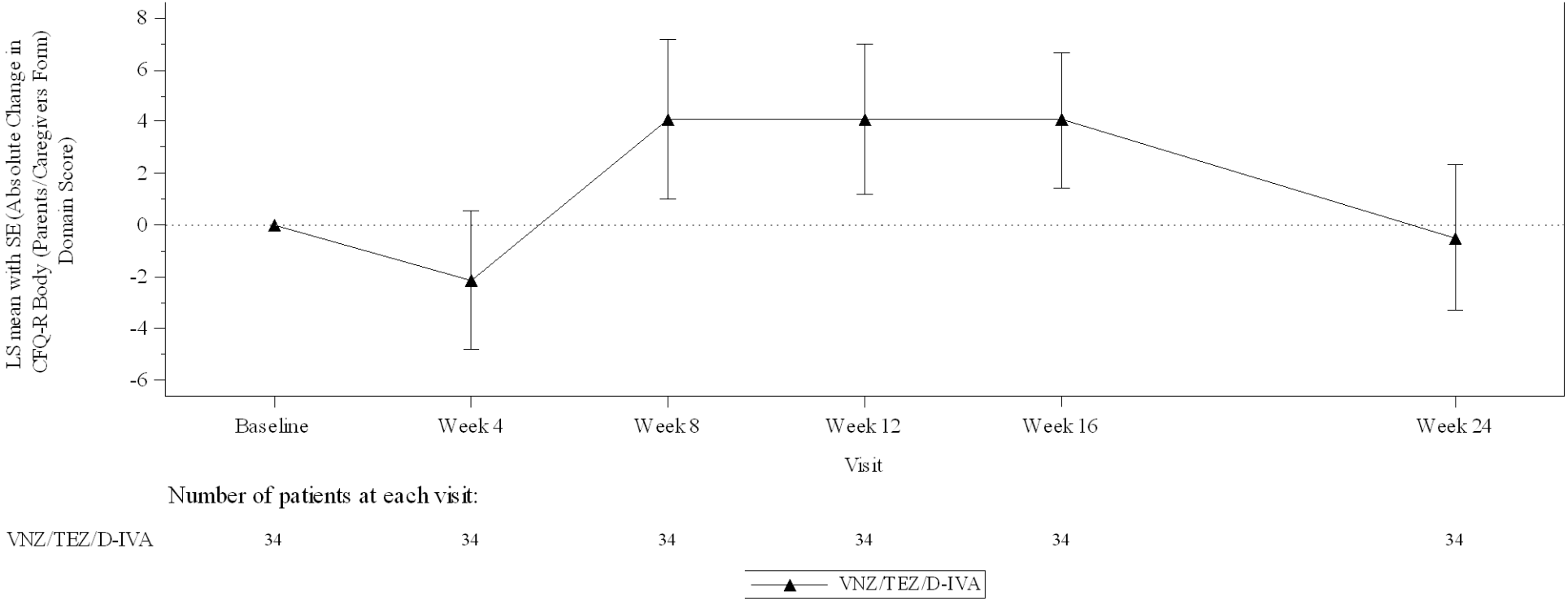
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Sex = Male



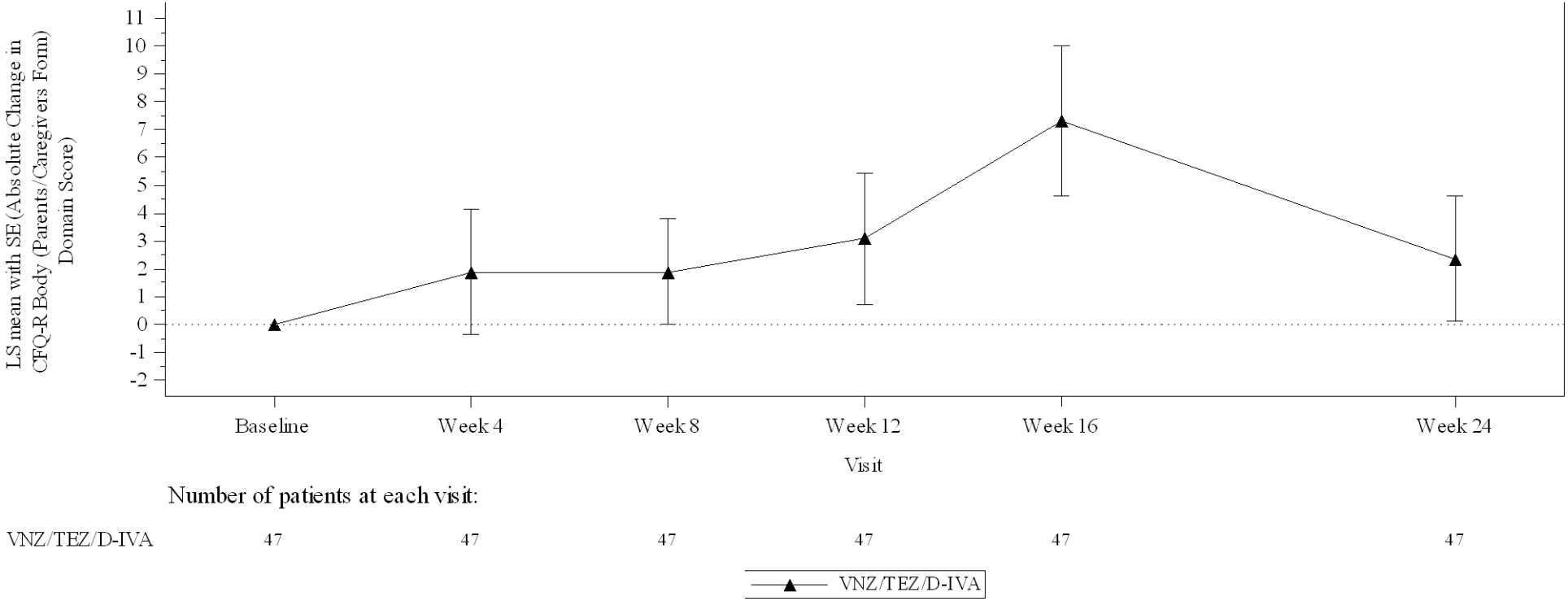
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Sex = Female



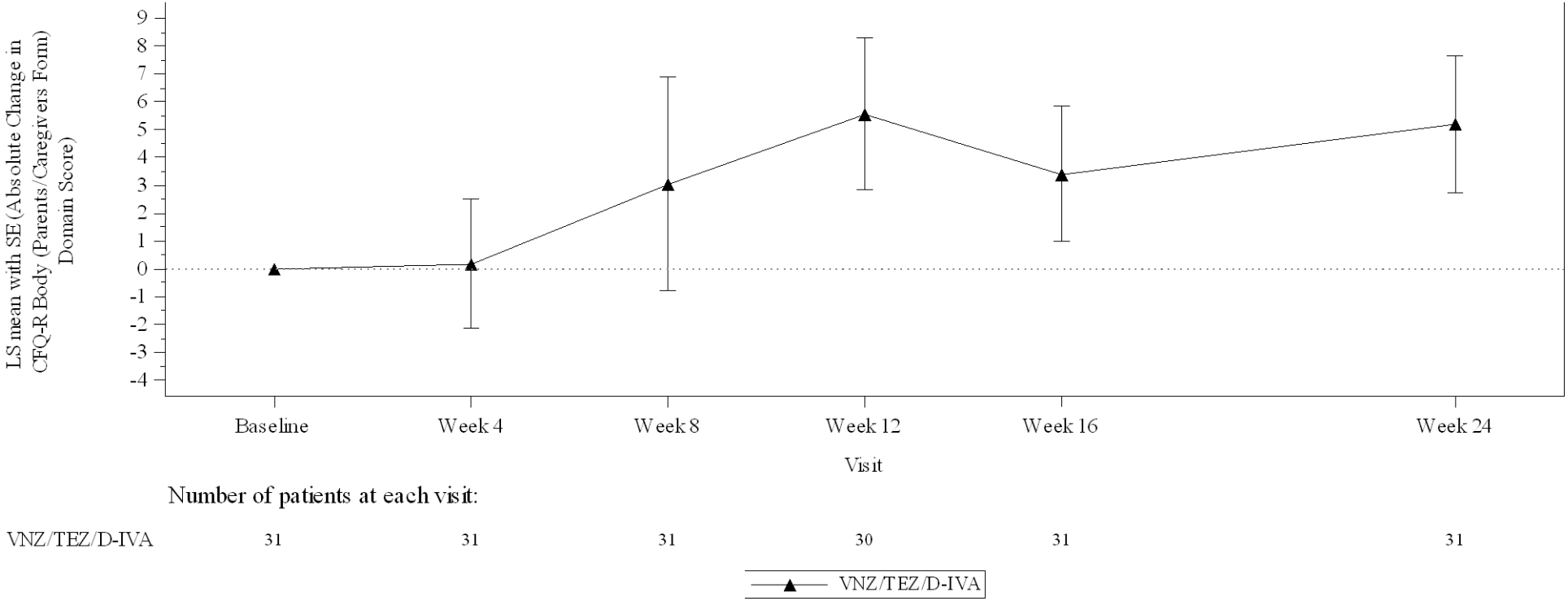
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Region = North America



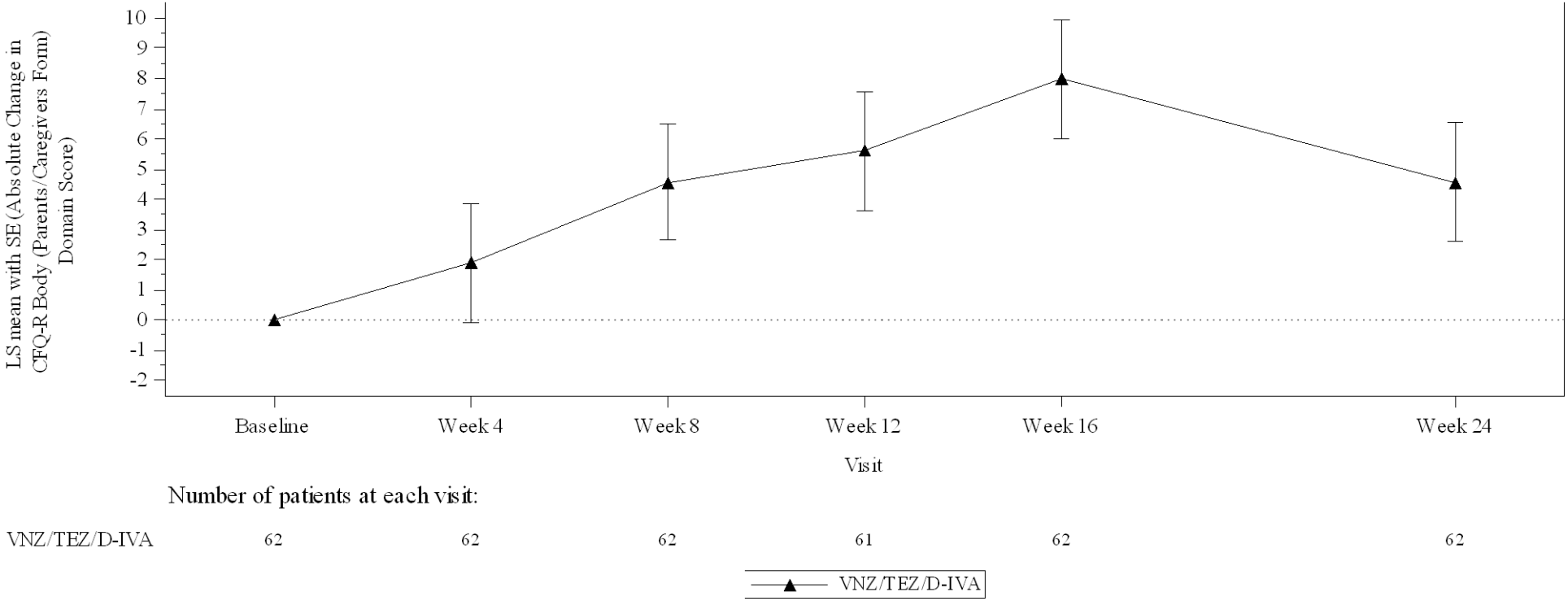
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
Region = Rest of World



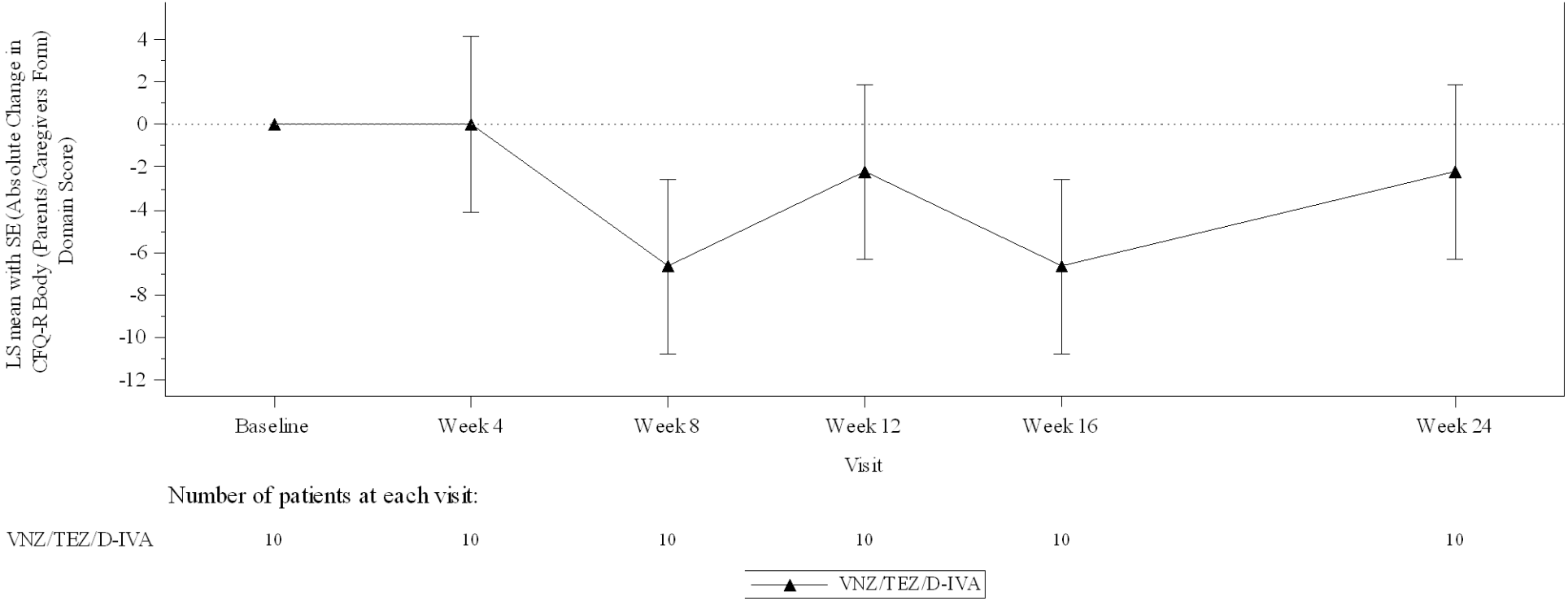
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



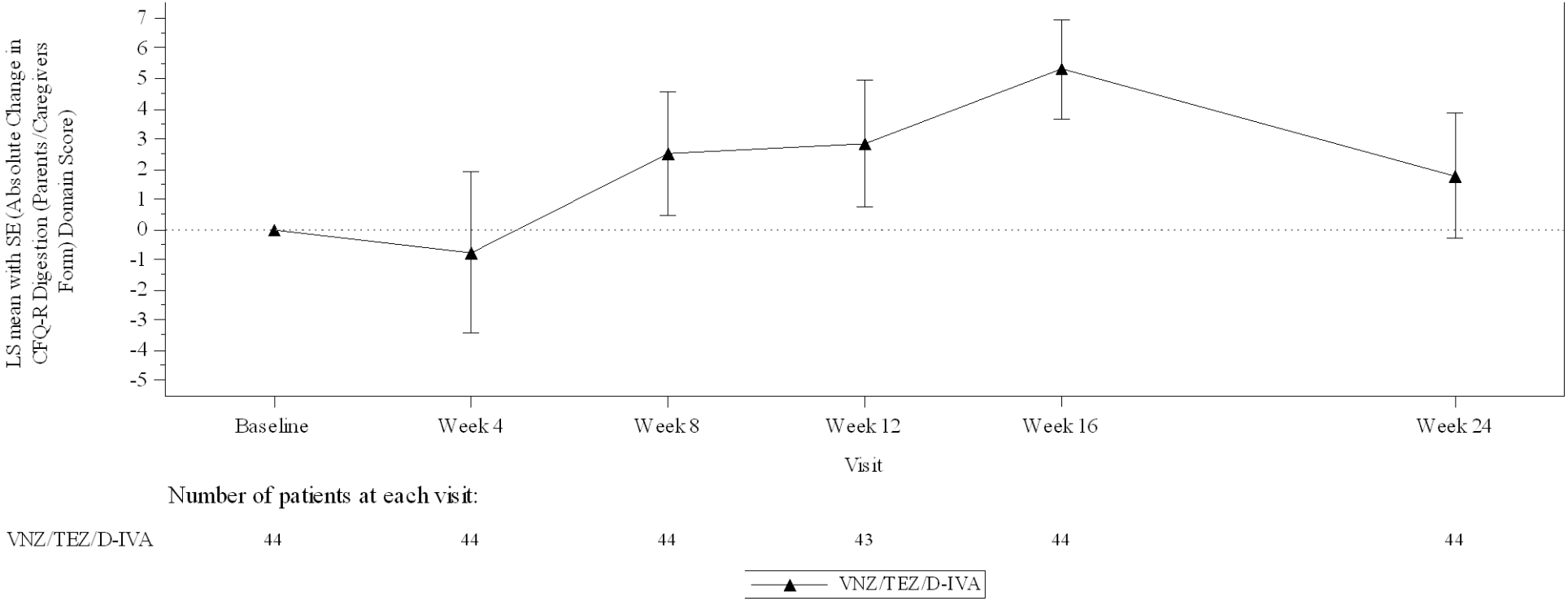
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Body (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



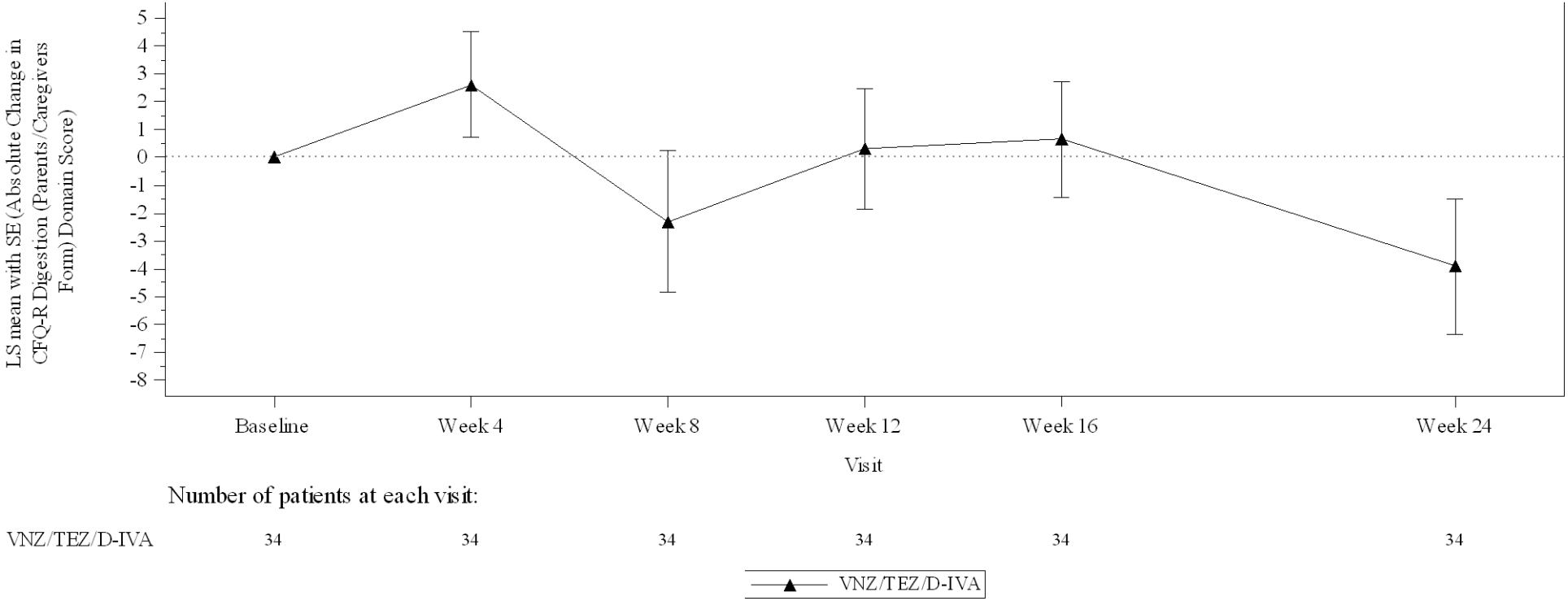
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Sex = Male



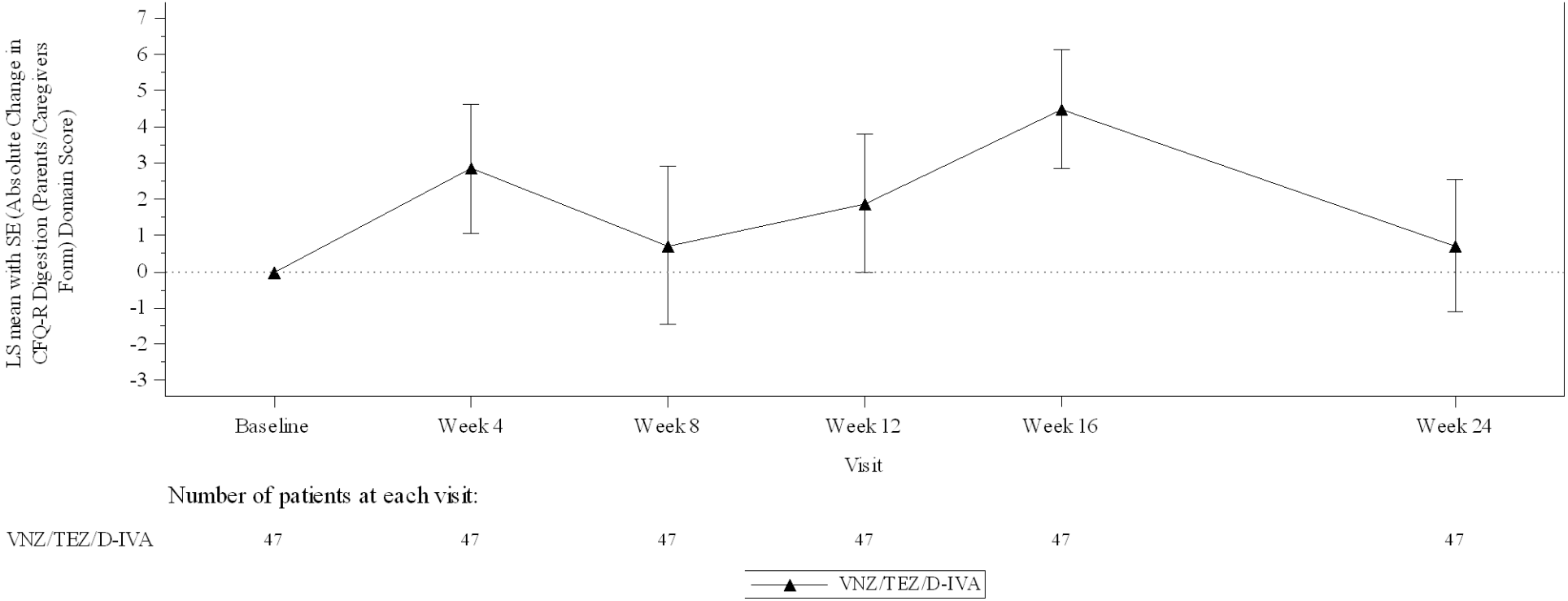
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Sex = Female



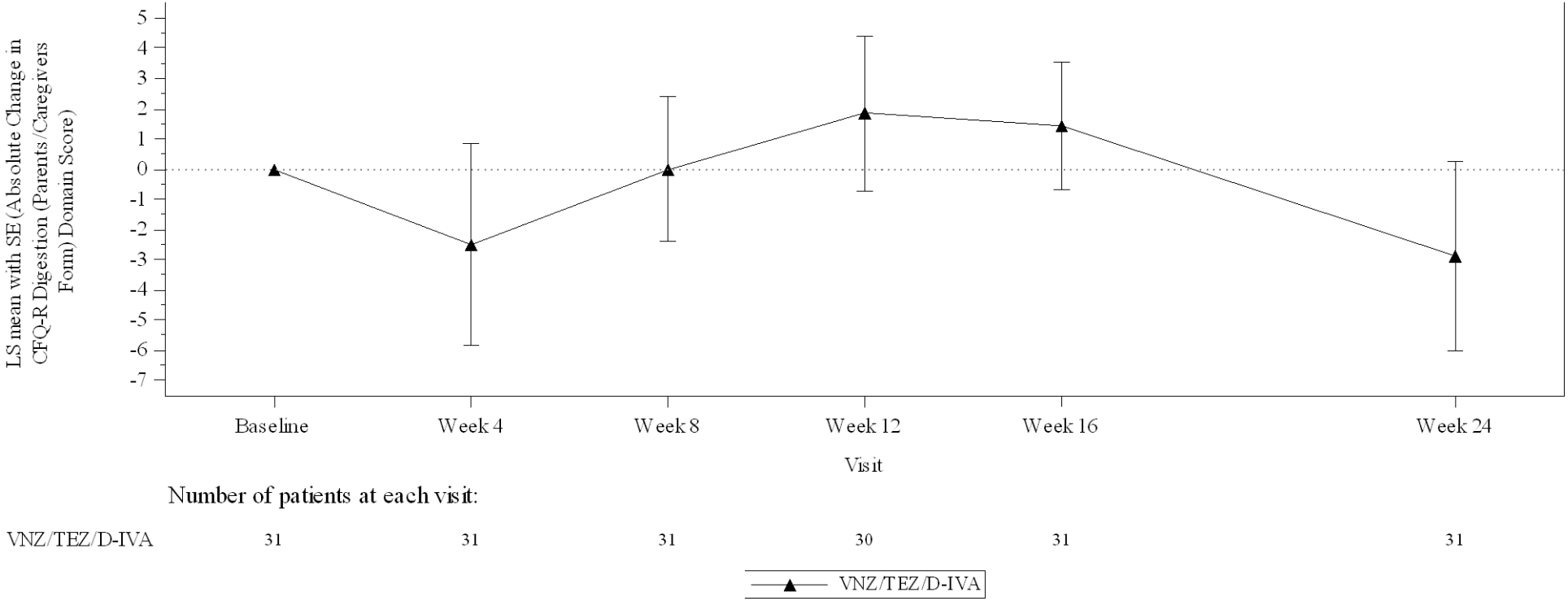
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
Region = North America



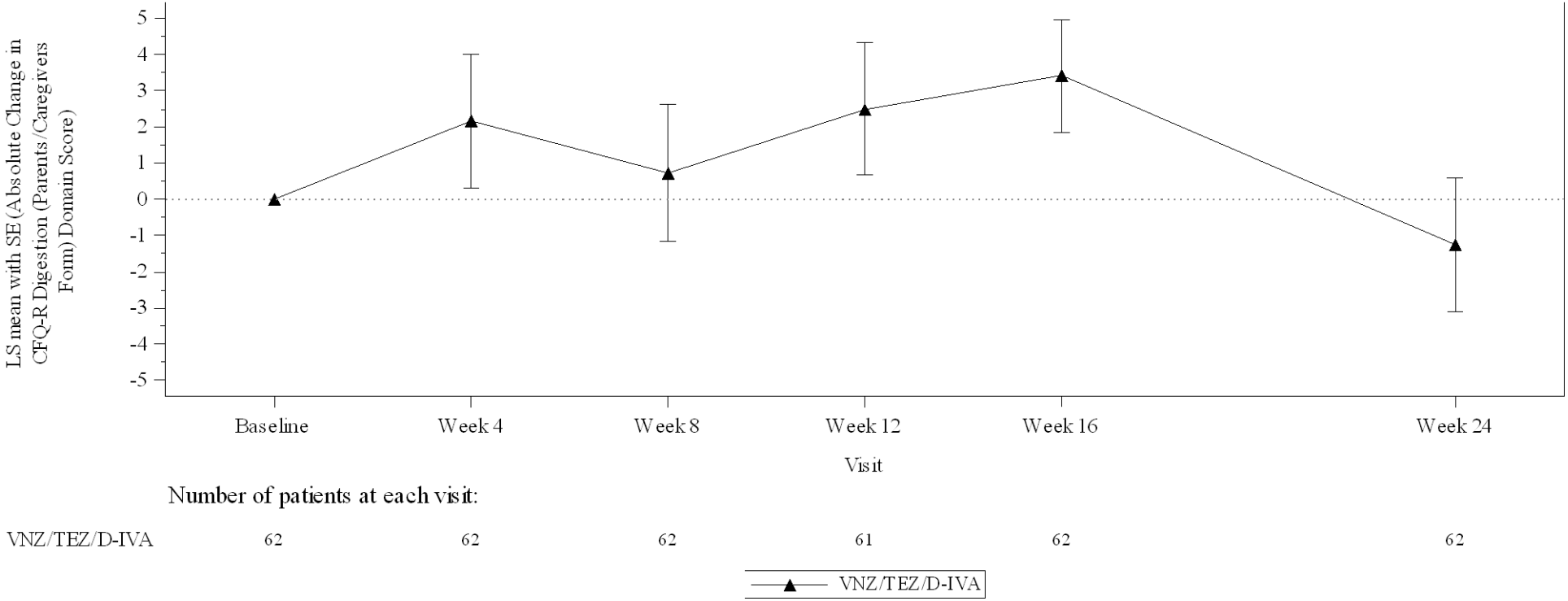
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
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Domain: Digestion (Parents/Caregivers Form)
Region = Rest of World



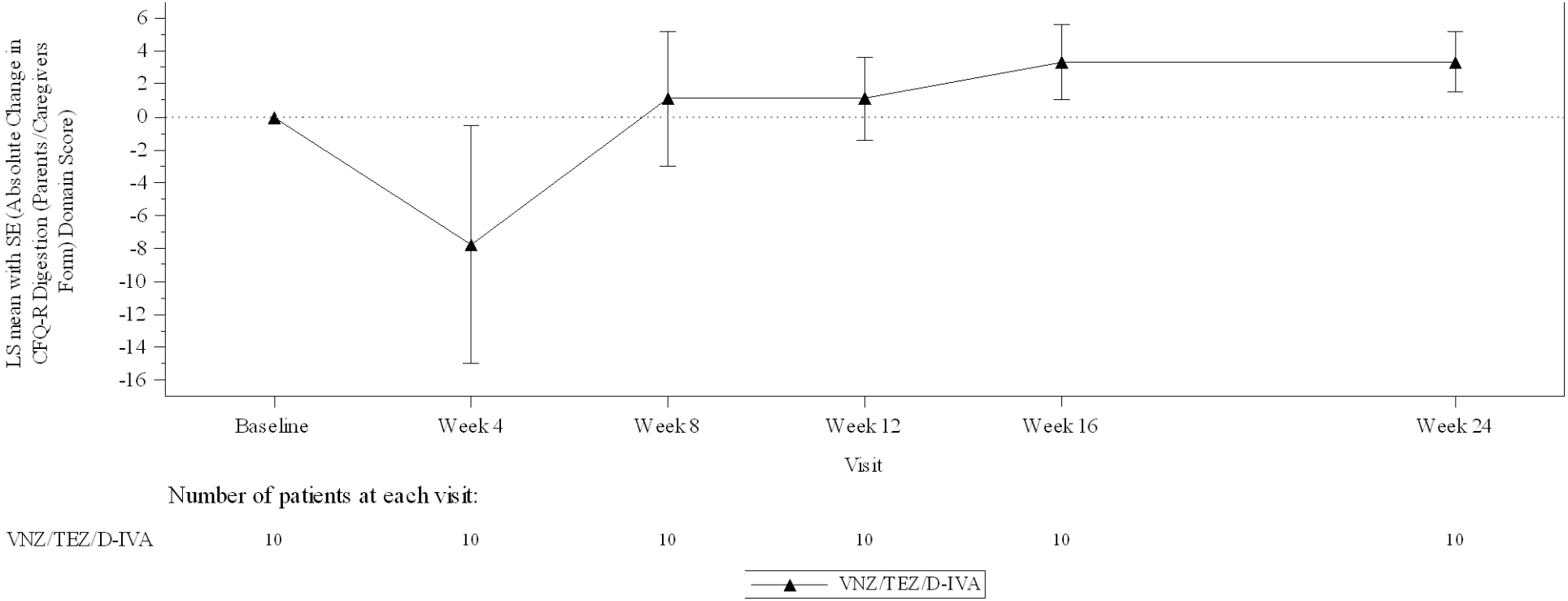
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



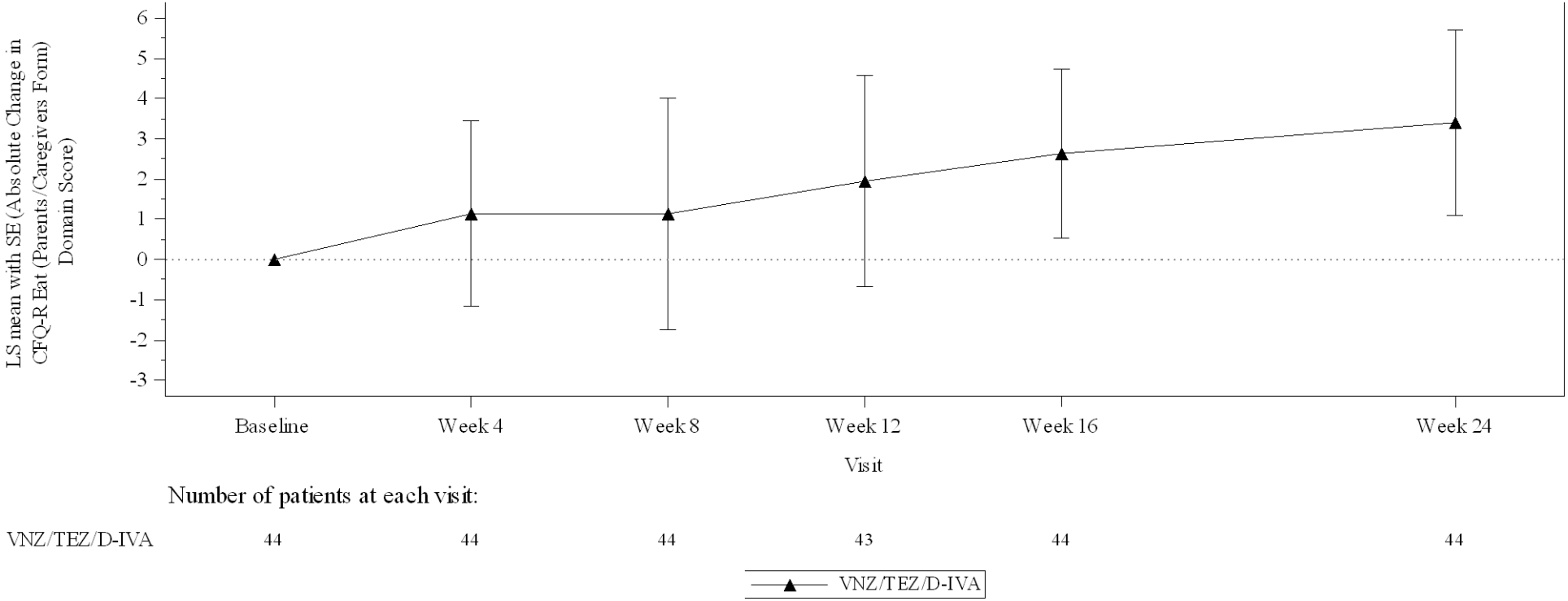
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Full Analysis Set
Domain: Digestion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



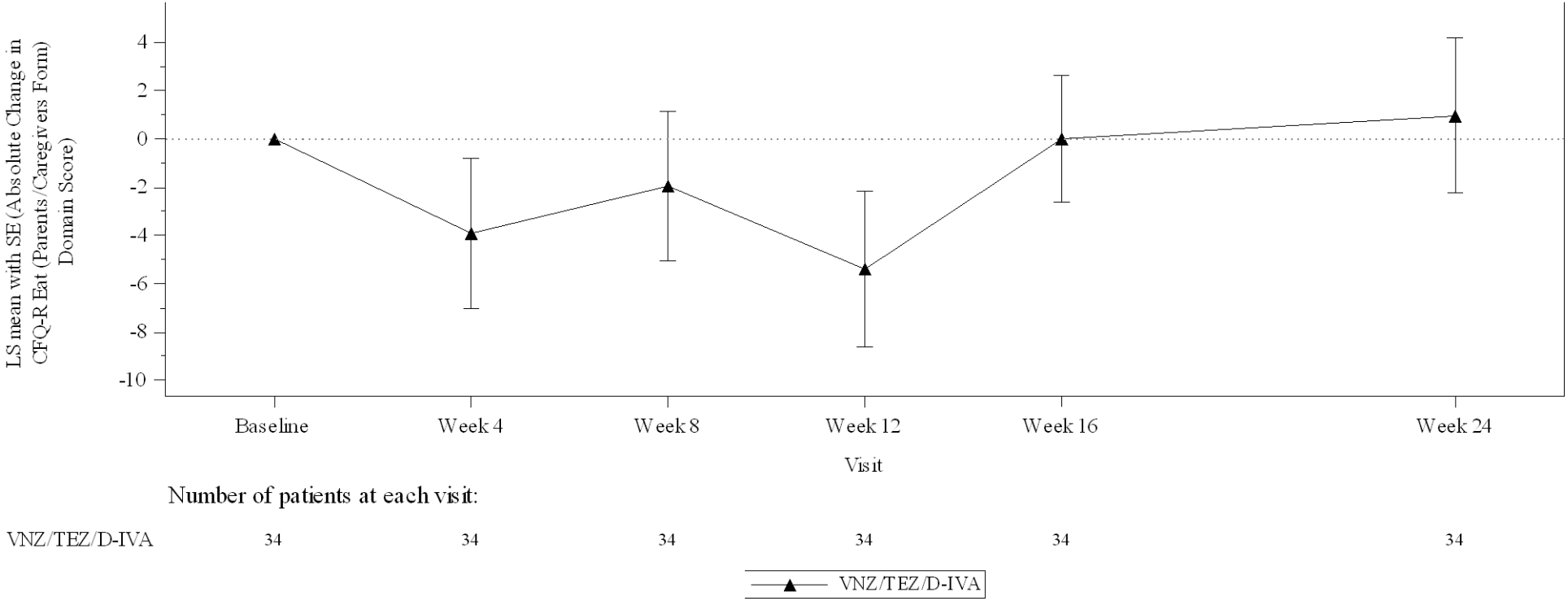
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Sex = Male



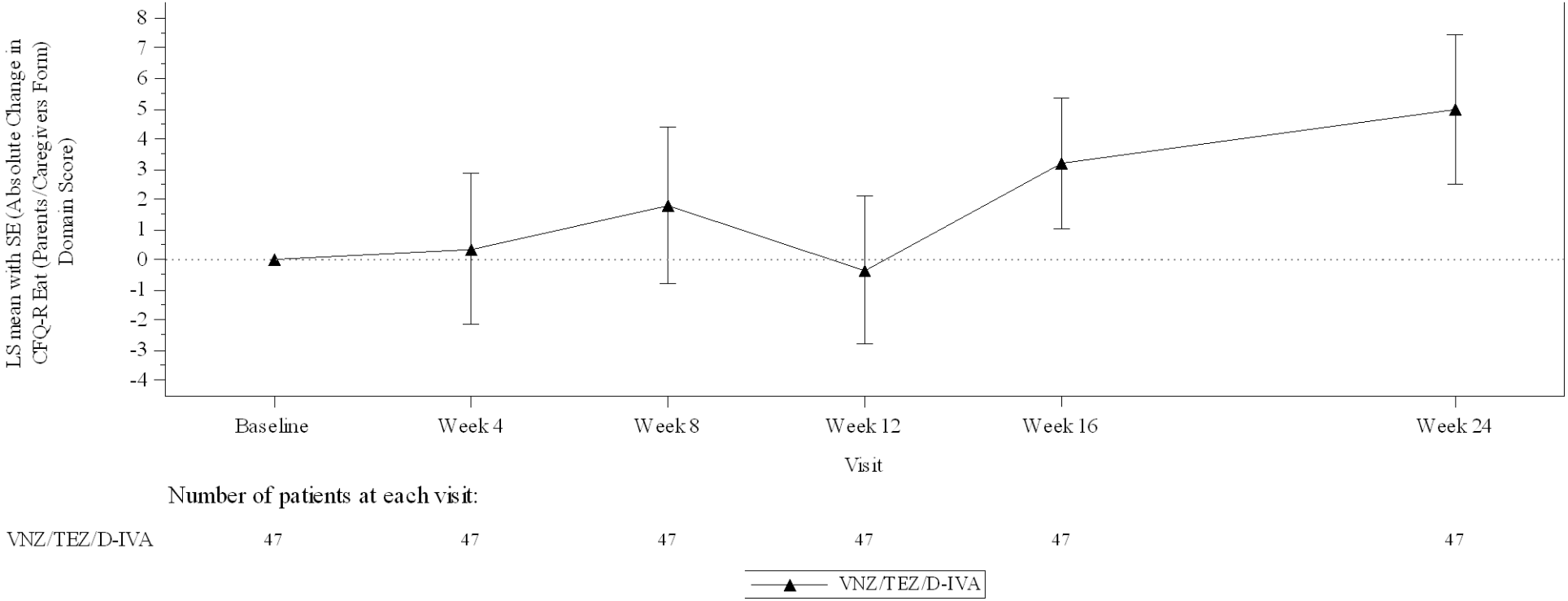
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Sex = Female



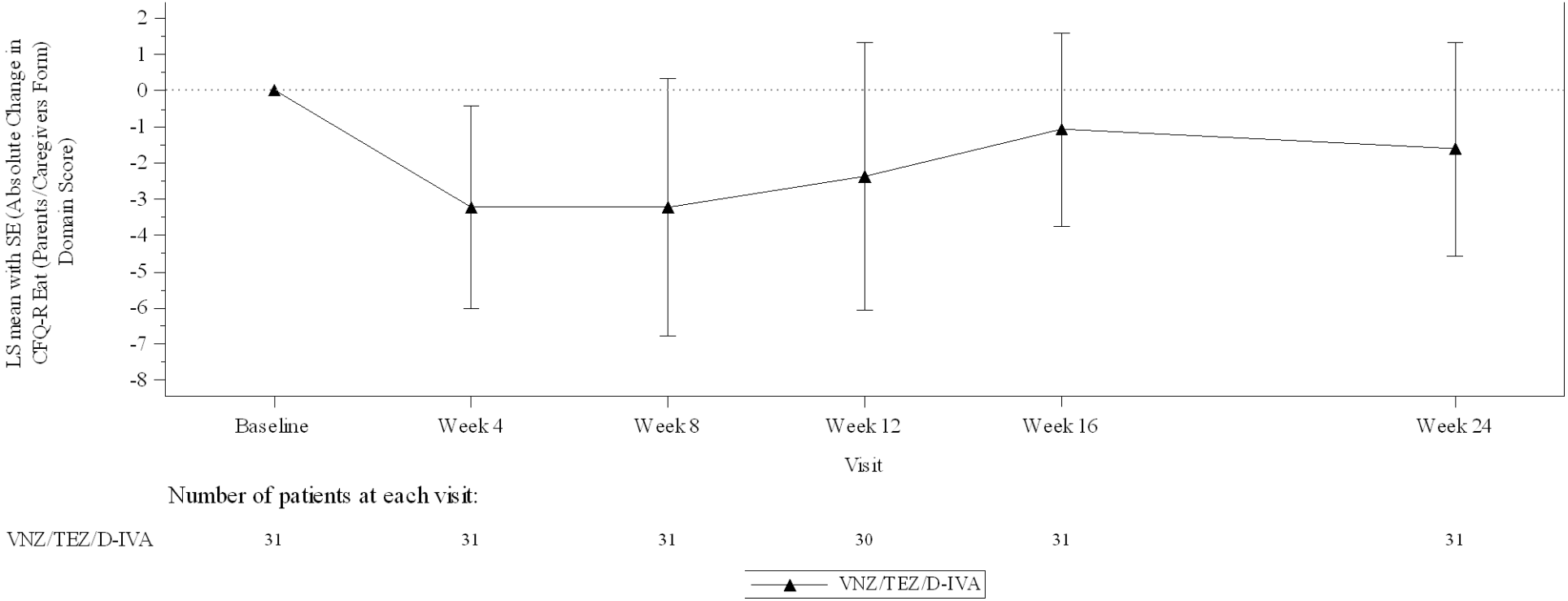
- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Eat (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Region = North America



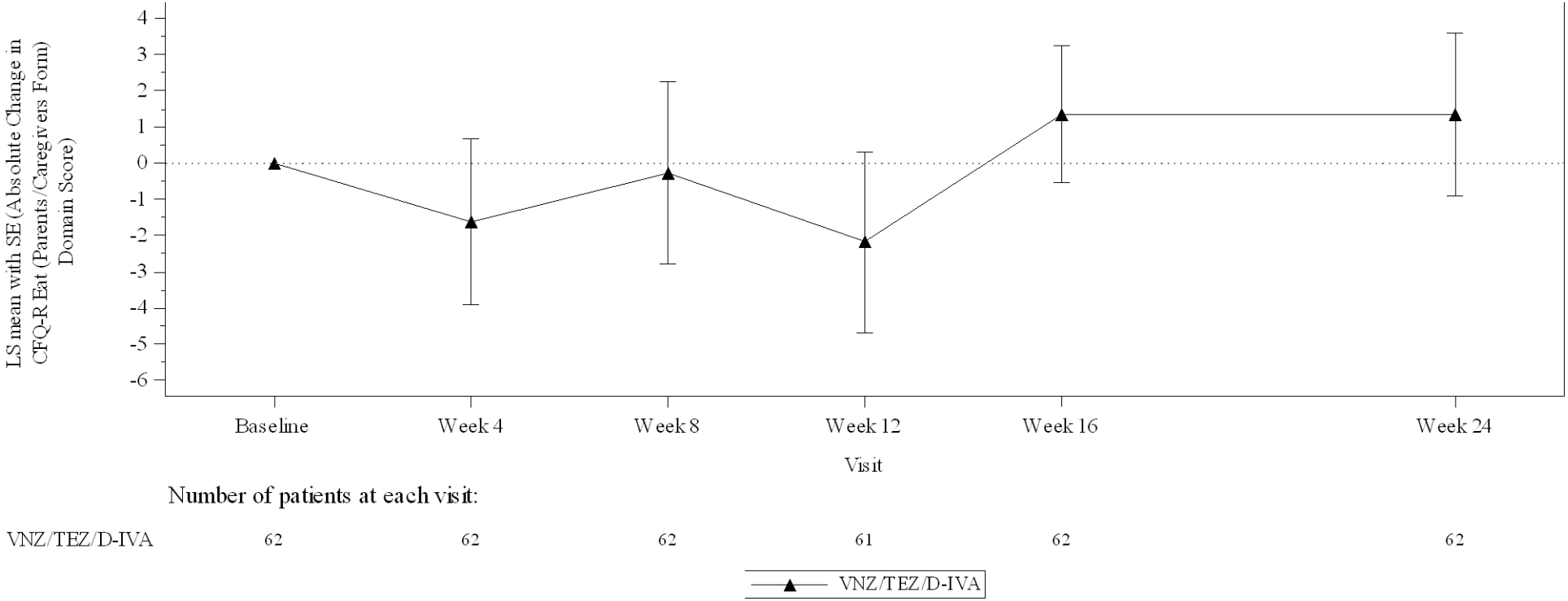
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
Region = Rest of World



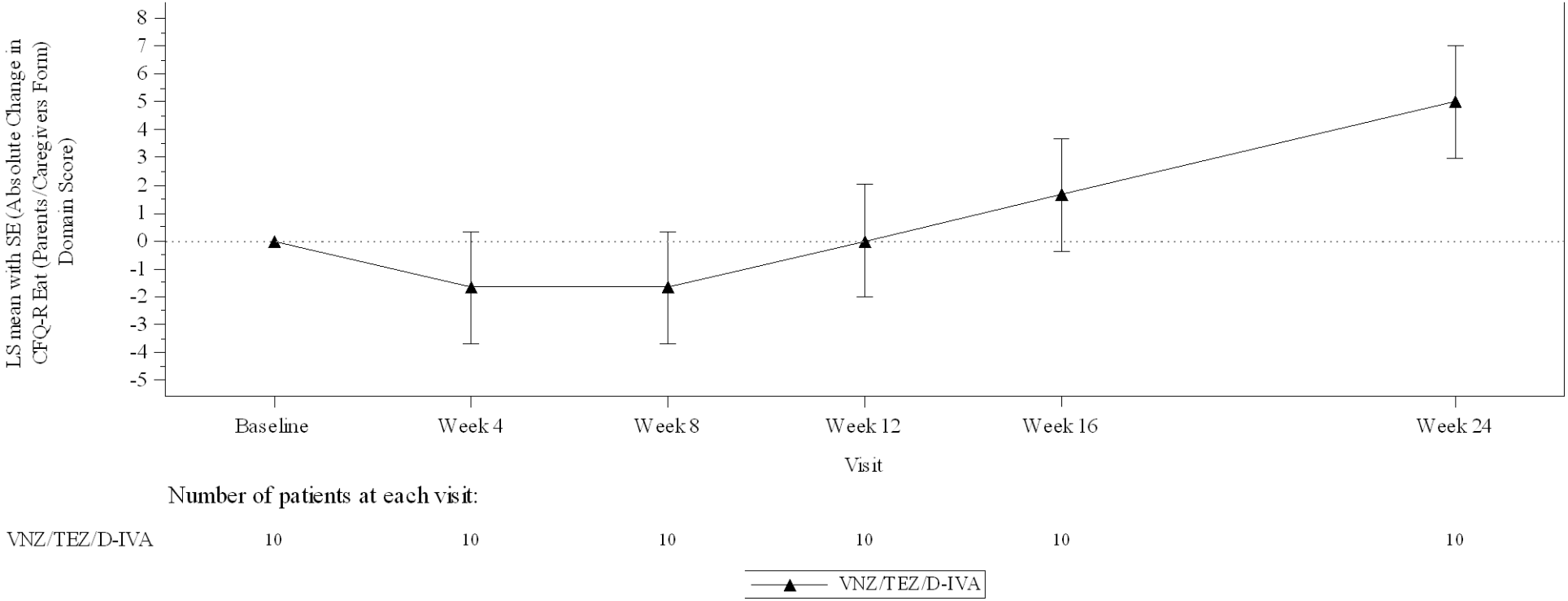
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



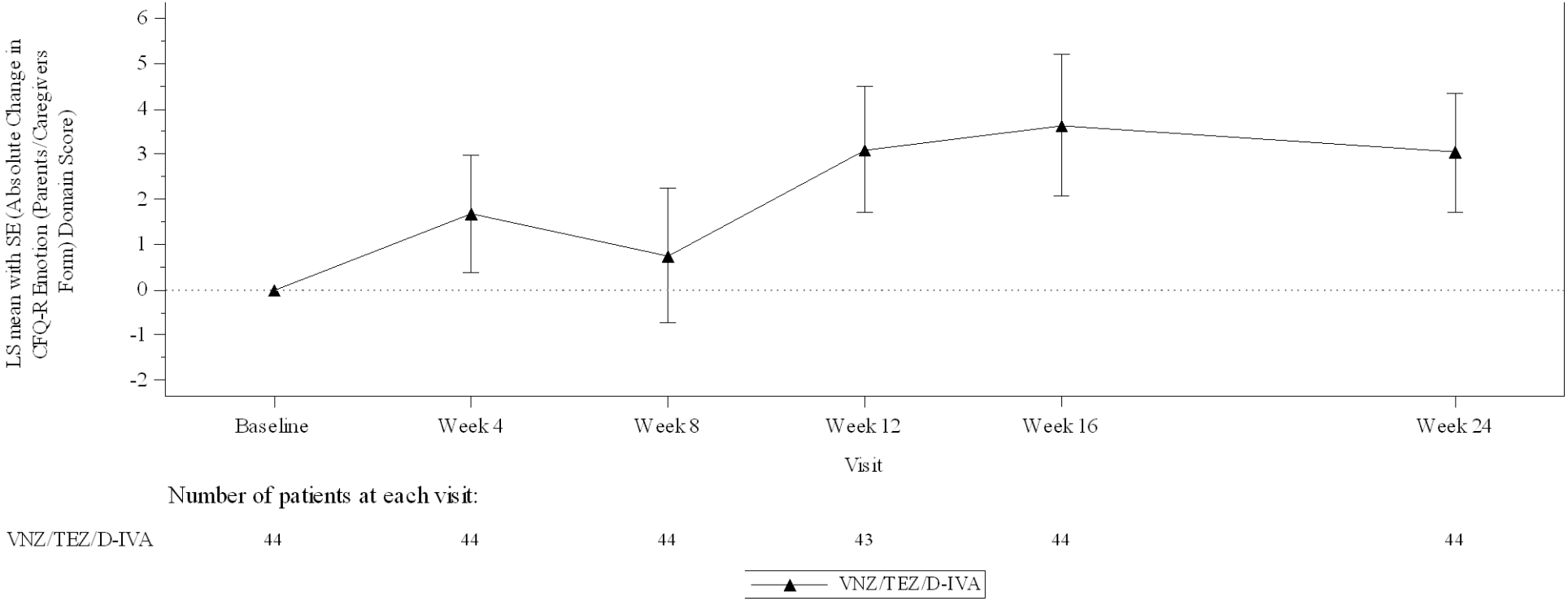
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Eat (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



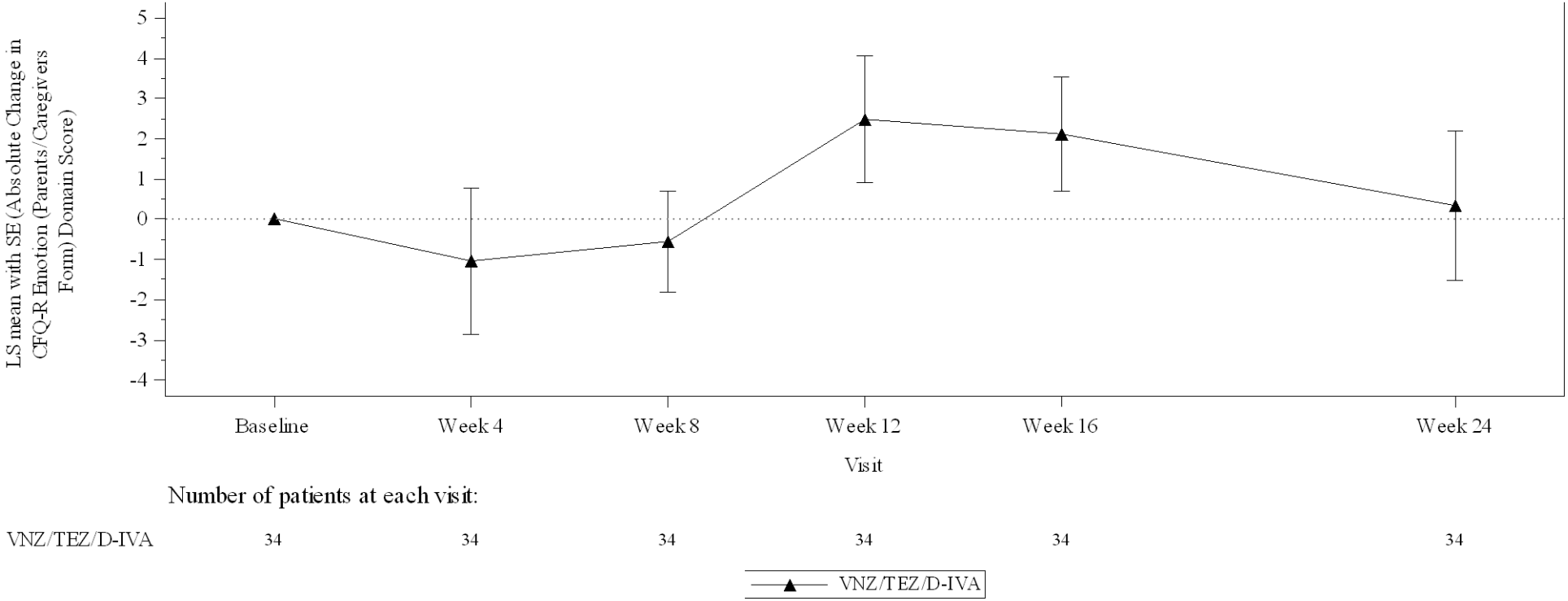
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Sex = Male



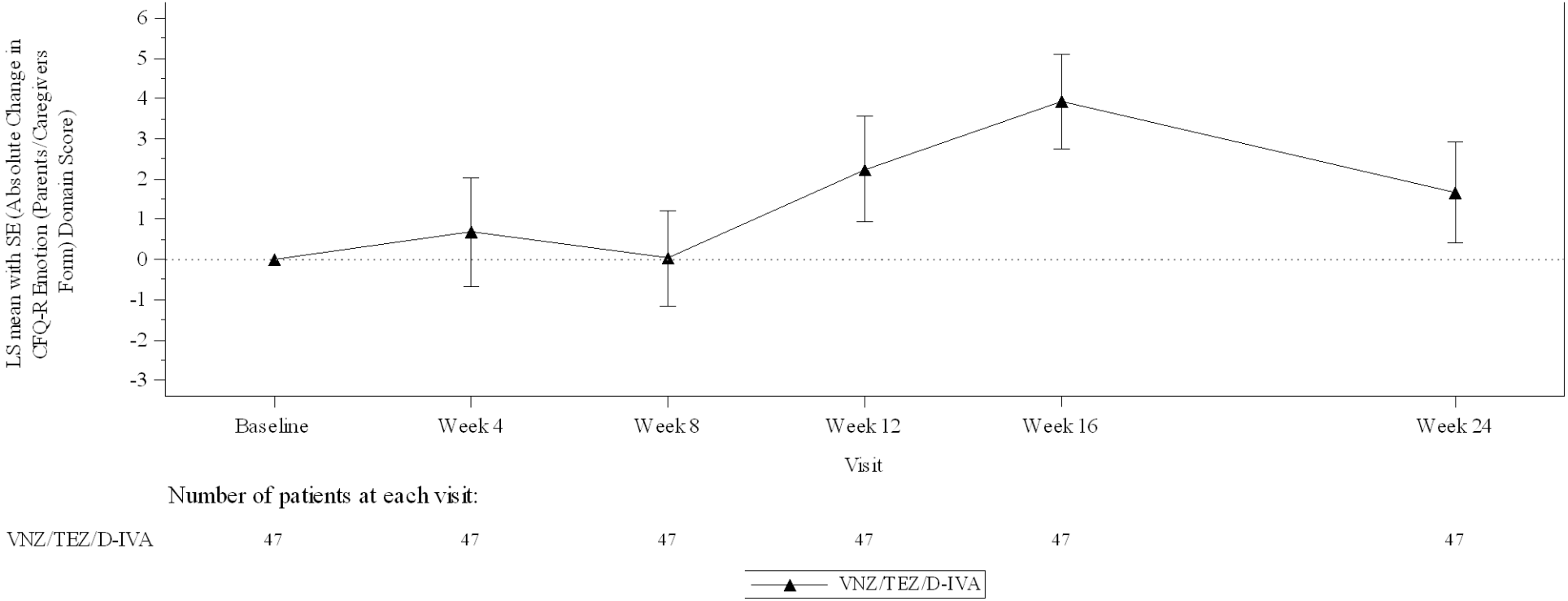
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Sex = Female



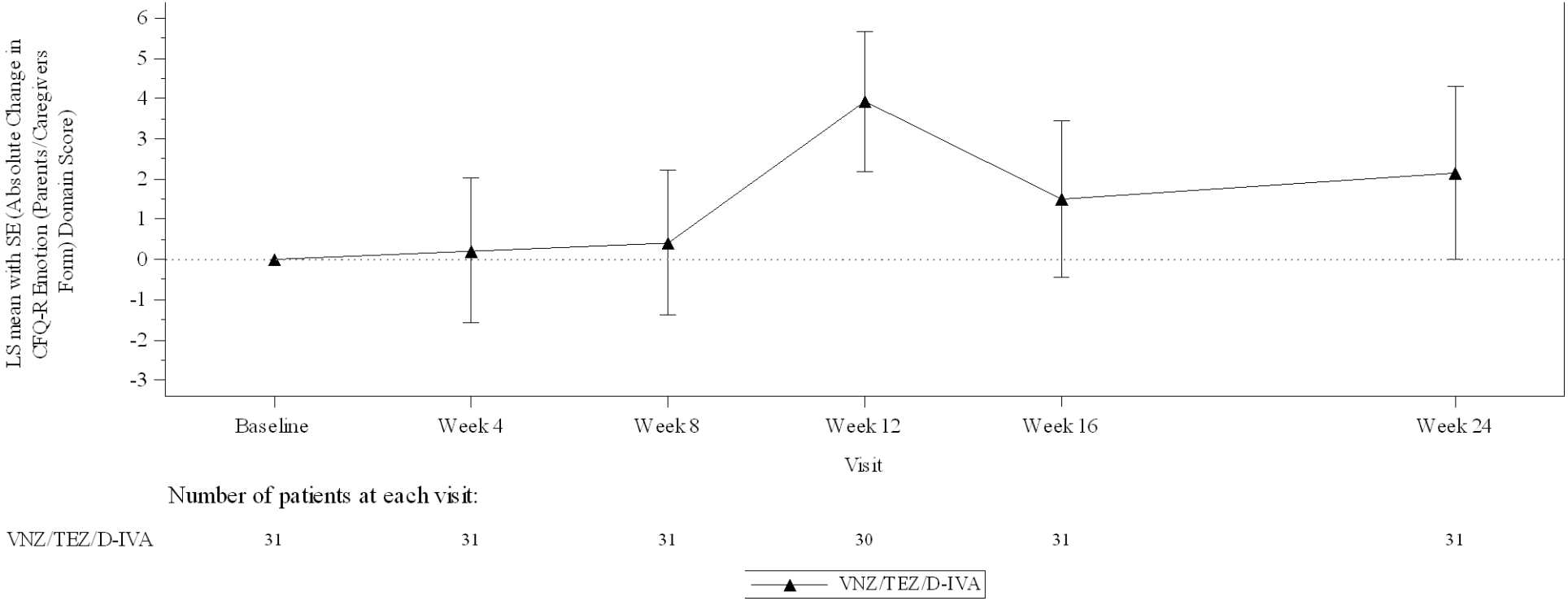
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Region = North America



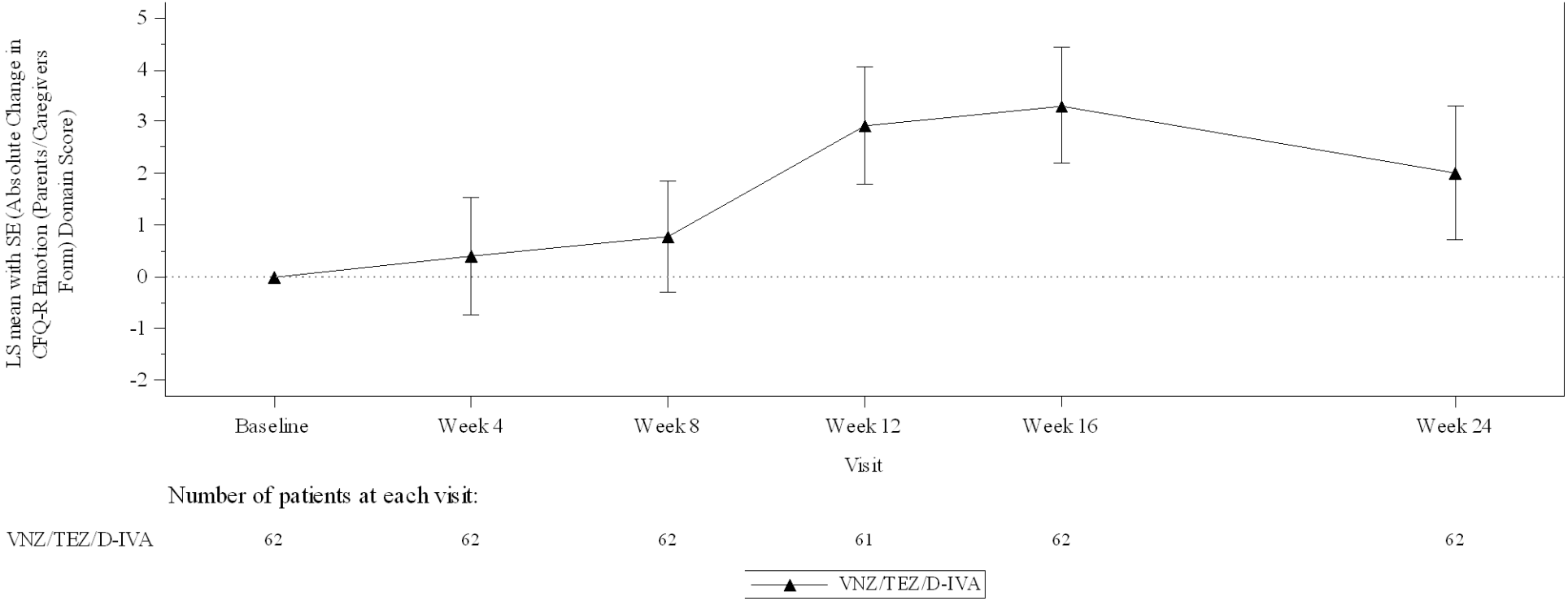
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
Region = Rest of World



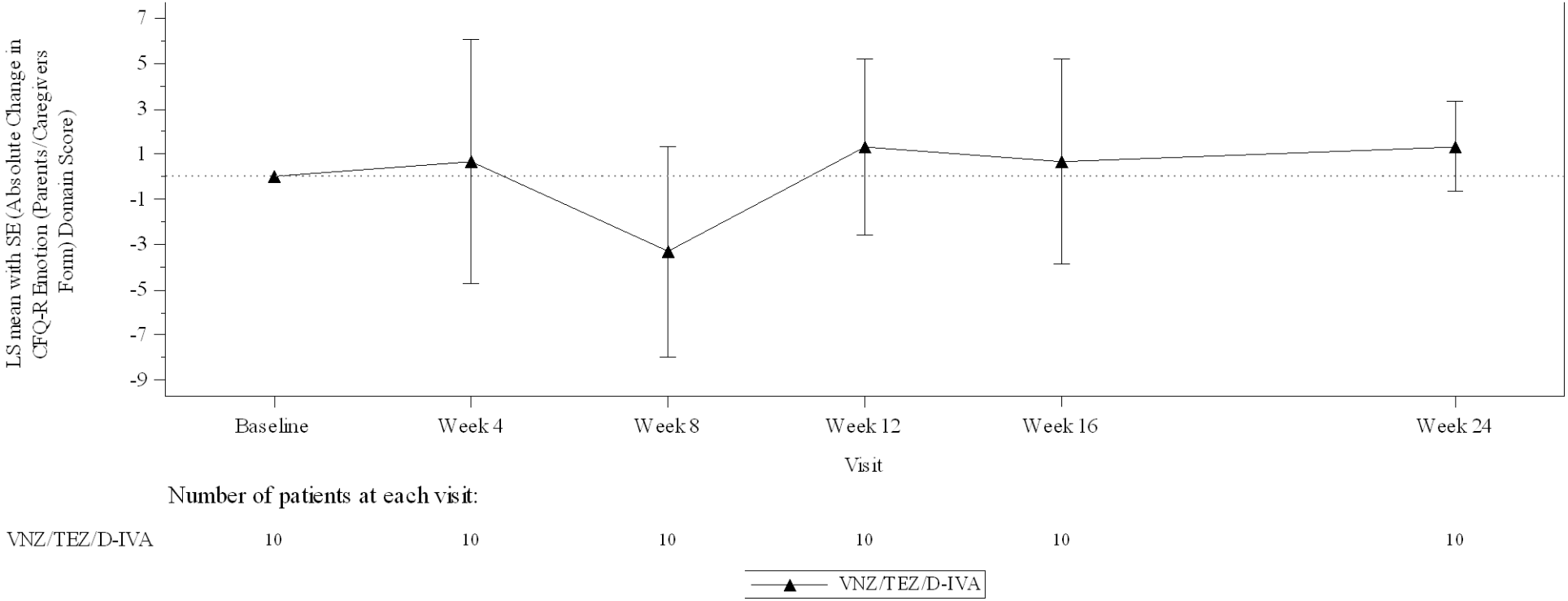
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



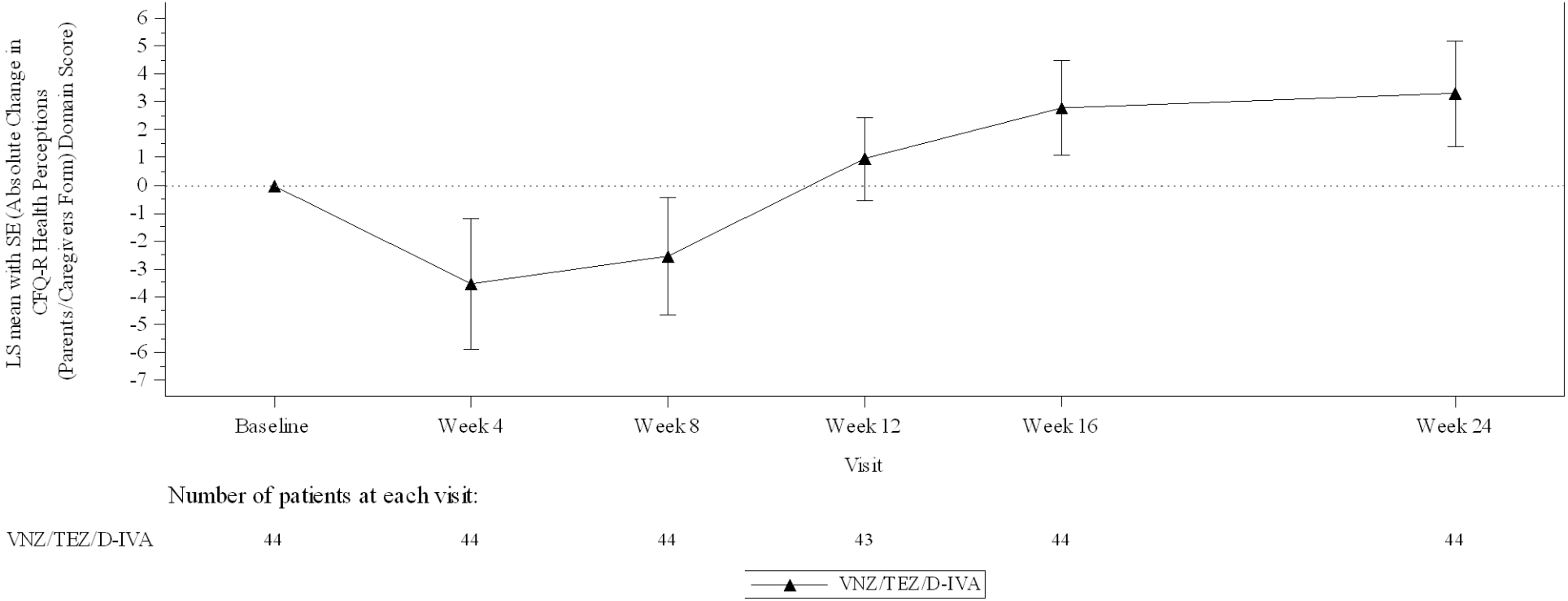
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Emotion (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Male



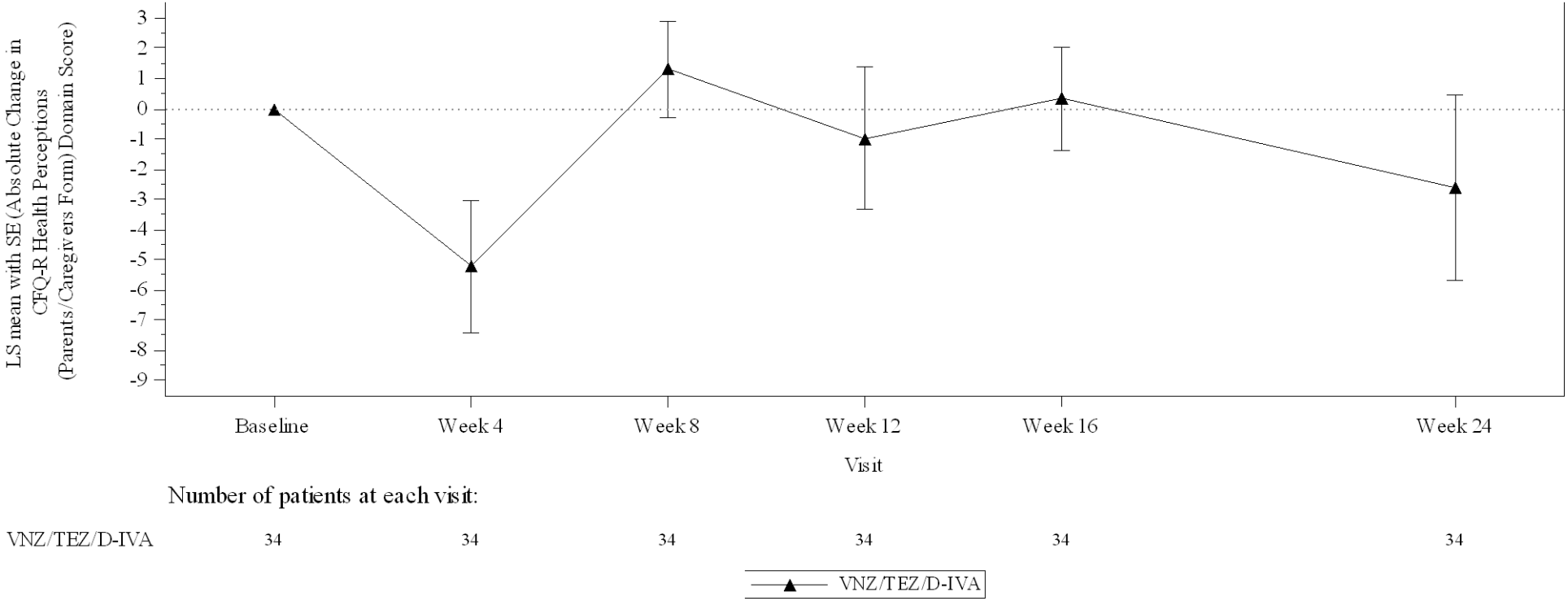
Number of patients at each visit:

VNZ/TEZ/D-IVA	44	44	44	43	44	44

VNZ/TEZ/D-IVA

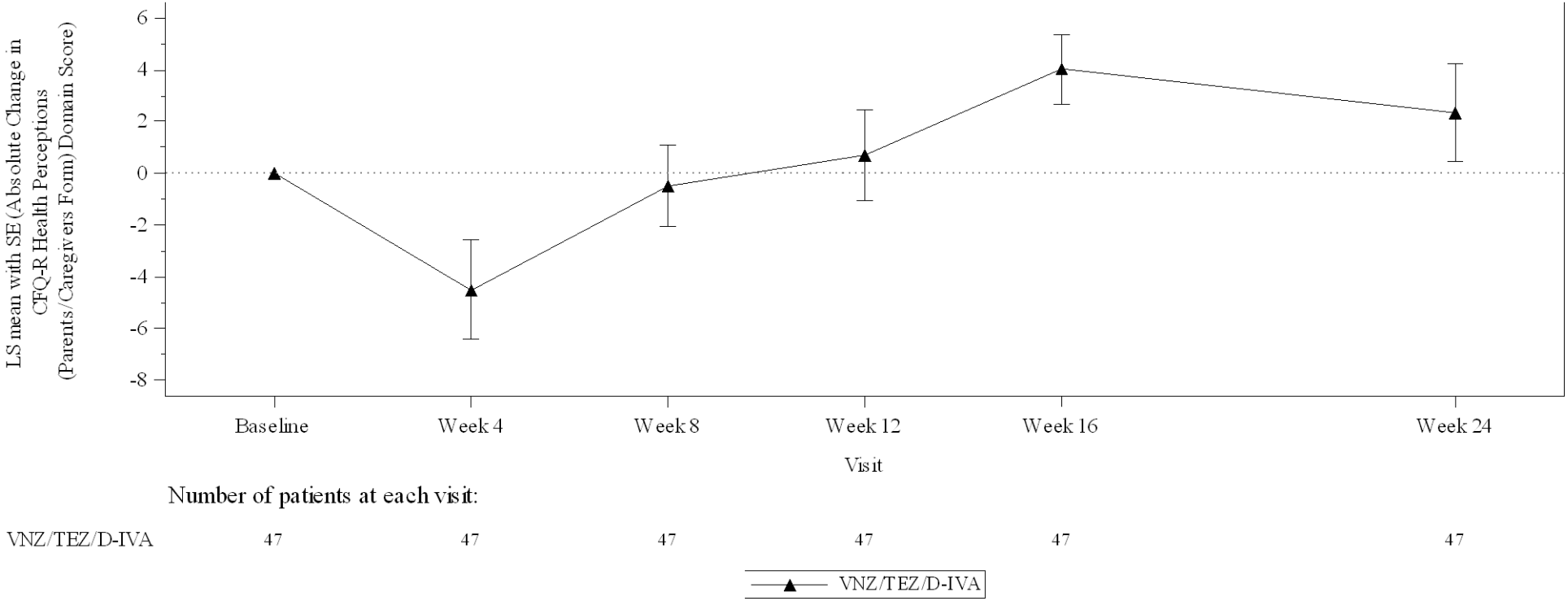
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Sex = Female



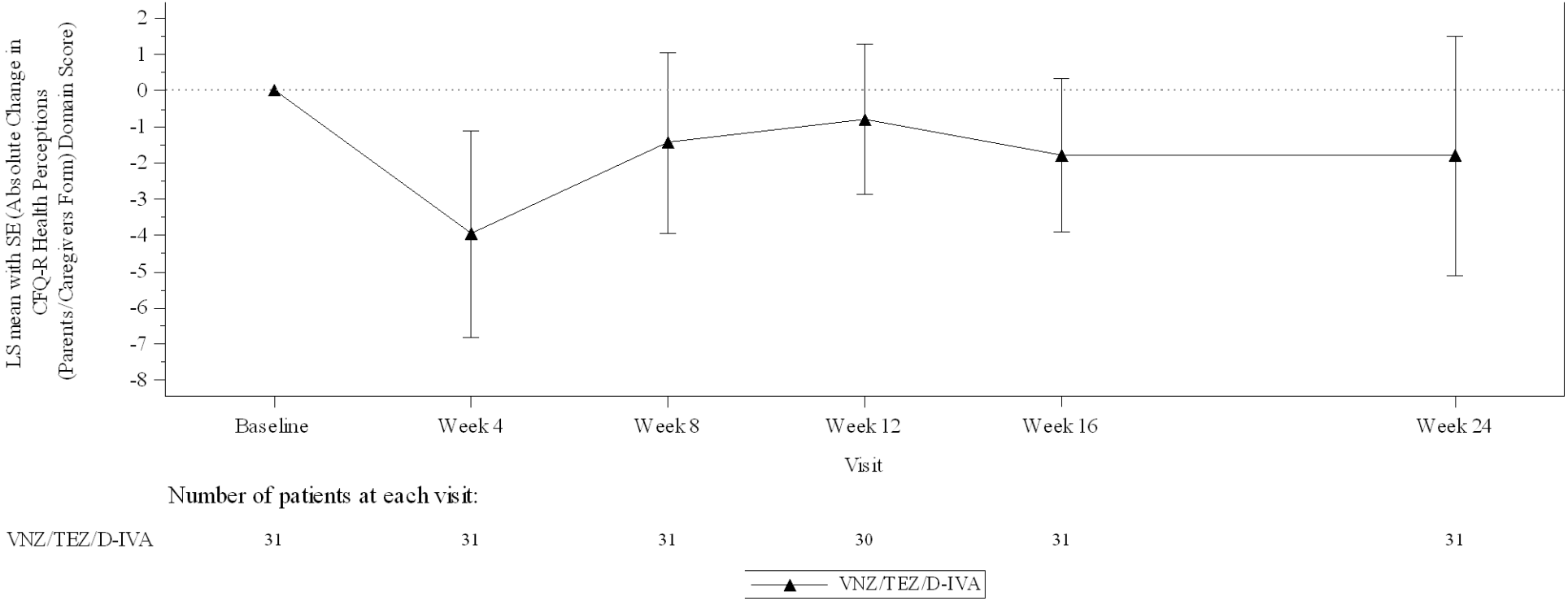
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Region = North America



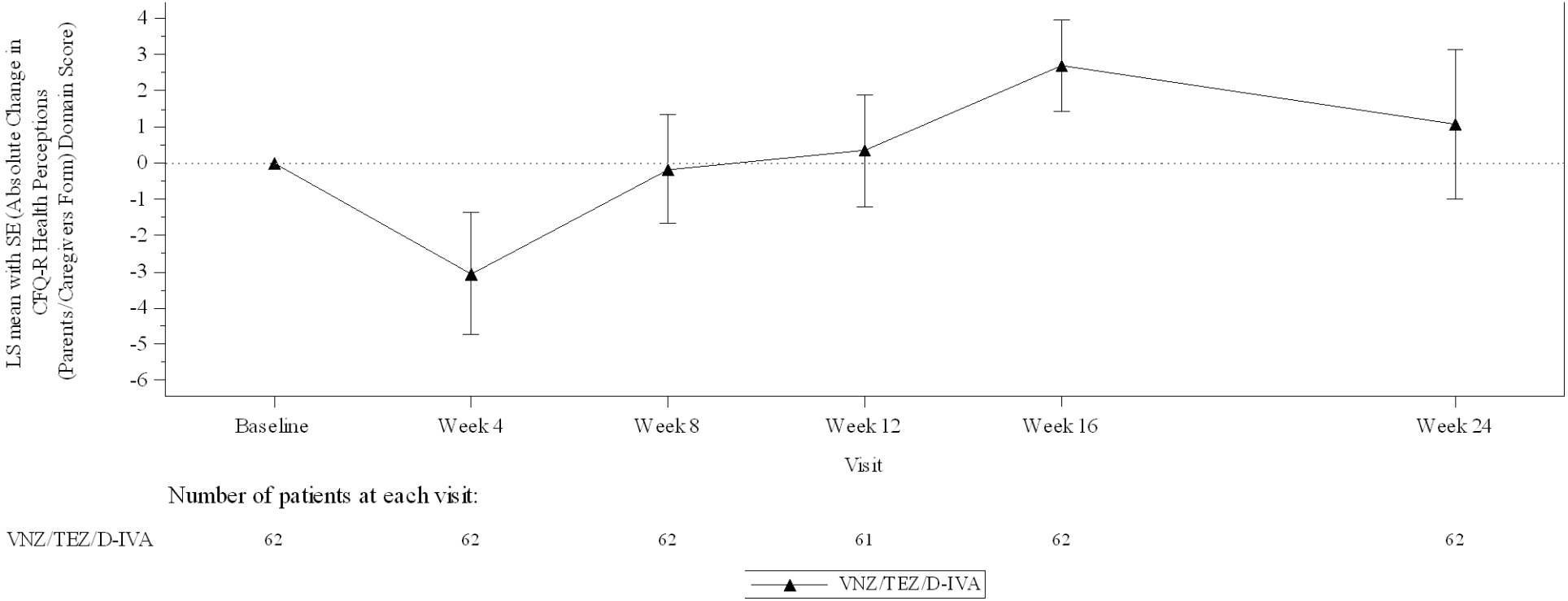
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
Region = Rest of World



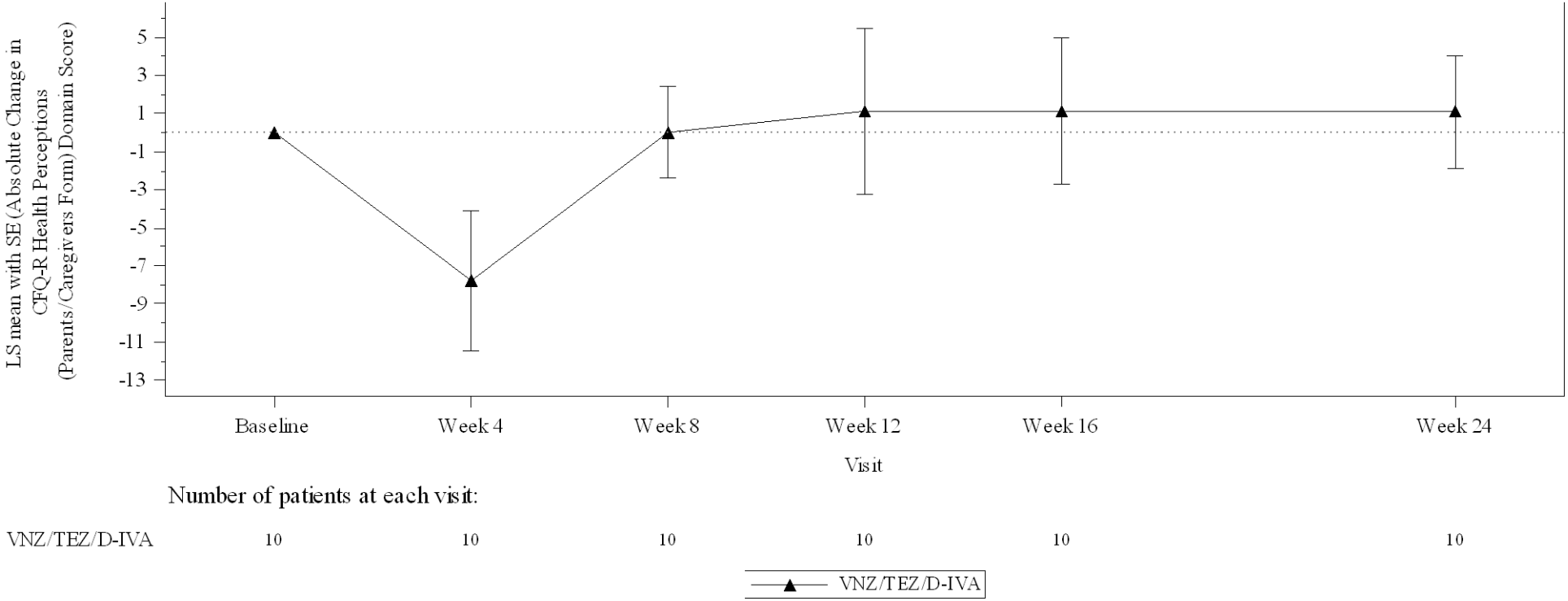
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



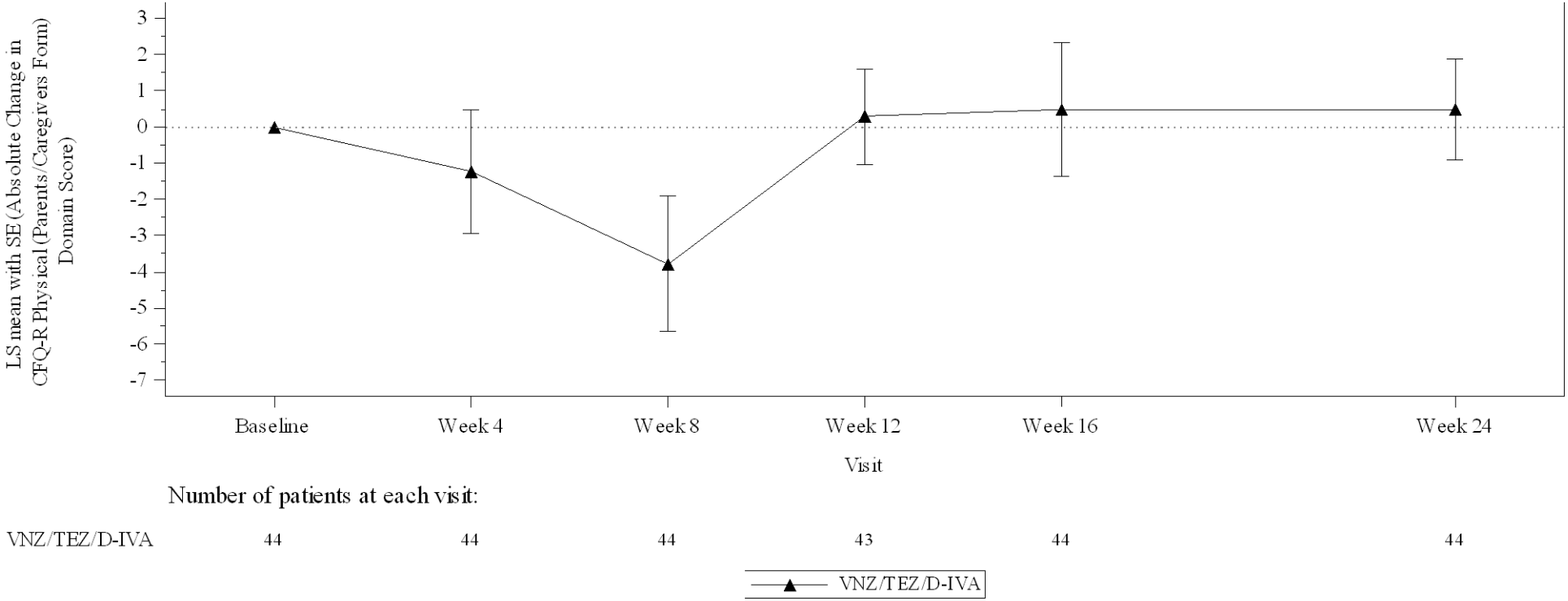
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Full Analysis Set
Domain: Health Perceptions (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



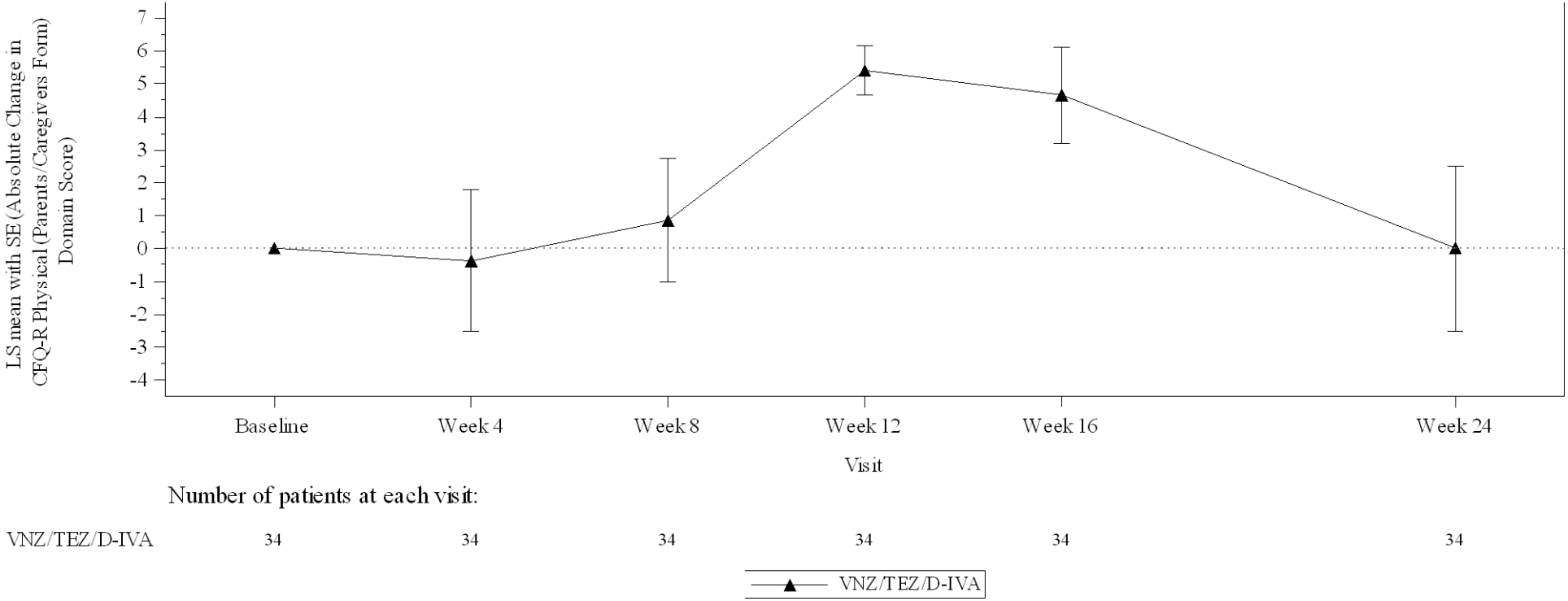
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Sex = Male



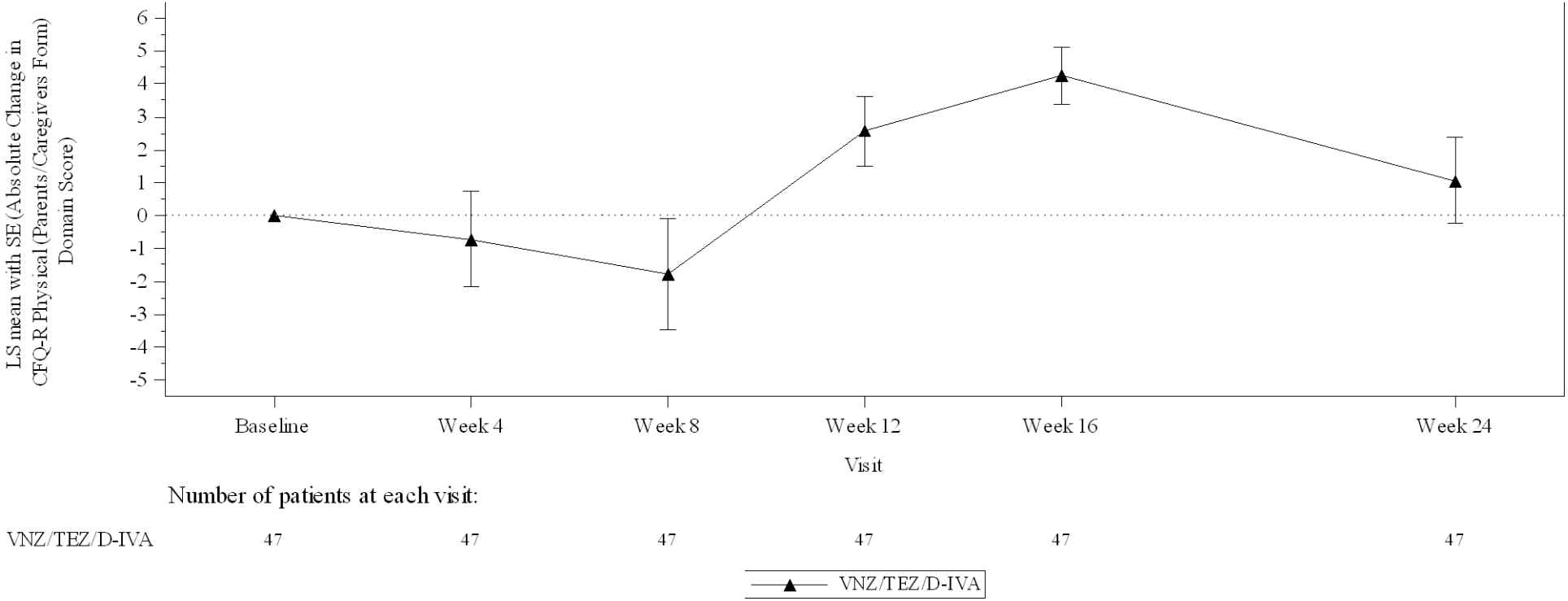
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Sex = Female



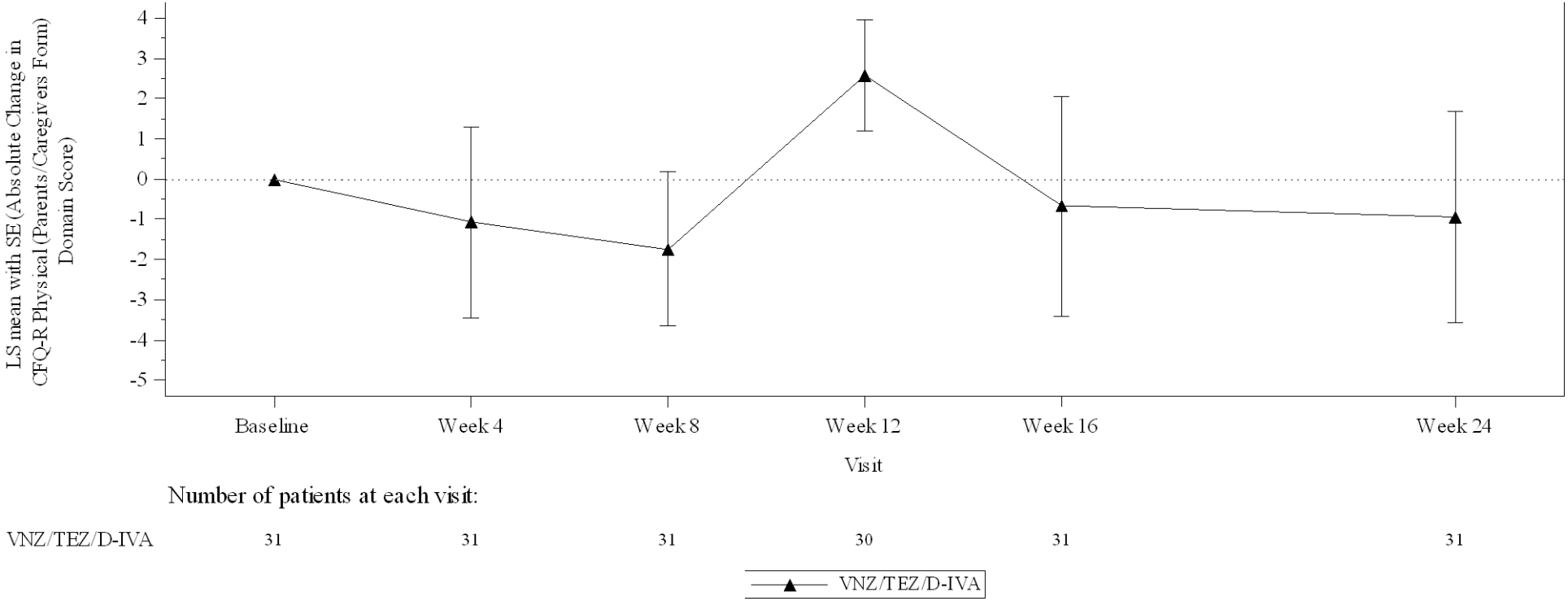
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Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
Region = North America



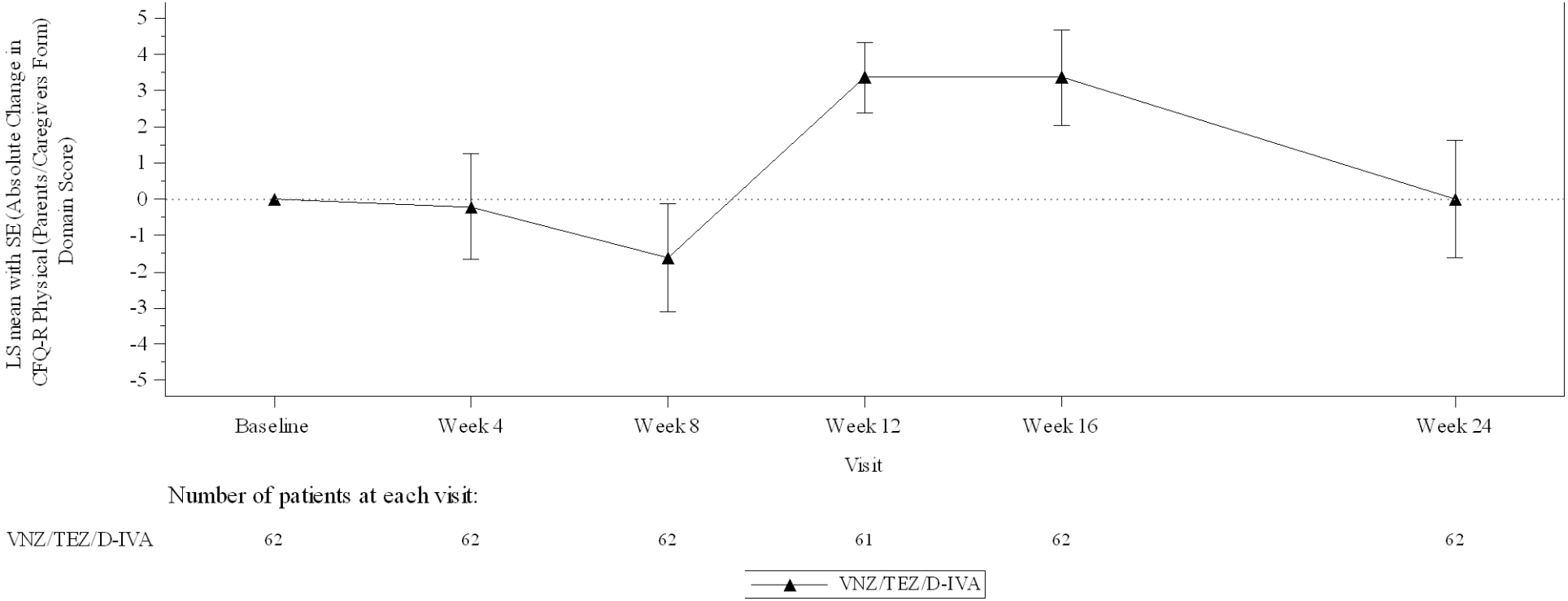
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Region = Rest of World



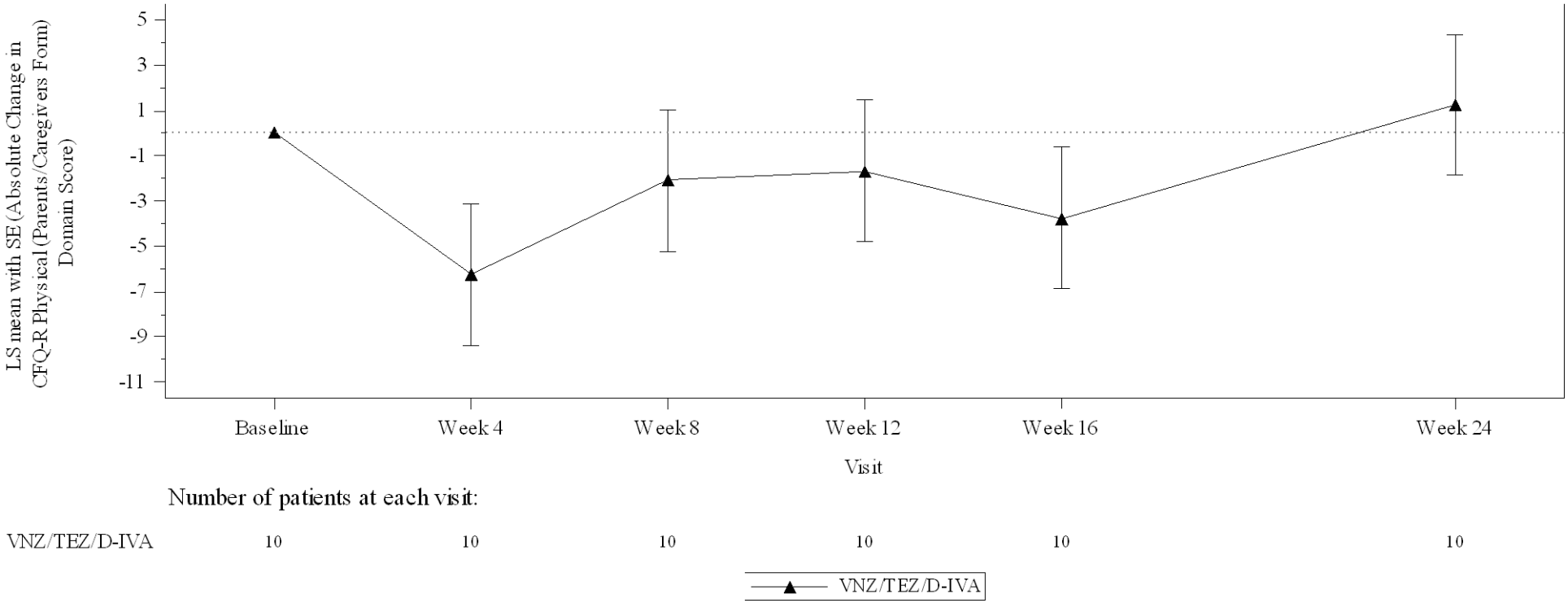
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Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



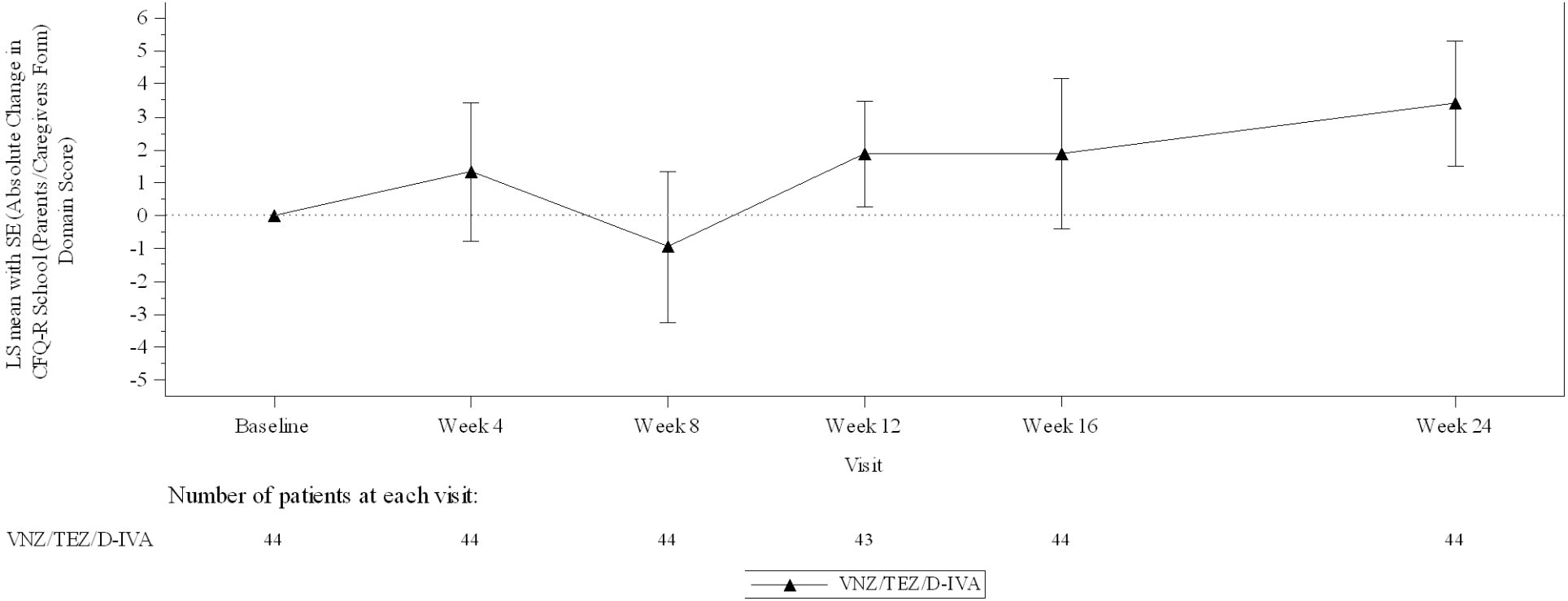
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Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Physical (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



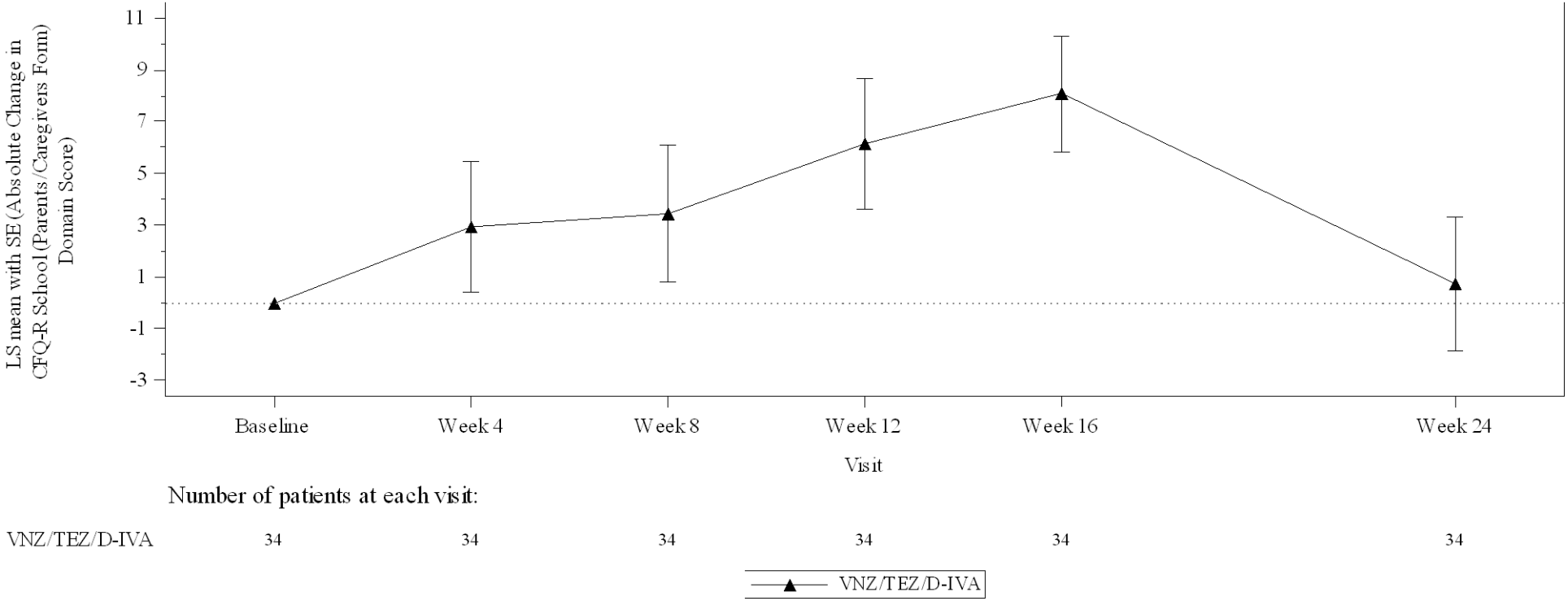
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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Physical (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=CS, DF=Kenward-Roger

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Sex = Male



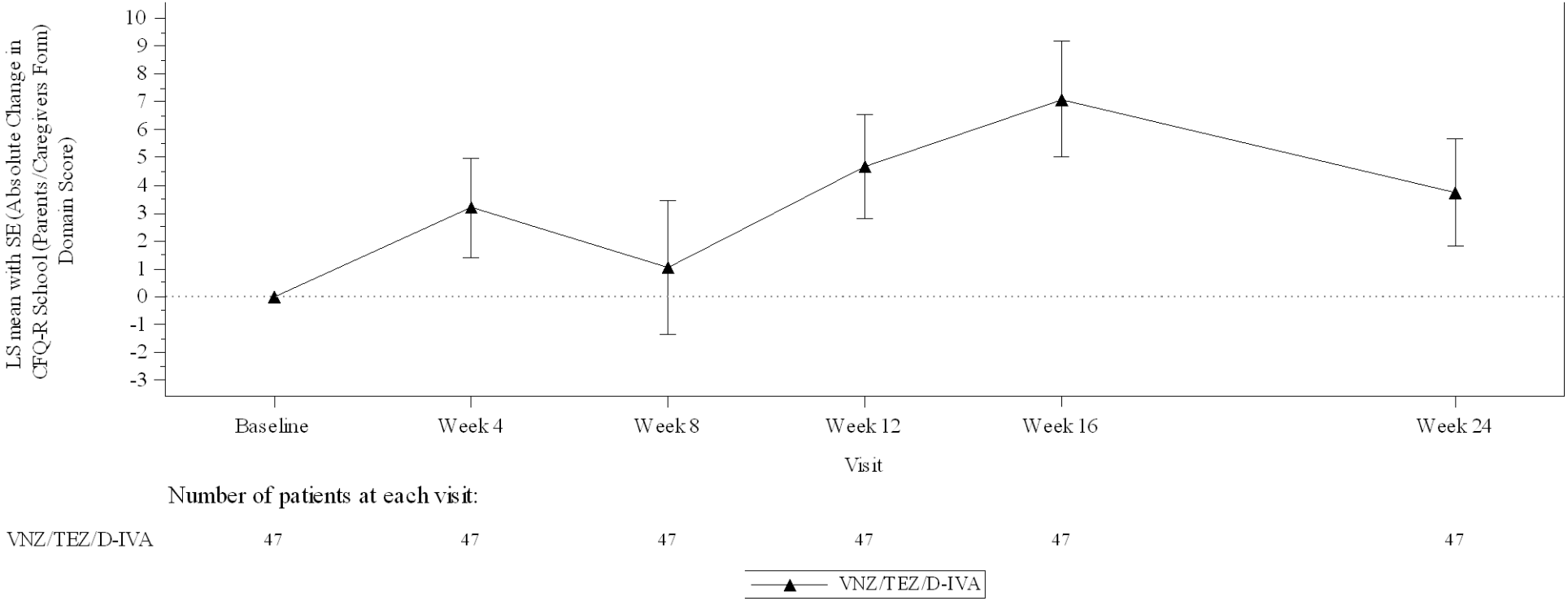
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- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R School (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Sex = Female



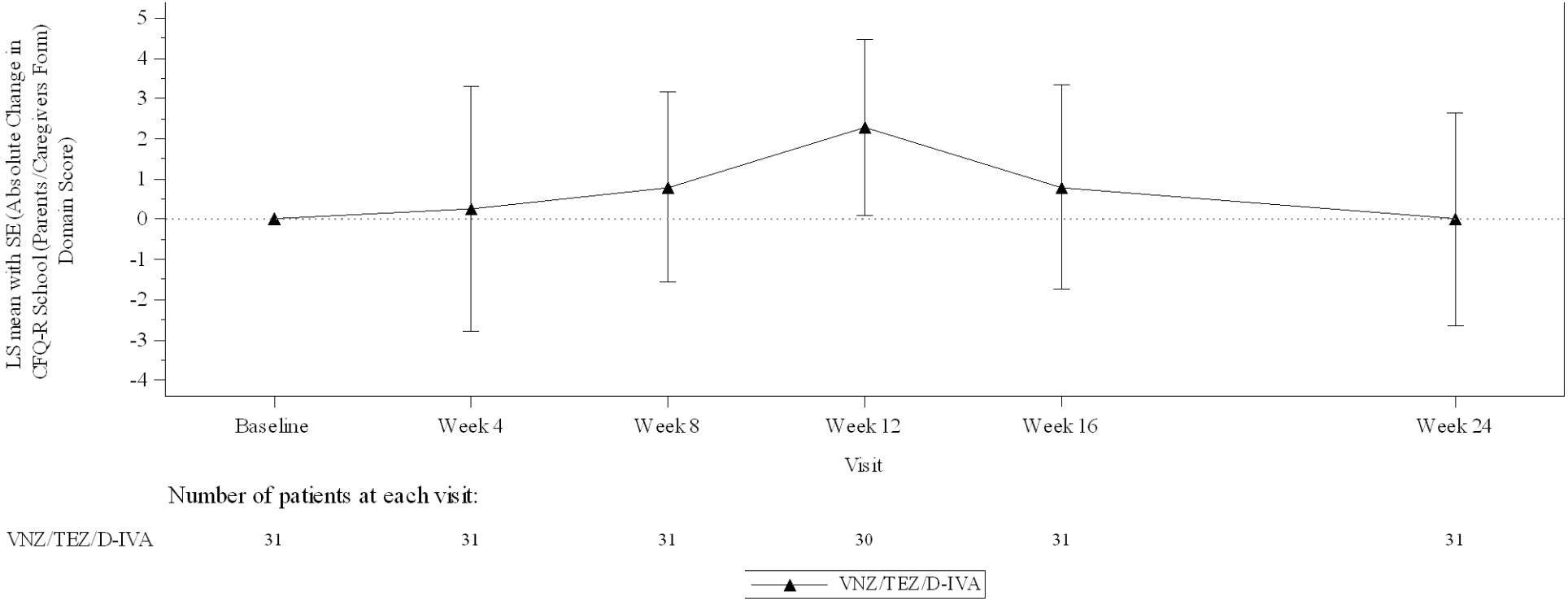
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Region = North America



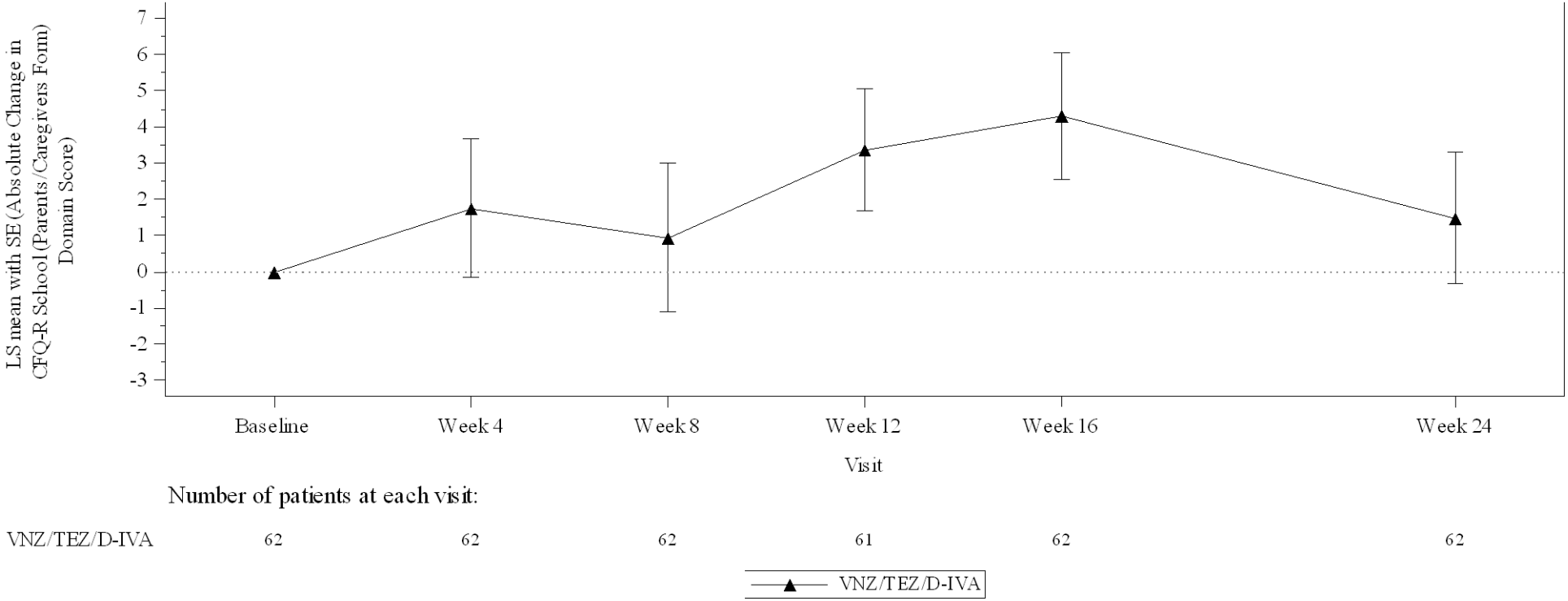
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: School (Parents/Caregivers Form)
Region = Rest of World



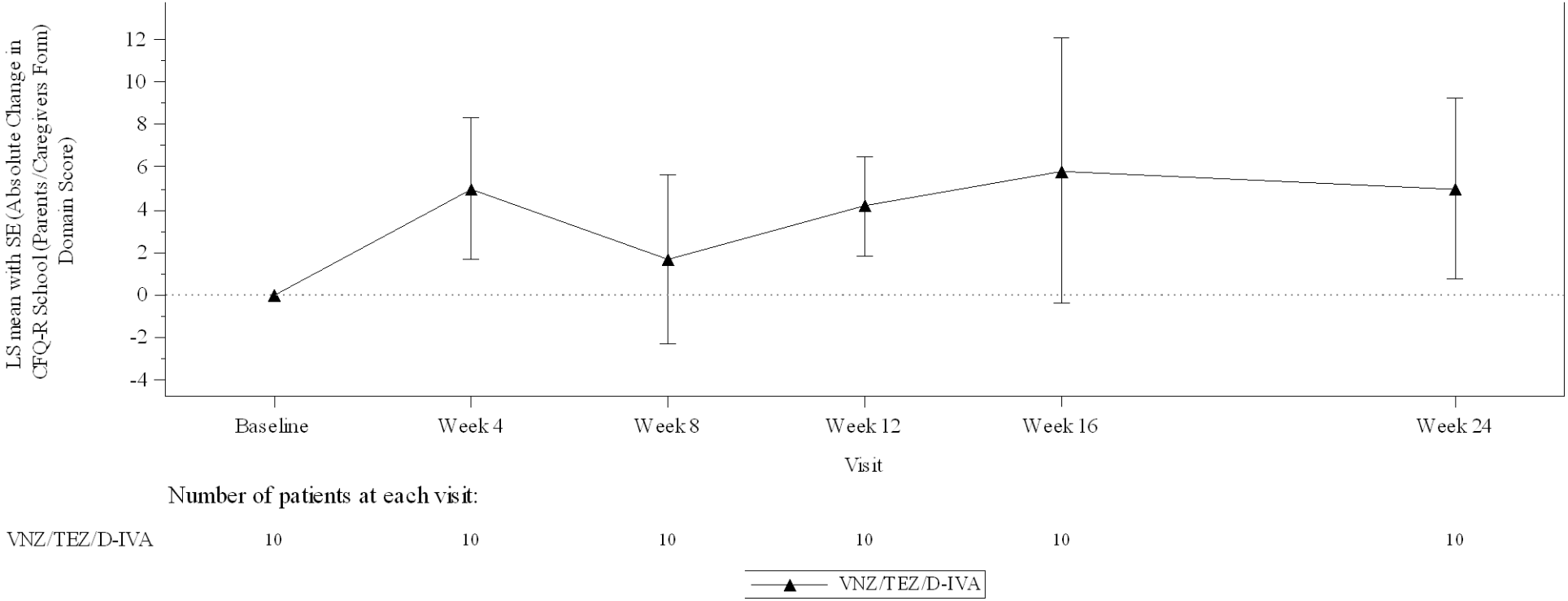
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



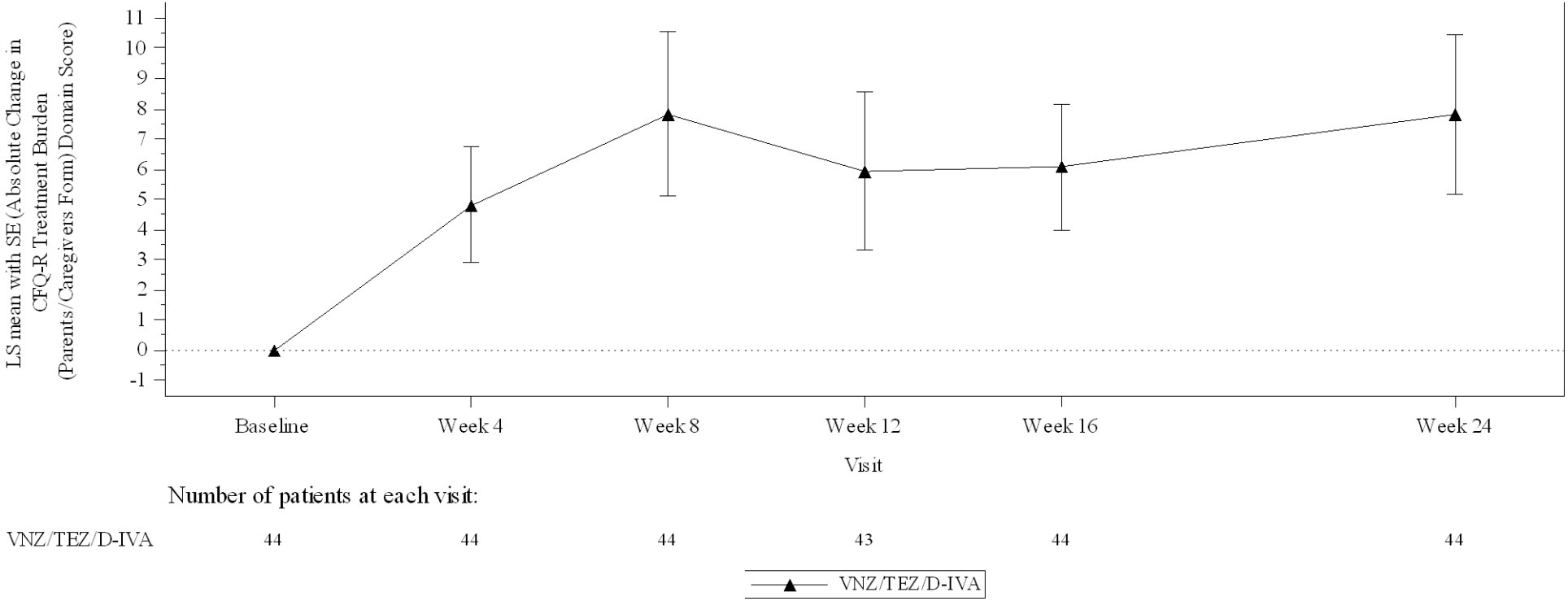
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: School (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



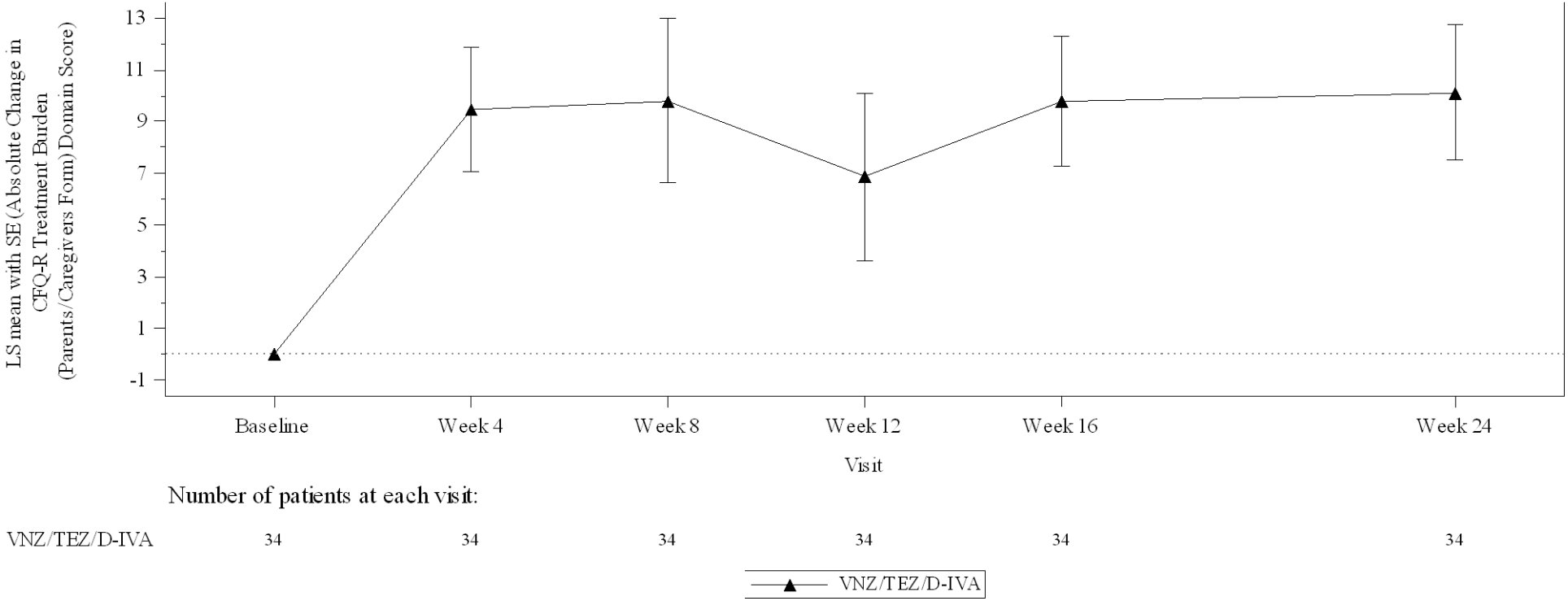
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Male



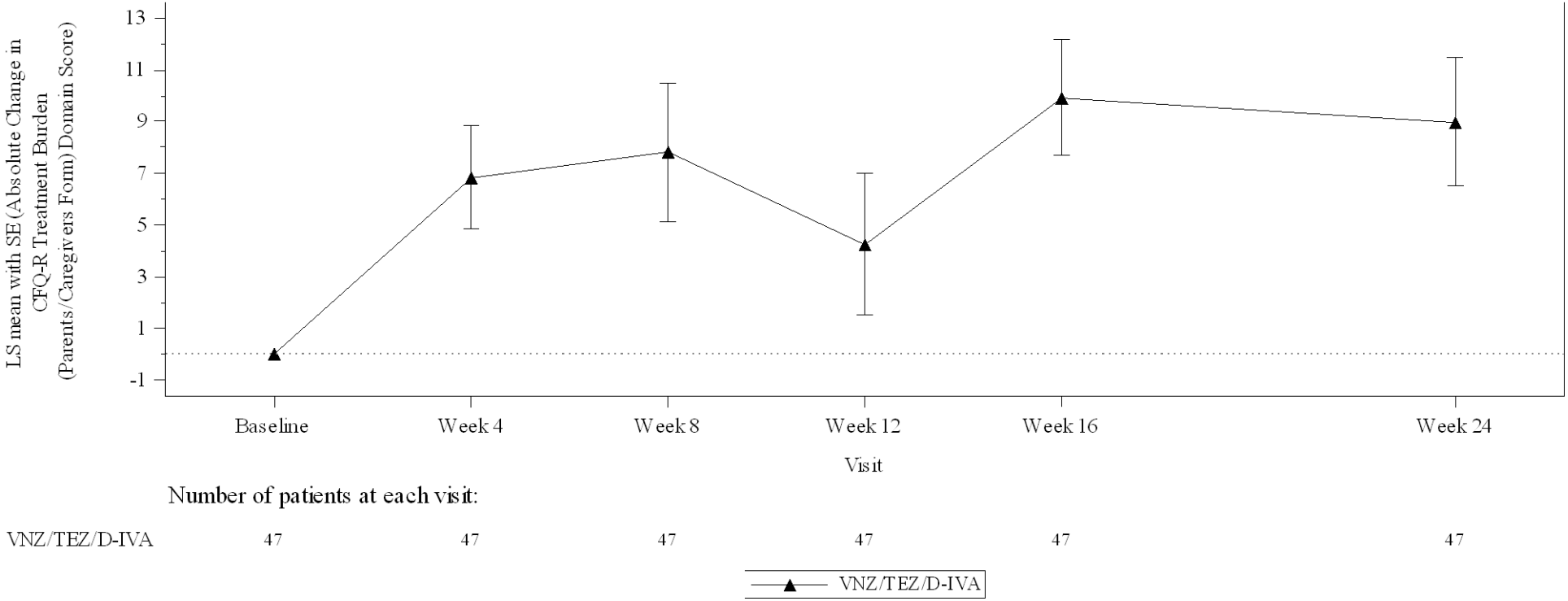
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- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Sex = Female



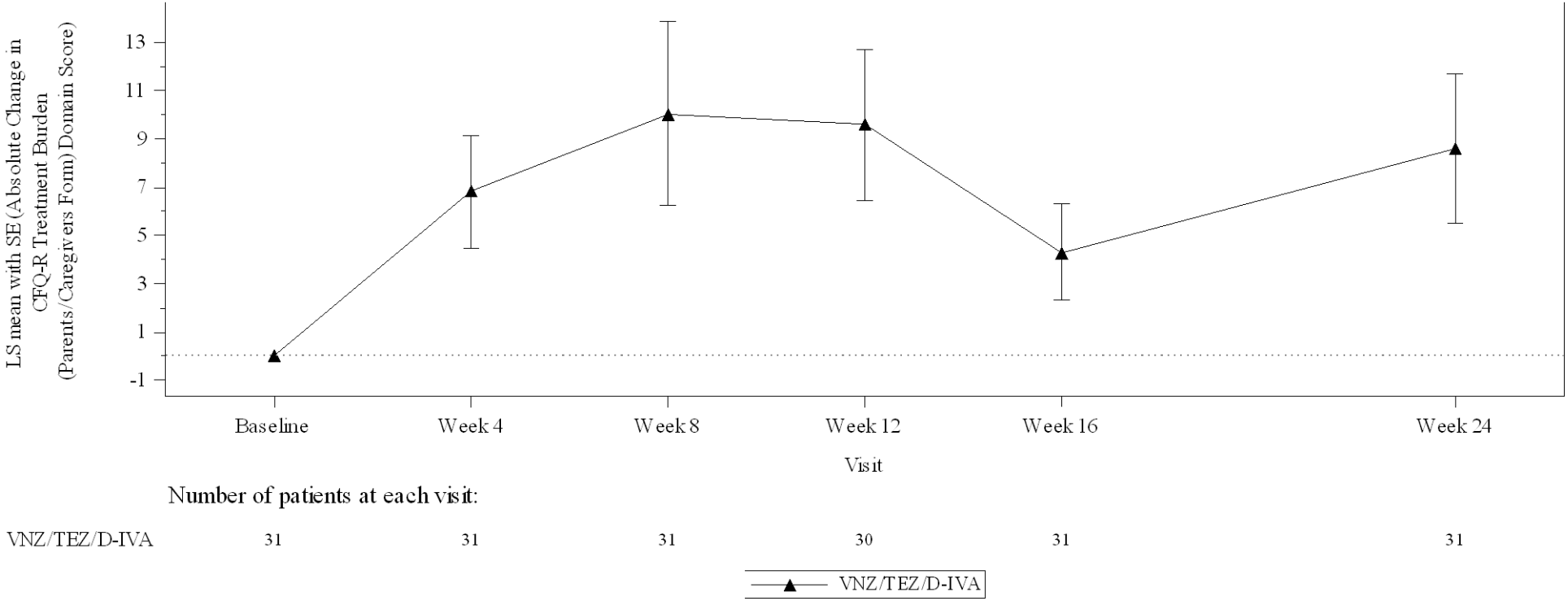
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Region = North America



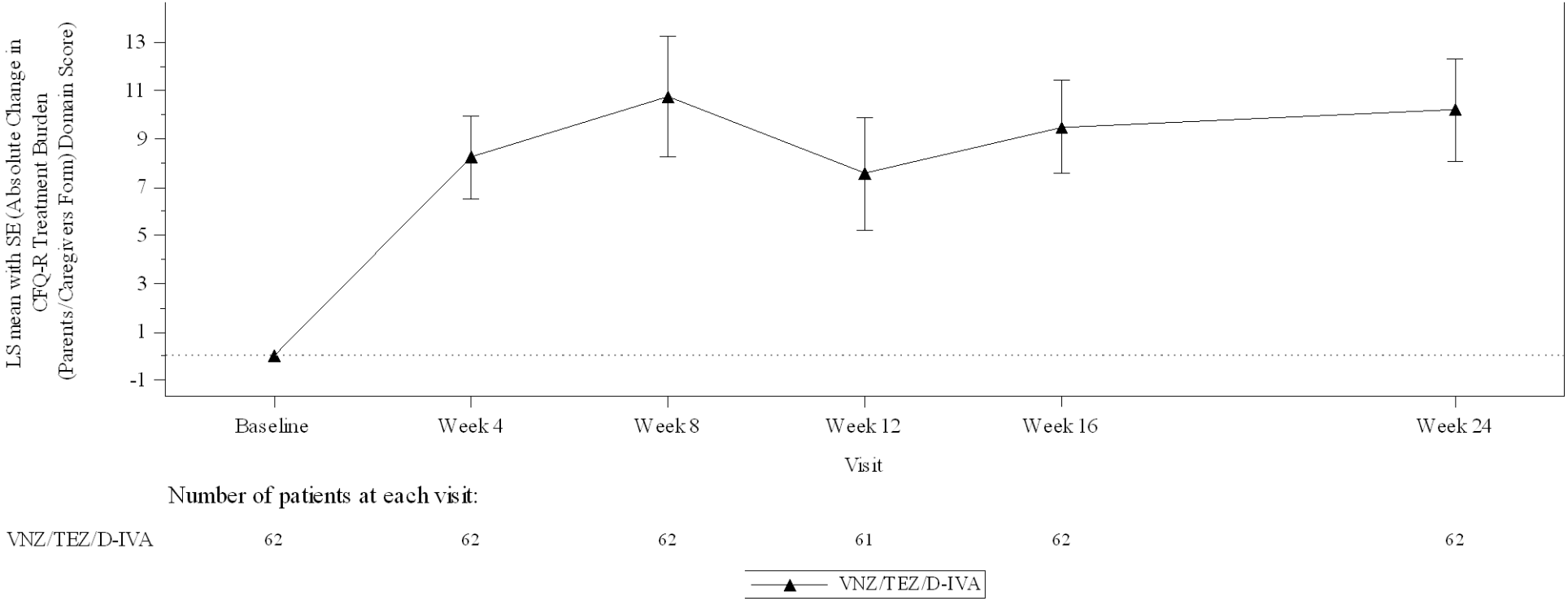
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
Region = Rest of World



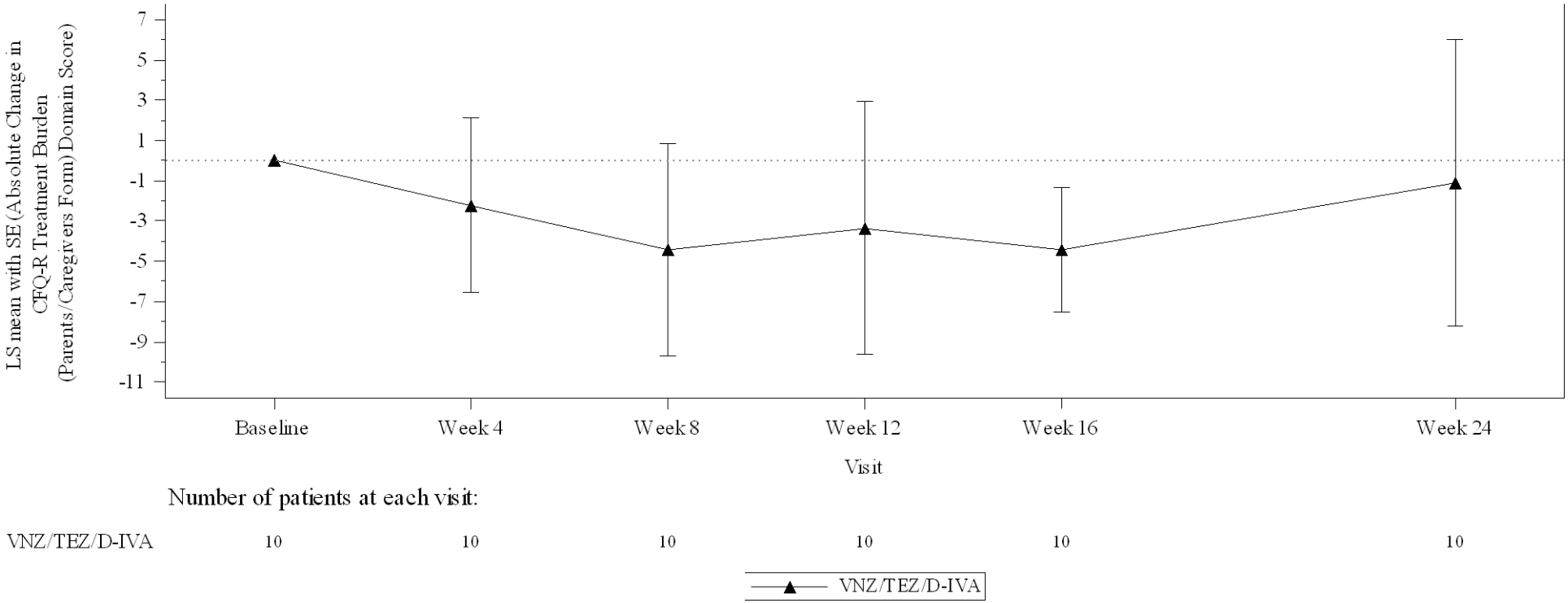
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



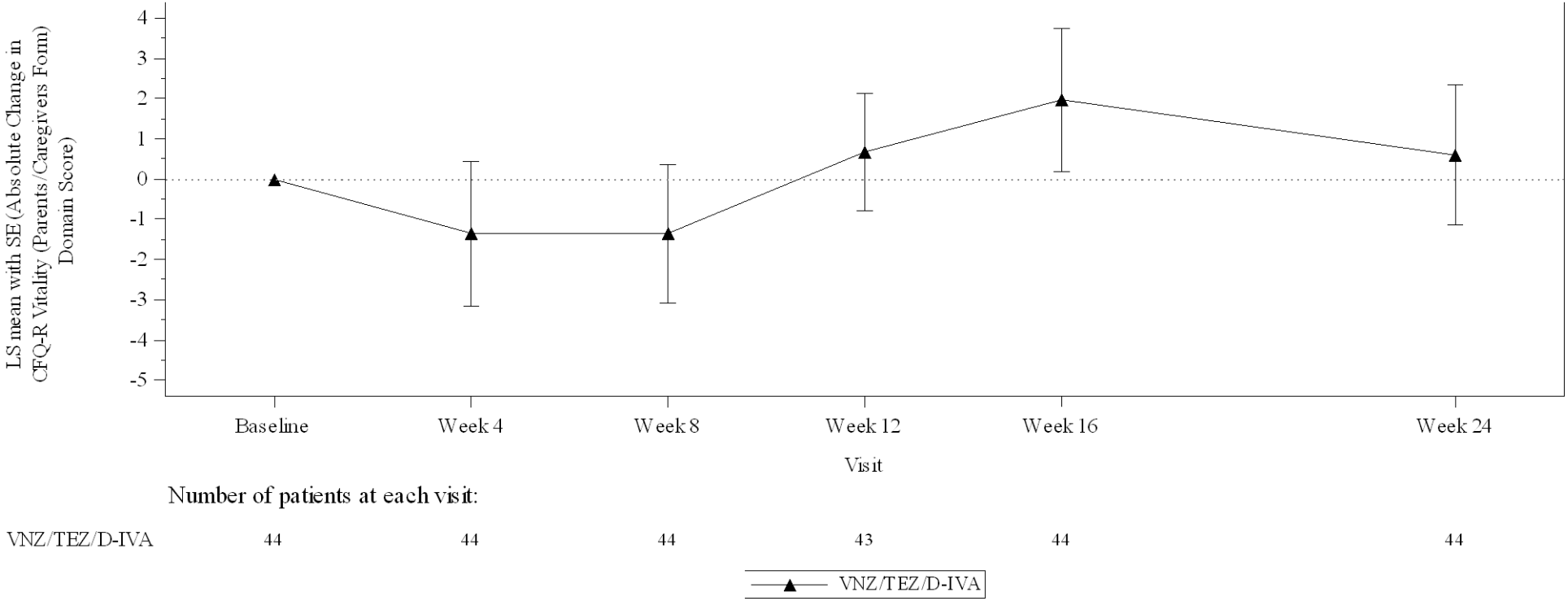
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Treatment Burden (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



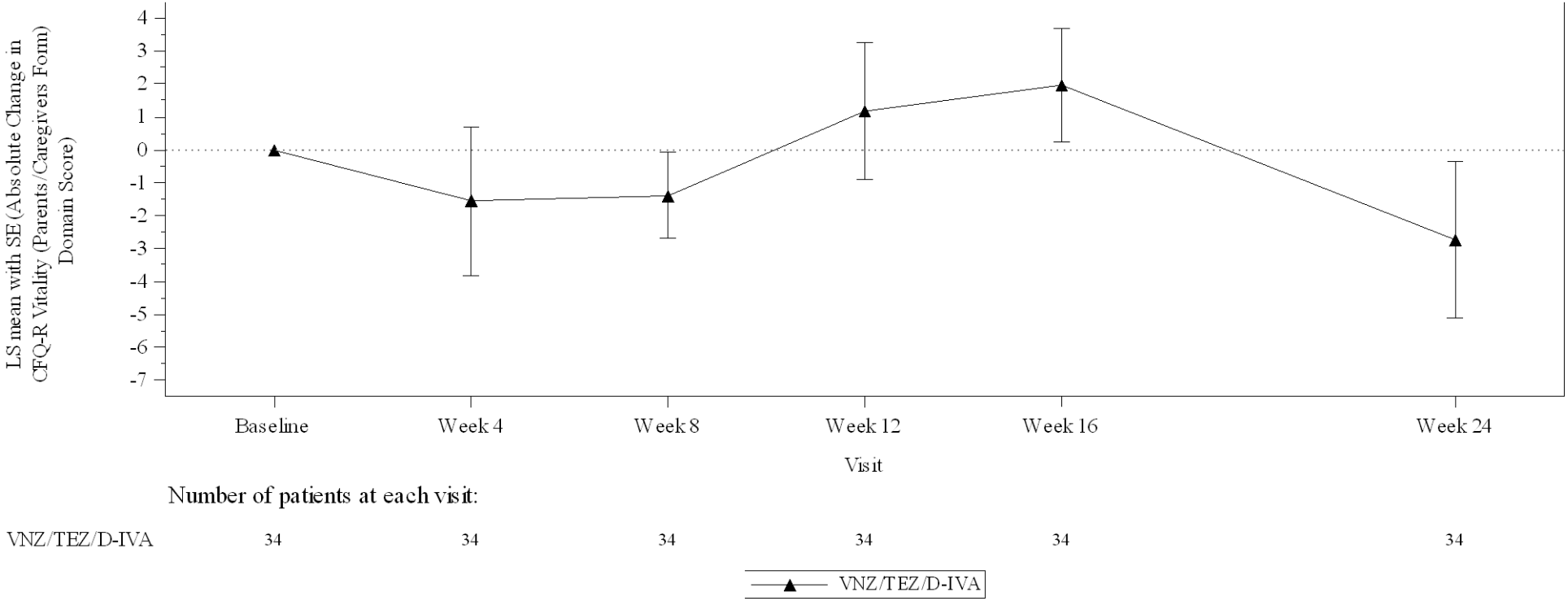
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Sex = Male



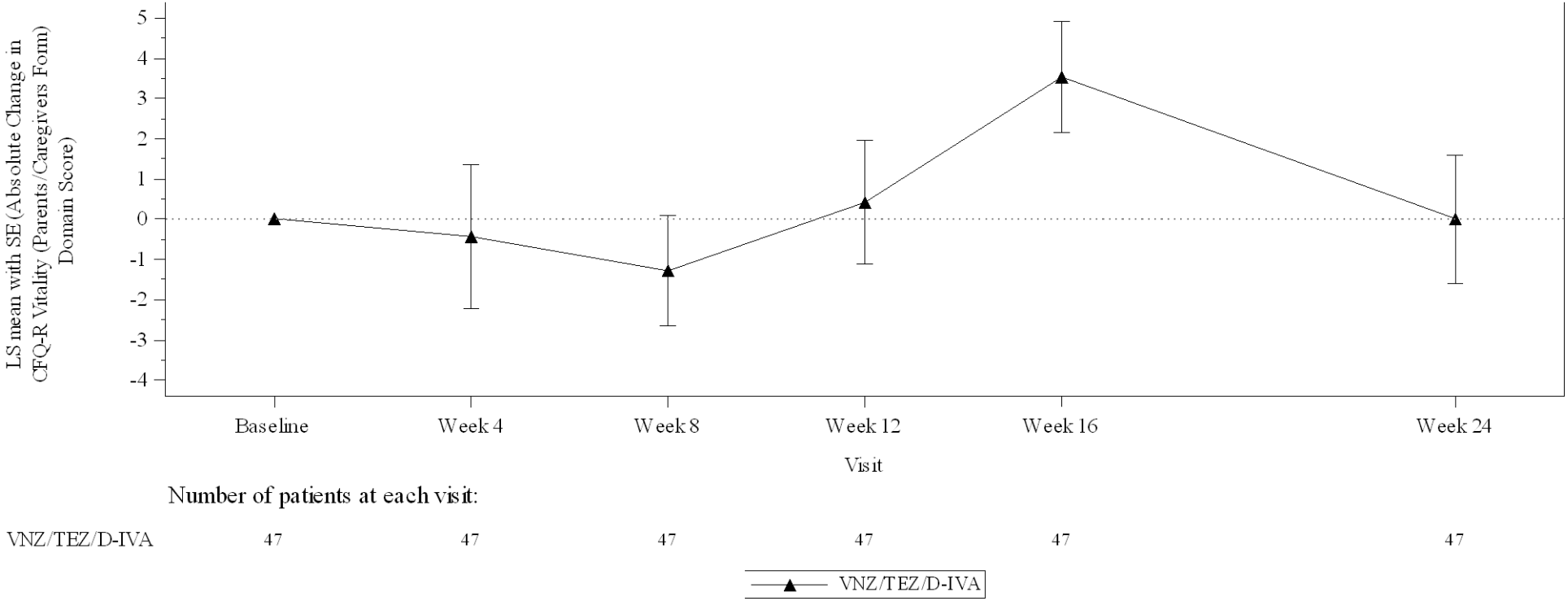
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Sex = Female



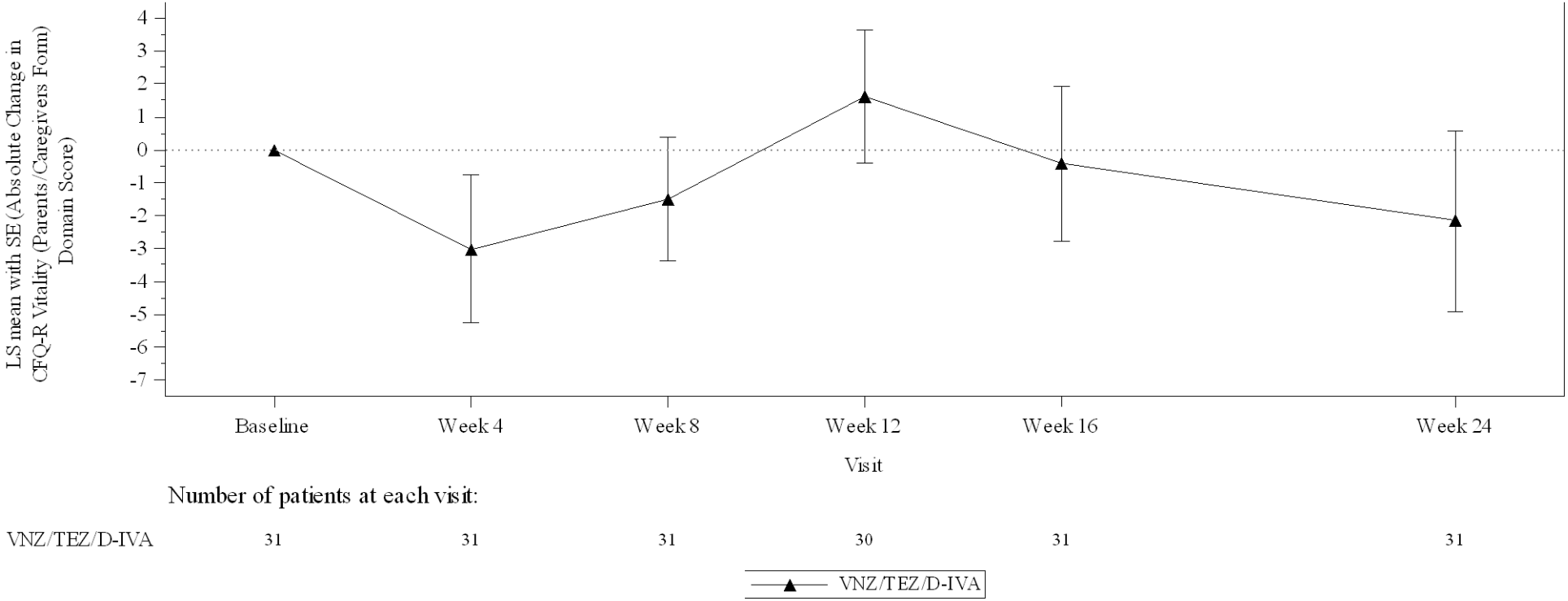
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Region = North America



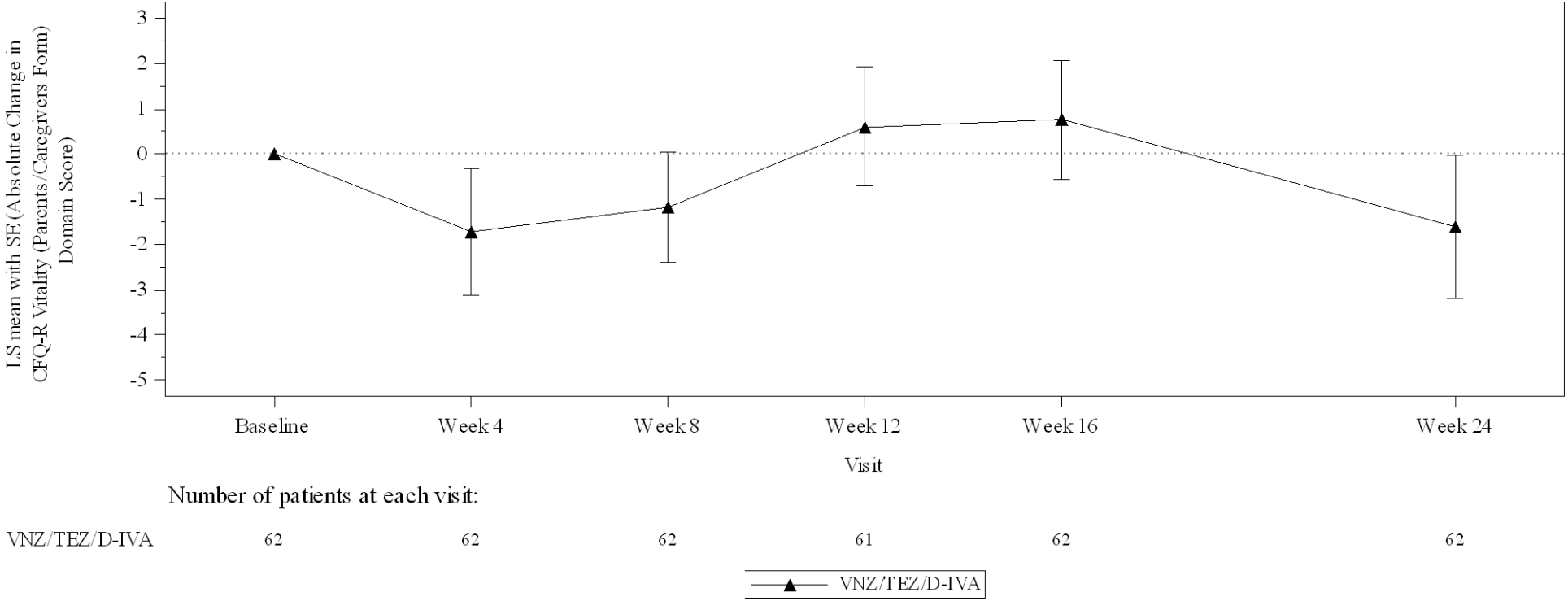
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
Region = Rest of World



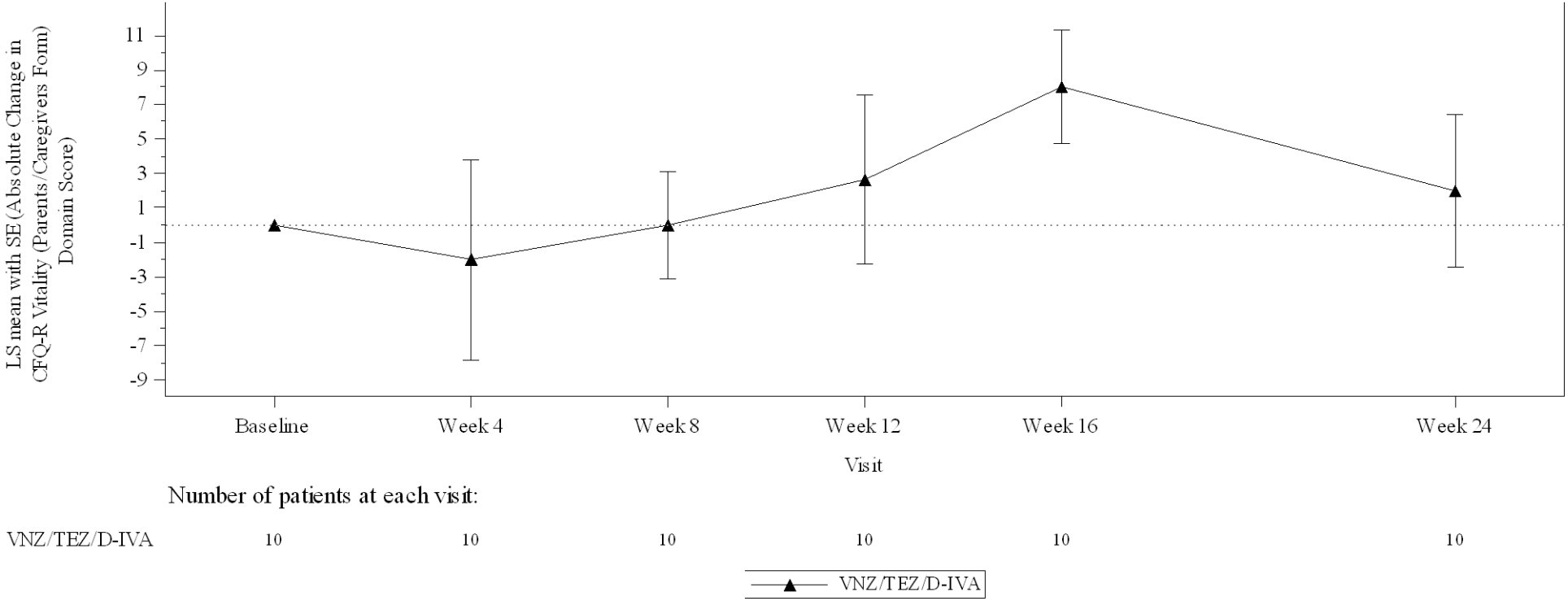
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Vitality (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



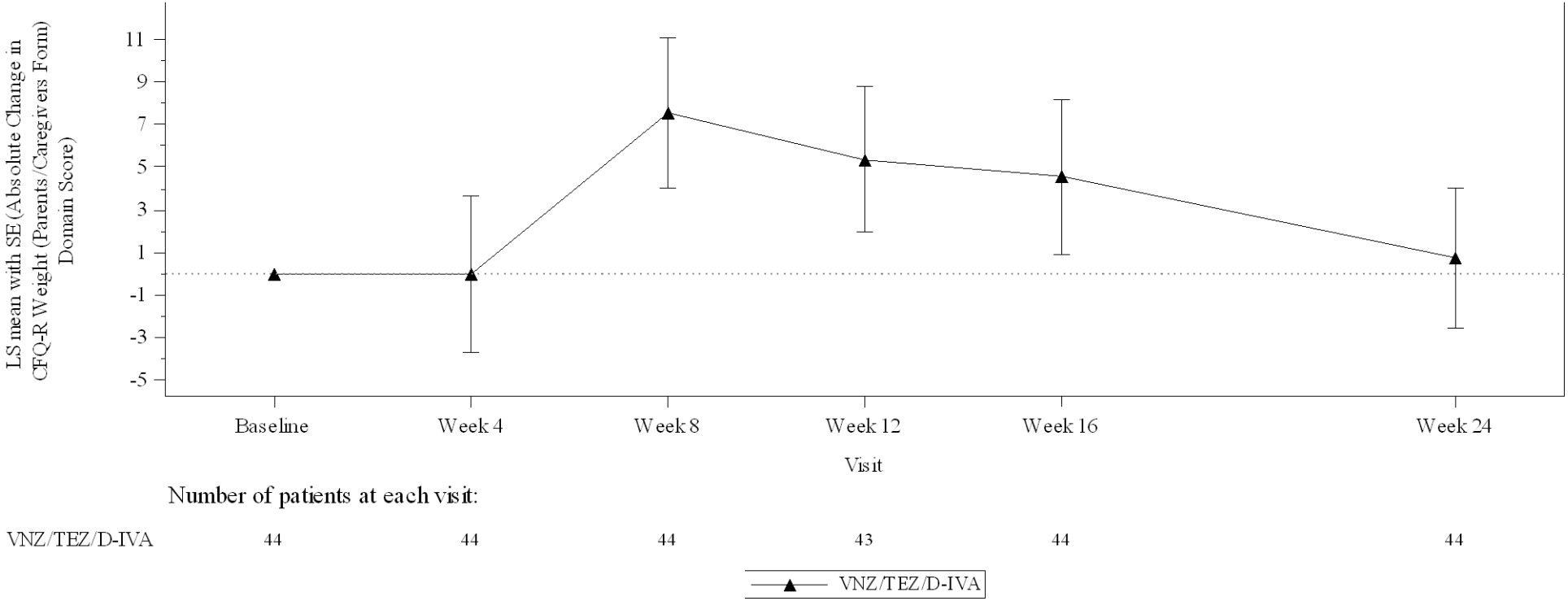
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
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$LCI_{2.5}$ at baseline ≥7.5



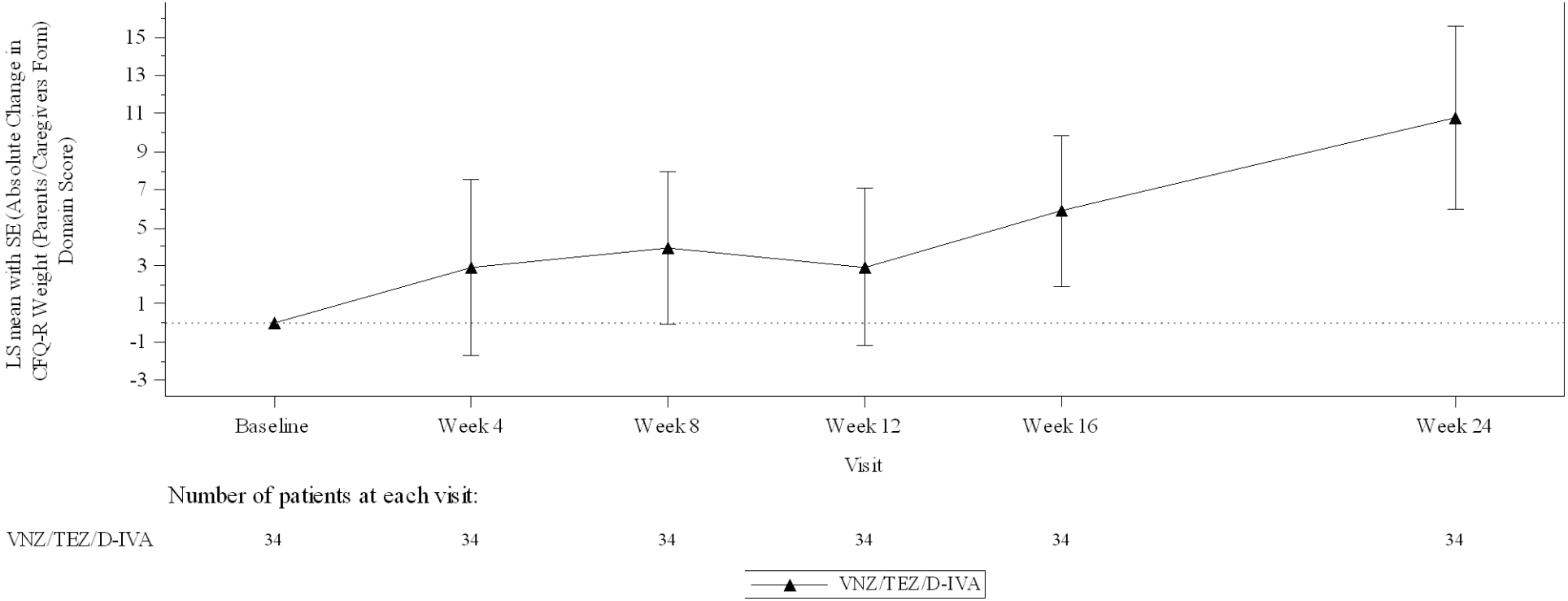
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Sex = Male



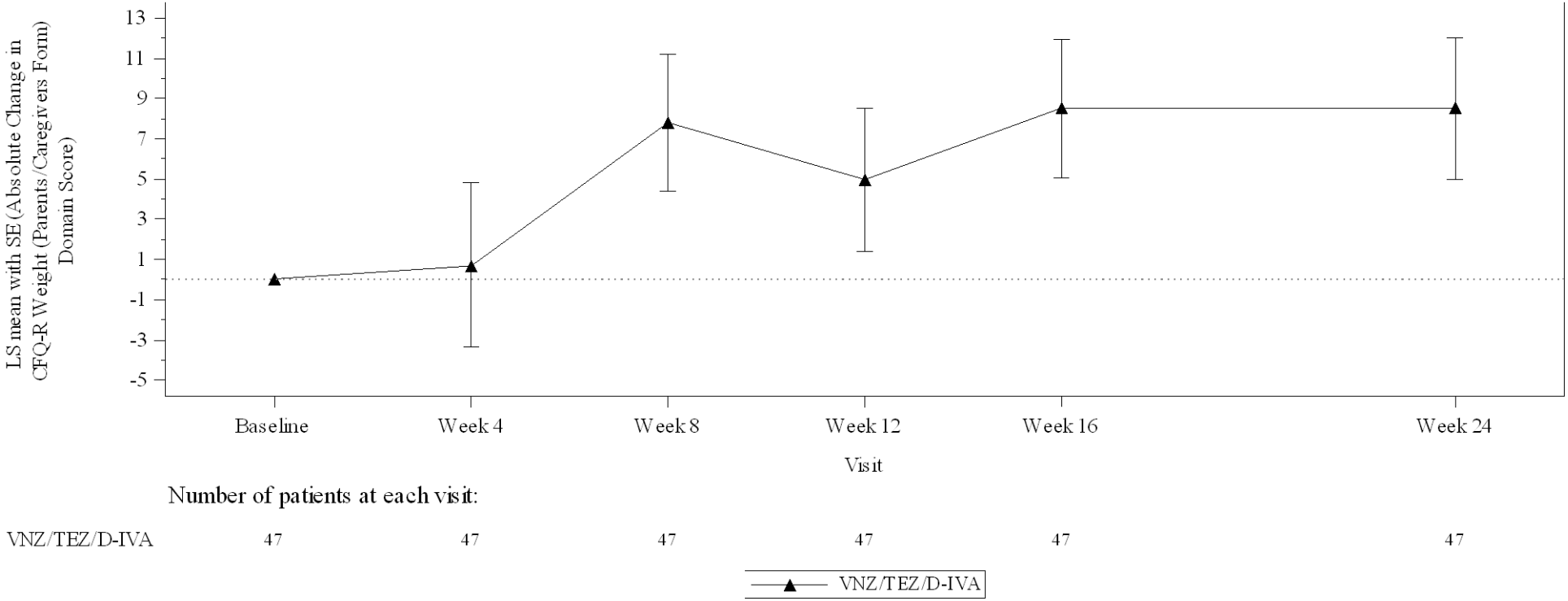
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Sex = Female



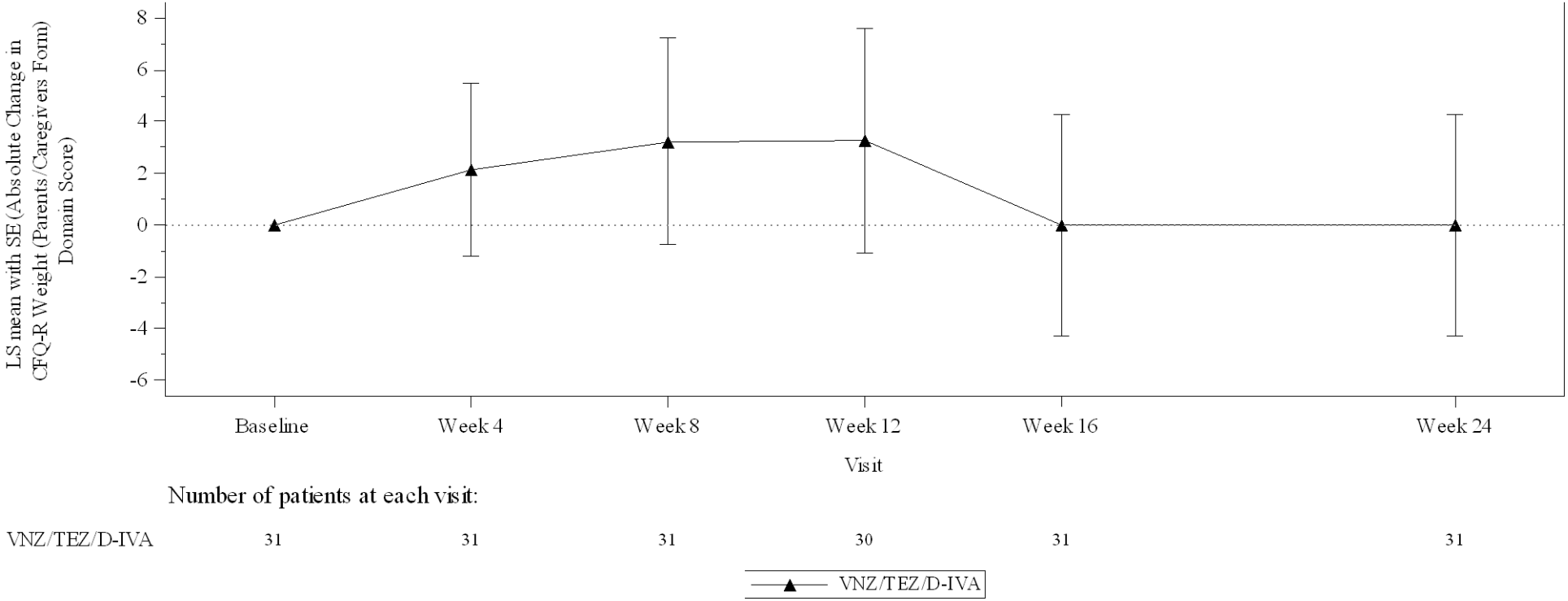
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Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
Region = North America



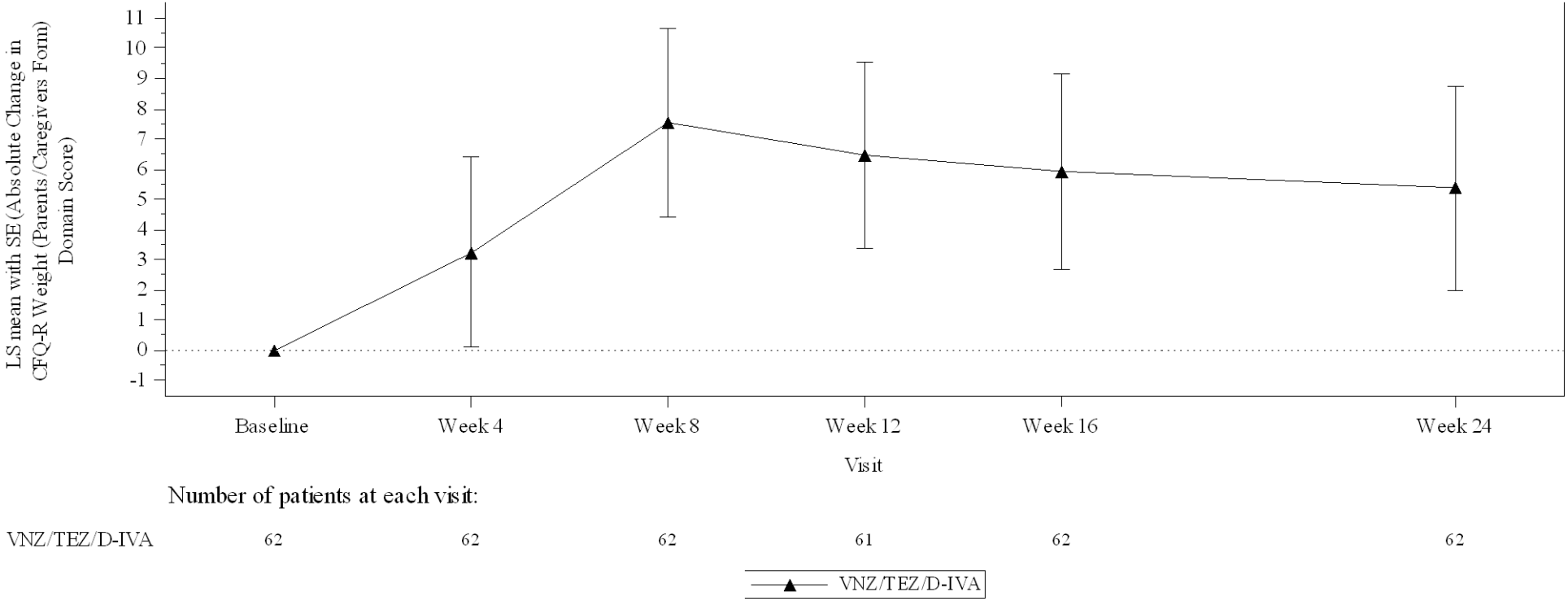
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
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Region = Rest of World



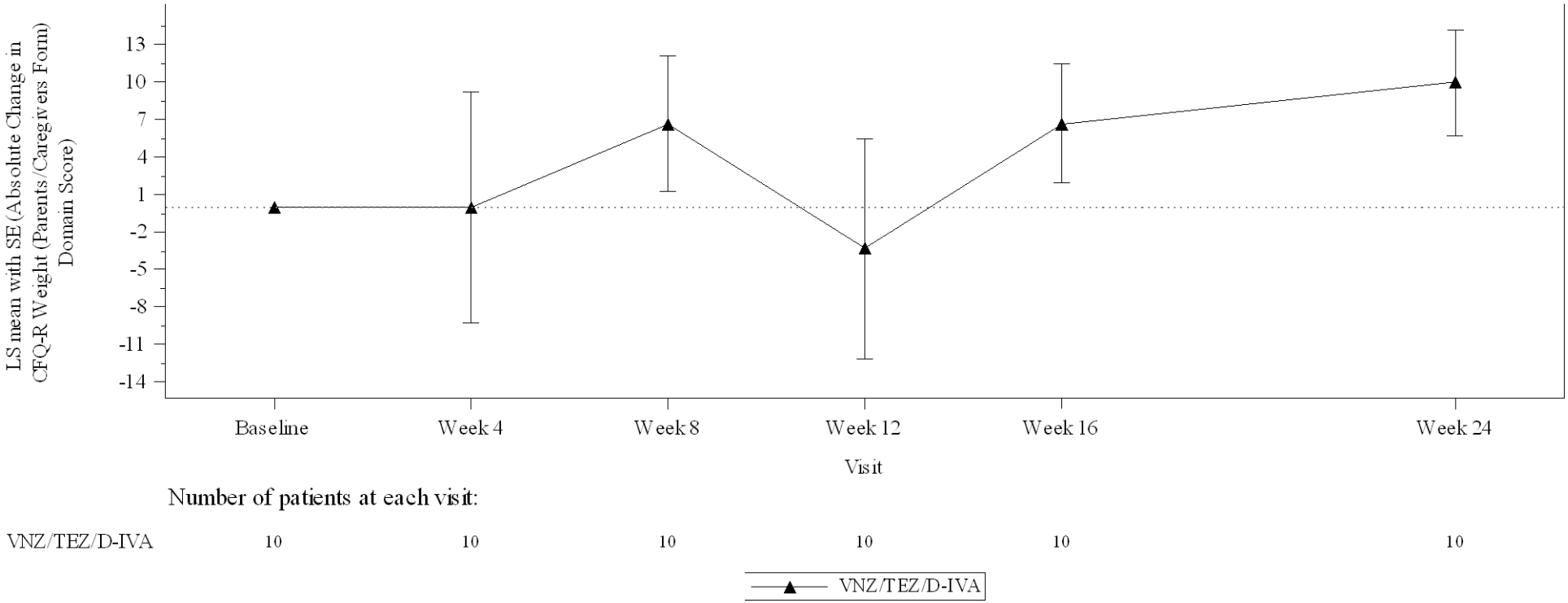
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Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline <7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

Figure 3.2.2.10.6
Study VX21-121-105: Plot of Absolute Change from Baseline in CFQ-R Domain Score (Parent's Version) at Each Visit up to Week 24 by Subgroups
Full Analysis Set
Domain: Weight (Parents/Caregivers Form)
$LCI_{2.5}$ at baseline ≥7.5



- Subgroup Criteria: subgroup analyses are performed only when the following conditions are fulfilled 1)at least 10 subjects in each subgroup (per factor), and 2)for dichotomous endpoints, at least 10 subjects with events occurred in at least one of subgroups (per factor).
- Baseline is defined as the pre-dose Day 1 value.
- MMRM includes data from all available visits up to Week 24. The model includes fixed categorical effect visit and genotype group (F/MF vs rest), with baseline CFQ-R Weight (Parents/Caregivers Form) Domain score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger

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Figure 14.2.4.2c1a.ph MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Parent's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

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Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Physical

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	75
Mean (SD)	87.3 (13.0)
Absolute change at Week 4	
n	75
LS mean (SE)	-0.3 (1.3)
95% CI of LS mean	(-3.0, 2.3)
Absolute change at Week 8	
n	75
LS mean (SE)	-1.8 (1.8)
95% CI of LS mean	(-5.4, 1.8)
Absolute change at Week 12	
n	74
LS mean (SE)	-1.0 (1.9)
95% CI of LS mean	(-4.7, 2.7)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Physical

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	75
LS mean (SE)	1.2 (1.7)
95% CI of LS mean	(-2.1, 4.5)
Absolute change at Week 24	
n	75
LS mean (SE)	3.3 (1.5)
95% CI of LS mean	(0.2, 6.3)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Physical

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	69
LS mean (SE)	-1.8 (2.0)
95% CI of LS mean	(-5.8, 2.2)
Absolute change at OL Part A Week 48	
n	68
LS mean (SE)	2.3 (1.5)
95% CI of LS mean	(-0.7, 5.3)
Absolute change at OL Part A Week 72	
n	68
LS mean (SE)	5.1 (1.3)
95% CI of LS mean	(2.6, 7.7)
Absolute change at OL Part A Week 96	
n	63
LS mean (SE)	4.5 (1.7)
95% CI of LS mean	(1.1, 8.0)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Physical

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	71
LS mean (SE)	2.5 (1.1)
95% CI of LS mean	(0.3, 4.8)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Vitality

	VNZ/TEZ/D-IVA

No data met the criteria for this table.

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Emotion

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	75
Mean (SD)	76.5 (14.7)
Absolute change at Week 4	
n	75
LS mean (SE)	0.0 (1.4)
95% CI of LS mean	(-2.9, 2.8)
Absolute change at Week 8	
n	75
LS mean (SE)	1.4 (1.5)
95% CI of LS mean	(-1.5, 4.3)
Absolute change at Week 12	
n	74
LS mean (SE)	3.0 (1.6)
95% CI of LS mean	(-0.2, 6.2)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Emotion

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	75
LS mean (SE)	3.7 (1.7)
95% CI of LS mean	(0.3, 7.0)
Absolute change at Week 24	
n	75
LS mean (SE)	3.7 (1.3)
95% CI of LS mean	(1.1, 6.3)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Emotion

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	69
LS mean (SE)	2.0 (1.7)
95% CI of LS mean	(-1.3, 5.3)
Absolute change at OL Part A Week 48	
n	68
LS mean (SE)	3.5 (1.5)
95% CI of LS mean	(0.5, 6.6)
Absolute change at OL Part A Week 72	
n	68
LS mean (SE)	2.4 (1.5)
95% CI of LS mean	(-0.7, 5.4)
Absolute change at OL Part A Week 96	
n	63
LS mean (SE)	3.6 (1.6)
95% CI of LS mean	(0.4, 6.9)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Emotion

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	71
LS mean (SE)	2.9 (1.3)
95% CI of LS mean	(0.3, 5.5)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Body

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	75
Mean (SD)	82.7 (23.5)
Absolute change at Week 4	
n	75
LS mean (SE)	2.2 (2.2)
95% CI of LS mean	(-2.1, 6.5)
Absolute change at Week 8	
n	75
LS mean (SE)	4.9 (2.0)
95% CI of LS mean	(0.8, 8.9)
Absolute change at Week 12	
n	74
LS mean (SE)	5.9 (1.8)
95% CI of LS mean	(2.3, 9.4)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Body

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	75
LS mean (SE)	8.6 (1.5)
95% CI of LS mean	(5.6, 11.6)
Absolute change at Week 24	
n	75
LS mean (SE)	5.6 (2.2)
95% CI of LS mean	(1.2, 10.0)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Body

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	69
LS mean (SE)	7.0 (1.3)
95% CI of LS mean	(4.4, 9.6)
Absolute change at OL Part A Week 48	
n	68
LS mean (SE)	4.8 (2.2)
95% CI of LS mean	(0.4, 9.2)
Absolute change at OL Part A Week 72	
n	68
LS mean (SE)	6.8 (1.7)
95% CI of LS mean	(3.4, 10.1)
Absolute change at OL Part A Week 96	
n	63
LS mean (SE)	4.0 (2.1)
95% CI of LS mean	(-0.2, 8.2)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Body

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	71
LS mean (SE)	5.6 (1.4)
95% CI of LS mean	(2.9, 8.4)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
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- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Eat

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	75
Mean (SD)	81.5 (21.4)
Absolute change at Week 4	
n	75
LS mean (SE)	0.3 (2.0)
95% CI of LS mean	(-3.8, 4.4)
Absolute change at Week 8	
n	75
LS mean (SE)	-1.6 (2.2)
95% CI of LS mean	(-6.1, 2.8)
Absolute change at Week 12	
n	74
LS mean (SE)	1.9 (2.2)
95% CI of LS mean	(-2.6, 6.4)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Eat

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	75
LS mean (SE)	3.0 (2.2)
95% CI of LS mean	(-1.4, 7.3)
Absolute change at Week 24	
n	75
LS mean (SE)	7.2 (1.7)
95% CI of LS mean	(3.9, 10.6)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Eat

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	69
LS mean (SE)	2.6 (2.1)
95% CI of LS mean	(-1.6, 6.8)
Absolute change at OL Part A Week 48	
n	68
LS mean (SE)	6.0 (1.6)
95% CI of LS mean	(2.9, 9.2)
Absolute change at OL Part A Week 72	
n	68
LS mean (SE)	8.3 (1.6)
95% CI of LS mean	(5.0, 11.5)
Absolute change at OL Part A Week 96	
n	63
LS mean (SE)	7.0 (2.0)
95% CI of LS mean	(3.0, 10.9)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Eat

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	71
LS mean (SE)	6.0 (1.2)
95% CI of LS mean	(3.5, 8.4)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Treatment Burden

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	75
Mean (SD)	76.4 (21.2)
Absolute change at Week 4	
n	75
LS mean (SE)	2.6 (1.7)
95% CI of LS mean	(-0.8, 6.0)
Absolute change at Week 8	
n	75
LS mean (SE)	3.1 (1.8)
95% CI of LS mean	(-0.5, 6.8)
Absolute change at Week 12	
n	74
LS mean (SE)	4.3 (1.8)
95% CI of LS mean	(0.8, 7.9)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
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- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Treatment Burden

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	75
LS mean (SE)	3.1 (2.3)
95% CI of LS mean	(-1.6, 7.7)
Absolute change at Week 24	
n	75
LS mean (SE)	5.3 (2.1)
95% CI of LS mean	(1.2, 9.4)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Treatment Burden

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	69
LS mean (SE)	5.4 (1.7)
95% CI of LS mean	(2.0, 8.8)
Absolute change at OL Part A Week 48	
n	68
LS mean (SE)	3.3 (2.1)
95% CI of LS mean	(-1.0, 7.6)
Absolute change at OL Part A Week 72	
n	68
LS mean (SE)	4.7 (1.9)
95% CI of LS mean	(1.0, 8.4)
Absolute change at OL Part A Week 96	
n	63
LS mean (SE)	5.5 (2.0)
95% CI of LS mean	(1.5, 9.5)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Treatment Burden

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	71
LS mean (SE)	4.7 (1.4)
95% CI of LS mean	(1.9, 7.6)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Health Perceptions

	VNZ/TEZ/D-IVA

No data met the criteria for this table.

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Weight

	VNZ/TEZ/D-IVA

No data met the criteria for this table.

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- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
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Table 2.2.1
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Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Digestion

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	74
Mean (SD)	79.7 (21.2)
Absolute change at Week 4	
n	74
LS mean (SE)	-2.3 (3.0)
95% CI of LS mean	(-8.2, 3.7)
Absolute change at Week 8	
n	74
LS mean (SE)	0.0 (2.7)
95% CI of LS mean	(-5.5, 5.5)
Absolute change at Week 12	
n	73
LS mean (SE)	0.3 (2.2)
95% CI of LS mean	(-4.0, 4.7)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
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- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Digestion

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	74
LS mean (SE)	4.0 (2.4)
95% CI of LS mean	(-0.8, 8.9)
Absolute change at Week 24	
n	74
LS mean (SE)	4.9 (2.5)
95% CI of LS mean	(-0.1, 10.0)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Digestion

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	67
LS mean (SE)	1.2 (2.8)
95% CI of LS mean	(-4.3, 6.8)
Absolute change at OL Part A Week 48	
n	67
LS mean (SE)	0.3 (2.6)
95% CI of LS mean	(-4.9, 5.6)
Absolute change at OL Part A Week 72	
n	67
LS mean (SE)	0.4 (3.2)
95% CI of LS mean	(-5.9, 6.8)
Absolute change at OL Part A Week 96	
n	62
LS mean (SE)	-0.7 (3.4)
95% CI of LS mean	(-7.4, 6.1)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
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Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Digestion

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	70
LS mean (SE)	0.3 (2.4)
95% CI of LS mean	(-4.4, 5.0)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
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Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Role

	VNZ/TEZ/D-IVA

No data met the criteria for this table.

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
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- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Social

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	75
Mean (SD)	67.0 (19.2)
Absolute change at Week 4	
n	75
LS mean (SE)	1.1 (1.6)
95% CI of LS mean	(-2.1, 4.3)
Absolute change at Week 8	
n	75
LS mean (SE)	2.0 (1.8)
95% CI of LS mean	(-1.6, 5.7)
Absolute change at Week 12	
n	74
LS mean (SE)	5.4 (1.7)
95% CI of LS mean	(2.0, 8.8)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

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MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Social

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	75
LS mean (SE)	5.7 (2.0)
95% CI of LS mean	(1.7, 9.7)
Absolute change at Week 24	
n	75
LS mean (SE)	8.7 (1.7)
95% CI of LS mean	(5.3, 12.0)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Social

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	69
LS mean (SE)	5.9 (1.9)
95% CI of LS mean	(2.1, 9.8)
Absolute change at OL Part A Week 48	
n	68
LS mean (SE)	8.6 (1.8)
95% CI of LS mean	(5.1, 12.1)
Absolute change at OL Part A Week 72	
n	68
LS mean (SE)	6.4 (2.1)
95% CI of LS mean	(2.3, 10.6)
Absolute change at OL Part A Week 96	
n	63
LS mean (SE)	6.0 (1.8)
95% CI of LS mean	(2.4, 9.6)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.1
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Child's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set - Cohort 1

Domain: Social

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	71
LS mean (SE)	6.7 (1.6)
95% CI of LS mean	(3.6, 9.9)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	91.9 (13.3)
Absolute change at Week 4	
n	78
LS mean (SE)	-0.9 (1.3)
95% CI of LS mean	(-3.4, 1.7)
Absolute change at Week 8	
n	78
LS mean (SE)	-1.8 (1.3)
95% CI of LS mean	(-4.3, 0.8)
Absolute change at Week 12	
n	77
LS mean (SE)	2.5 (0.8)
95% CI of LS mean	(0.9, 4.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	2.3 (1.2)
95% CI of LS mean	(-0.1, 4.7)
Absolute change at Week 24	
n	78
LS mean (SE)	0.3 (1.3)
95% CI of LS mean	(-2.3, 2.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	74
LS mean (SE)	0.2 (1.5)
95% CI of LS mean	(-2.8, 3.3)
Absolute change at OL Part A Week 48	
n	72
LS mean (SE)	0.9 (1.1)
95% CI of LS mean	(-1.3, 3.2)
Absolute change at OL Part A Week 72	
n	70
LS mean (SE)	-0.8 (1.9)
95% CI of LS mean	(-4.7, 3.1)
Absolute change at OL Part A Week 96	
n	65
LS mean (SE)	0.4 (1.5)
95% CI of LS mean	(-2.7, 3.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Physical (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	74
LS mean (SE)	0.2 (1.1)
95% CI of LS mean	(-2.0, 2.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	76.7 (12.5)
Absolute change at Week 4	
n	78
LS mean (SE)	-1.5 (1.4)
95% CI of LS mean	(-4.2, 1.3)
Absolute change at Week 8	
n	78
LS mean (SE)	-1.4 (1.1)
95% CI of LS mean	(-3.6, 0.8)
Absolute change at Week 12	
n	77
LS mean (SE)	0.9 (1.2)
95% CI of LS mean	(-1.5, 3.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	2.0 (1.3)
95% CI of LS mean	(-0.5, 4.5)
Absolute change at Week 24	
n	78
LS mean (SE)	-0.9 (1.4)
95% CI of LS mean	(-3.7, 2.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	74
LS mean (SE)	-1.8 (1.6)
95% CI of LS mean	(-5.1, 1.4)
Absolute change at OL Part A Week 48	
n	72
LS mean (SE)	1.4 (1.3)
95% CI of LS mean	(-1.1, 4.0)
Absolute change at OL Part A Week 72	
n	70
LS mean (SE)	-0.4 (1.7)
95% CI of LS mean	(-3.8, 3.0)
Absolute change at OL Part A Week 96	
n	65
LS mean (SE)	0.8 (1.7)
95% CI of LS mean	(-2.7, 4.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Vitality (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	74
LS mean (SE)	0.0 (1.1)
95% CI of LS mean	(-2.2, 2.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	86.5 (12.9)
Absolute change at Week 4	
n	78
LS mean (SE)	0.5 (1.1)
95% CI of LS mean	(-1.7, 2.7)
Absolute change at Week 8	
n	78
LS mean (SE)	0.2 (1.0)
95% CI of LS mean	(-1.8, 2.2)
Absolute change at Week 12	
n	77
LS mean (SE)	2.9 (1.0)
95% CI of LS mean	(0.8, 4.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	3.0 (1.1)
95% CI of LS mean	(0.8, 5.1)
Absolute change at Week 24	
n	78
LS mean (SE)	1.9 (1.1)
95% CI of LS mean	(-0.4, 4.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	74
LS mean (SE)	1.6 (1.4)
95% CI of LS mean	(-1.2, 4.5)
Absolute change at OL Part A Week 48	
n	72
LS mean (SE)	0.9 (1.2)
95% CI of LS mean	(-1.6, 3.4)
Absolute change at OL Part A Week 72	
n	70
LS mean (SE)	0.5 (1.5)
95% CI of LS mean	(-2.5, 3.4)
Absolute change at OL Part A Week 96	
n	65
LS mean (SE)	1.2 (1.3)
95% CI of LS mean	(-1.5, 3.9)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Emotion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	74
LS mean (SE)	1.0 (1.0)
95% CI of LS mean	(-1.0, 3.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	80.4 (17.4)
Absolute change at Week 4	
n	78
LS mean (SE)	2.0 (1.6)
95% CI of LS mean	(-1.2, 5.2)
Absolute change at Week 8	
n	78
LS mean (SE)	1.0 (1.7)
95% CI of LS mean	(-2.4, 4.3)
Absolute change at Week 12	
n	77
LS mean (SE)	3.8 (1.4)
95% CI of LS mean	(0.9, 6.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	4.6 (1.6)
95% CI of LS mean	(1.4, 7.8)
Absolute change at Week 24	
n	78
LS mean (SE)	2.2 (1.6)
95% CI of LS mean	(-0.9, 5.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	74
LS mean (SE)	0.7 (1.7)
95% CI of LS mean	(-2.6, 4.0)
Absolute change at OL Part A Week 48	
n	72
LS mean (SE)	2.5 (1.6)
95% CI of LS mean	(-0.7, 5.7)
Absolute change at OL Part A Week 72	
n	70
LS mean (SE)	-0.5 (2.0)
95% CI of LS mean	(-4.4, 3.5)
Absolute change at OL Part A Week 96	
n	65
LS mean (SE)	0.9 (1.7)
95% CI of LS mean	(-2.5, 4.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: School (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	74
LS mean (SE)	0.9 (1.2)
95% CI of LS mean	(-1.6, 3.4)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	80.1 (26.1)
Absolute change at Week 4	
n	78
LS mean (SE)	1.2 (1.7)
95% CI of LS mean	(-2.1, 4.6)
Absolute change at Week 8	
n	78
LS mean (SE)	2.4 (1.8)
95% CI of LS mean	(-1.2, 5.9)
Absolute change at Week 12	
n	77
LS mean (SE)	4.0 (1.7)
95% CI of LS mean	(0.6, 7.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	5.8 (1.9)
95% CI of LS mean	(2.1, 9.5)
Absolute change at Week 24	
n	78
LS mean (SE)	3.5 (1.6)
95% CI of LS mean	(0.2, 6.7)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	74
LS mean (SE)	5.8 (1.7)
95% CI of LS mean	(2.3, 9.2)
Absolute change at OL Part A Week 48	
n	72
LS mean (SE)	3.6 (2.0)
95% CI of LS mean	(-0.4, 7.5)
Absolute change at OL Part A Week 72	
n	70
LS mean (SE)	1.4 (2.5)
95% CI of LS mean	(-3.6, 6.4)
Absolute change at OL Part A Week 96	
n	65
LS mean (SE)	2.4 (2.3)
95% CI of LS mean	(-2.2, 7.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Body (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	74
LS mean (SE)	3.3 (1.8)
95% CI of LS mean	(-0.2, 6.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	79.5 (25.6)
Absolute change at Week 4	
n	78
LS mean (SE)	-1.1 (1.9)
95% CI of LS mean	(-4.8, 2.7)
Absolute change at Week 8	
n	78
LS mean (SE)	-0.2 (2.1)
95% CI of LS mean	(-4.4, 4.0)
Absolute change at Week 12	
n	77
LS mean (SE)	-1.3 (2.1)
95% CI of LS mean	(-5.4, 2.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	1.5 (1.7)
95% CI of LS mean	(-1.8, 4.8)
Absolute change at Week 24	
n	78
LS mean (SE)	2.4 (1.9)
95% CI of LS mean	(-1.5, 6.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	74
LS mean (SE)	2.2 (2.4)
95% CI of LS mean	(-2.6, 7.1)
Absolute change at OL Part A Week 48	
n	72
LS mean (SE)	5.5 (2.0)
95% CI of LS mean	(1.6, 9.4)
Absolute change at OL Part A Week 72	
n	70
LS mean (SE)	4.0 (2.1)
95% CI of LS mean	(-0.3, 8.2)
Absolute change at OL Part A Week 96	
n	65
LS mean (SE)	6.6 (2.2)
95% CI of LS mean	(2.2, 11.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Eat (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	74
LS mean (SE)	4.6 (1.8)
95% CI of LS mean	(1.1, 8.1)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	69.4 (21.2)
Absolute change at Week 4	
n	78
LS mean (SE)	6.8 (1.5)
95% CI of LS mean	(3.8, 9.9)
Absolute change at Week 8	
n	78
LS mean (SE)	8.7 (2.2)
95% CI of LS mean	(4.4, 13.0)
Absolute change at Week 12	
n	77
LS mean (SE)	6.3 (2.0)
95% CI of LS mean	(2.3, 10.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	7.7 (1.6)
95% CI of LS mean	(4.5, 10.9)
Absolute change at Week 24	
n	78
LS mean (SE)	8.8 (1.9)
95% CI of LS mean	(5.0, 12.7)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	74
LS mean (SE)	8.1 (2.0)
95% CI of LS mean	(4.2, 12.0)
Absolute change at OL Part A Week 48	
n	72
LS mean (SE)	9.8 (1.8)
95% CI of LS mean	(6.1, 13.5)
Absolute change at OL Part A Week 72	
n	70
LS mean (SE)	8.5 (2.0)
95% CI of LS mean	(4.4, 12.6)
Absolute change at OL Part A Week 96	
n	65
LS mean (SE)	11.6 (2.0)
95% CI of LS mean	(7.5, 15.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Treatment Burden (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	74
LS mean (SE)	9.5 (1.5)
95% CI of LS mean	(6.4, 12.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	86.8 (13.8)
Absolute change at Week 4	
n	78
LS mean (SE)	-4.3 (1.6)
95% CI of LS mean	(-7.4, -1.1)
Absolute change at Week 8	
n	78
LS mean (SE)	-0.9 (1.4)
95% CI of LS mean	(-3.6, 1.9)
Absolute change at Week 12	
n	77
LS mean (SE)	0.1 (1.3)
95% CI of LS mean	(-2.5, 2.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	1.7 (1.2)
95% CI of LS mean	(-0.7, 4.1)
Absolute change at Week 24	
n	78
LS mean (SE)	0.7 (1.7)
95% CI of LS mean	(-2.8, 4.2)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	74
LS mean (SE)	-3.4 (1.9)
95% CI of LS mean	(-7.2, 0.4)
Absolute change at OL Part A Week 48	
n	72
LS mean (SE)	-2.6 (1.7)
95% CI of LS mean	(-6.1, 0.9)
Absolute change at OL Part A Week 72	
n	70
LS mean (SE)	-3.2 (1.9)
95% CI of LS mean	(-6.9, 0.6)
Absolute change at OL Part A Week 96	
n	65
LS mean (SE)	-1.9 (1.9)
95% CI of LS mean	(-5.7, 1.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Health Perceptions (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	74
LS mean (SE)	-2.8 (1.4)
95% CI of LS mean	(-5.6, 0.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	69.2 (35.5)
Absolute change at Week 4	
n	78
LS mean (SE)	1.3 (2.9)
95% CI of LS mean	(-4.5, 7.1)
Absolute change at Week 8	
n	78
LS mean (SE)	6.0 (2.6)
95% CI of LS mean	(0.7, 11.2)
Absolute change at Week 12	
n	77
LS mean (SE)	4.3 (2.7)
95% CI of LS mean	(-1.2, 9.7)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	5.1 (2.7)
95% CI of LS mean	(-0.2, 10.4)
Absolute change at Week 24	
n	78
LS mean (SE)	5.1 (2.8)
95% CI of LS mean	(-0.5, 10.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	74
LS mean (SE)	5.2 (3.1)
95% CI of LS mean	(-1.1, 11.4)
Absolute change at OL Part A Week 48	
n	72
LS mean (SE)	2.5 (3.6)
95% CI of LS mean	(-4.6, 9.6)
Absolute change at OL Part A Week 72	
n	70
LS mean (SE)	8.4 (3.1)
95% CI of LS mean	(2.2, 14.6)
Absolute change at OL Part A Week 96	
n	65
LS mean (SE)	7.6 (3.0)
95% CI of LS mean	(1.7, 13.6)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Weight (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	74
LS mean (SE)	5.9 (2.4)
95% CI of LS mean	(1.0, 10.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	82.2 (17.4)
Absolute change at Week 4	
n	78
LS mean (SE)	0.7 (1.7)
95% CI of LS mean	(-2.7, 4.2)
Absolute change at Week 8	
n	78
LS mean (SE)	0.4 (1.6)
95% CI of LS mean	(-2.8, 3.7)
Absolute change at Week 12	
n	77
LS mean (SE)	1.8 (1.5)
95% CI of LS mean	(-1.3, 4.8)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	3.3 (1.3)
95% CI of LS mean	(0.7, 5.8)
Absolute change at Week 24	
n	78
LS mean (SE)	-0.7 (1.6)
95% CI of LS mean	(-3.9, 2.5)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	74
LS mean (SE)	-0.6 (1.9)
95% CI of LS mean	(-4.3, 3.1)
Absolute change at OL Part A Week 48	
n	72
LS mean (SE)	-0.7 (1.8)
95% CI of LS mean	(-4.3, 2.9)
Absolute change at OL Part A Week 72	
n	70
LS mean (SE)	-1.3 (1.8)
95% CI of LS mean	(-4.9, 2.3)
Absolute change at OL Part A Week 96	
n	65
LS mean (SE)	-0.4 (1.9)
95% CI of LS mean	(-4.2, 3.3)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 2.2.2
MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Non-Respiratory Domain Score (Parent's Version) at Each Visit and through OL Week 96 - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Full Analysis Set - Cohort B1 and OL Full Analysis Set Cohort 1

Domain: Digestion (Parents/Caregivers Form)

	VNZ/TEZ/D-IVA
Average change through OL Part A Week 96	
n	74
LS mean (SE)	-0.8 (1.4)
95% CI of LS mean	(-3.6, 2.0)

- Parent study baseline is defined as the pre-dose Day 1 value in the parent study.
- N is the number of subjects in the parent study FAS (Parent Study Efficacy Period) and OL FAS (OL Efficacy Period for Part A), respectively.
- For the Parent Study Efficacy Period, MMRM is based on the parent study Full Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes all OL visits up to OL Week 96 and is based on the OL Full Analysis Set for subjects enrolled in parent study.
- MMRM model uses absolute change from parent study baseline as the dependent variable. The model includes fixed categorical effects for genotype group and visit, with baseline CFQ-R non-RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.
- Average change through OL Part A Week 96 for treatment effect is estimated by averaging from OL Part A Week 24 up to OL Part A Week 96.

Table 14.1.1c1a
Disposition - Part A
OL All Subjects Set - Cohort 1

Disposition/Reason	VNZ/TEZ/D-IVA n (%)
OL All Subjects Set	75
OL Safety Set	75
OL Full Analysis Set	75
Enrolled but not dosed	0
Completed treatment in Part A	69 (92.0)
Discontinued treatment in Part A	6 (8.0)
Reason for discontinuation of treatment in Part A	
Adverse event	2 (2.7)
Subject refused further dosing (not due to AE)	1 (1.3)
Lost to follow-up	0
Commercial drug is available for subject	0
Death	0
Did not meet eligibility criteria	0
Non-compliance with study drug	1 (1.3)
Other non-compliance	1 (1.3)
Physician decision	1 (1.3)
Pregnancy	0
Requires prohibited medication	0
Sponsor decision	0
Study terminated by sponsor	0
Other	0

- OL All Subjects Set: all subjects who were enrolled in the OL study
- OL Safety Set: all subjects who received at least 1 dose of the study drug in the OL study
- OL Full Analysis Set: all enrolled subjects who received at least 1 dose of the study drug in the OL study
- Percentages are based on the number of subjects in the OL Full Analysis Set.

Table 14.1.1c1a
Disposition - Part A
OL All Subjects Set - Cohort 1

Disposition/Reason	VNZ/TEZ/D-IVA n (%)
Completed study in Part A	69 (92.0)
Discontinued study in Part A	6 (8.0)
Reason for discontinuation from study in Part A	
Adverse event	1 (1.3)
Withdrawal of consent (not due to AE)	2 (2.7)
Lost to follow-up	0
Commercial drug is available for subject	0
Death	0
Other non-compliance	1 (1.3)
Physician decision	2 (2.7)
Sponsor decision	0
Study terminated by sponsor	0
Other	0
Rolled over to Part B	65 (86.7)

- OL All Subjects Set: all subjects who were enrolled in the OL study
- OL Safety Set: all subjects who received at least 1 dose of the study drug in the OL study
- OL Full Analysis Set: all enrolled subjects who received at least 1 dose of the study drug in the OL study
- Percentages are based on the number of subjects in the OL Full Analysis Set.

Zusatzanalysen zur Studie VX22-121-106

Table 14.1.3c1a
Demographics - Part A
OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA N = 75
Sex, n (%)	
Male	42 (56.0)
Female	33 (44.0)
Childbearing potential[1], n (%)	
Yes	18 (54.5)
No	15 (45.5)
Reason not of childbearing potential[2], n (%)	
Surgical Procedure	0
Postmenopausal	0
Premenarchal	15 (100.0)
Other	0
Age at Day 1 in the parent study (years)	
n	75
Mean (SD)	9.1 (1.7)
Median	9.4
Min, max	6.2, 12.0

- [1]: Female n is the denominator
- [2]: Female n with no childbearing potential is the denominator
- Sex and childbearing potential are based on data collected in the OL study. Race and Ethnicity are based on data collected in the parent study.
- For reporting purposes, North America includes subjects from the United States, and Rest of the World includes subjects from Europe and Australia.

Table 14.1.3c1a
Demographics - Part A
OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA N = 75
Race, n (%)	
White	69 (92.0)
Black or African American	1 (1.3)
Asian	0
Northeast Asian	0
Southeast Asian	0
Other Asian	0
Asian, Region Not Reported	0
American Indian or Alaska Native	0
Native Hawaiian or Other Pacific Islander	0
Other	0
More than one race	1 (1.3)
Not Collected per Local Regulations	4 (5.3)
Ethnicity, n (%)	
Hispanic or Latino	9 (12.0)
Not Hispanic or Latino	60 (80.0)
Not Collected per Local Regulations	6 (8.0)
Geographic Region, n (%)	
North America	45 (60.0)
Rest of the World	30 (40.0)

- [1]: Female n is the denominator
- [2]: Female n with no childbearing potential is the denominator
- Sex and childbearing potential are based on data collected in the OL study. Race and Ethnicity are based on data collected in the parent study.
- For reporting purposes, North America includes subjects from the United States, and Rest of the World includes subjects from Europe and Australia.

Table 14.1.4c1a
Parent Study Baseline Characteristics - Part A
OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA N = 75
Weight (kg)	
n	75
Mean (SD)	30.08 (7.01)
Median	29.00
Min, max	19.30, 47.50
Weight-for-age z-score	
n	75
Mean (SD)	-0.01 (0.88)
Median	0.00
Min, max	-1.89, 1.48
Weight category, n (%)	
<40 kg	68 (90.7)
≥40 kg	7 (9.3)
Height (cm)	
n	75
Mean (SD)	132.9 (10.4)
Median	133.1
Min, max	111.5, 153.7
Height-for-age z-score	
n	75
Mean (SD)	-0.05 (0.95)
Median	-0.06
Min, max	-2.18, 2.06

- Prior CFTR modulator use includes the most recent CFTRm prior to parent study informed consent for each subject.
- *: Includes medications administered during the 28 days before the first dose of study drug in the parent study Treatment Period. For ELX/TEZ/IVA-naive subjects, this includes medications administered during the 56 days before the first dose of study drug in the parent study Treatment Period excluding the ones that started in the Run-in Period.

Table 14.1.4c1a
Parent Study Baseline Characteristics - Part A
OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA N = 75
BMI (kg/m^2)	
n	75
Mean (SD)	16.80 (2.02)
Median	16.39
Min, max	13.40, 23.43
BMI-for-age z-score	
n	75
Mean (SD)	0.07 (0.86)
Median	0.09
Min, max	-1.75, 1.84
Genotype group, n (%)	
F/MF	24 (32.0)
F/F	36 (48.0)
F/G	2 (2.7)
F/RF	1 (1.3)
F/other	1 (1.3)
TCR/any	11 (14.7)
TCR/F	5 (6.7)
TCR/non-F	6 (8.0)
$ppFEV_1$ (percentage points)	
n	74
Mean (SD)	99.9 (15.3)
Median	101.3
Min, max	29.3, 146.0

- Prior CFTR modulator use includes the most recent CFTRm prior to parent study informed consent for each subject.
- *: Includes medications administered during the 28 days before the first dose of study drug in the parent study Treatment Period. For ELX/TEZ/IVA-naive subjects, this includes medications administered during the 56 days before the first dose of study drug in the parent study Treatment Period excluding the ones that started in the Run-in Period.

Table 14.1.4c1a
Parent Study Baseline Characteristics - Part A
OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA N = 75
$ppFEV_1$ category, n (%)	
<40 percentage points	1 (1.3)
≥40 to <70 percentage points	1 (1.3)
≥70 to ≤90 percentage points	14 (18.7)
>90 percentage points	58 (77.3)
Missing	1 (1.3)
Sweat chloride (mmol/L)	
n	74
Mean (SD)	40.8 (21.2)
Median	39.0
Min, max	11.5, 109.5
Sweat chloride category, n (%)	
<30 mmol/L	29 (38.7)
≥30 to <60 mmol/L	33 (44.0)
≥60 mmol/L	12 (16.0)
Missing	1 (1.3)
CFQ-R respiratory domain score (child version)	
n	72
Mean (SD)	84.7 (16.4)
Median	91.7
Min, max	16.7, 100.0

- Prior CFTR modulator use includes the most recent CFTRm prior to parent study informed consent for each subject.
- *: Includes medications administered during the 28 days before the first dose of study drug in the parent study Treatment Period. For ELX/TEZ/IVA-naive subjects, this includes medications administered during the 56 days before the first dose of study drug in the parent study Treatment Period excluding the ones that started in the Run-in Period.

Table 14.1.4c1a
Parent Study Baseline Characteristics - Part A
OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA N = 75
Prior CFTR modulator use, n (%)	
Yes	63 (84.0)
Kalydeco	2 (2.7)
Orkambi	2 (2.7)
Symdeko/Symkevi	0
Trikafta/Kaftrio	59 (78.7)
No	12 (16.0)
Prior use of dornase alfa*, n (%)	
Yes	48 (64.0)
No	27 (36.0)
Prior use of azithromycin*, n (%)	
Yes	10 (13.3)
No	65 (86.7)
Prior use of inhaled antibiotic*, n (%)	
Yes	3 (4.0)
No	72 (96.0)
Prior use of any bronchodilator*, n (%)	
Yes	60 (80.0)
No	15 (20.0)
Prior use of inhaled hypertonic saline*, n (%)	
Yes	57 (76.0)
No	18 (24.0)

- Prior CFTR modulator use includes the most recent CFTRm prior to parent study informed consent for each subject.
- *: Includes medications administered during the 28 days before the first dose of study drug in the parent study Treatment Period. For ELX/TEZ/IVA-naive subjects, this includes medications administered during the 56 days before the first dose of study drug in the parent study Treatment Period excluding the ones that started in the Run-in Period.

Table 14.1.4c1a
Parent Study Baseline Characteristics - Part A
OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA N = 75
Infection with *Pseudomonas aeruginosa* within 2 years prior to screening in the parent study, n (%)	
Positive	10 (13.3)
Negative	65 (86.7)

- Prior CFTR modulator use includes the most recent CFTRm prior to parent study informed consent for each subject.
- *: Includes medications administered during the 28 days before the first dose of study drug in the parent study Treatment Period. For ELX/TEZ/IVA-naive subjects, this includes medications administered during the 56 days before the first dose of study drug in the parent study Treatment Period excluding the ones that started in the Run-in Period.

Table 14.2.1.1c1a
Summary of Sweat Chloride (mmol/L) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	74
	Mean (SD)	40.8 (21.3)
	Median	39.0
	Min, max	11.0, 109.5
OL Part A Week 24	n	71
	Mean (SD)	32.8 (19.9)
	Median	28.0
	Min, max	10.0, 110.5
Change at OL Part A Week 24	n	71
	Mean (SD)	-8.6 (16.5)
	Median	-6.5
	Min, max	-66.0, 61.0
OL Part A Week 48	n	71
	Mean (SD)	35.4 (17.8)
	Median	32.5
	Min, max	10.0, 108.5
Change at OL Part A Week 48	n	70
	Mean (SD)	-6.6 (15.3)
	Median	-6.0
	Min, max	-58.0, 35.5

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.1.1c1a
Summary of Sweat Chloride (mmol/L) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	65
	Mean (SD)	36.9 (21.7)
	Median	33.0
	Min, max	10.0, 113.0
Change at OL Part A Week 72	n	65
	Mean (SD)	-5.2 (17.1)
	Median	-4.0
	Min, max	-45.5, 48.5
OL Part A Week 96	n	63
	Mean (SD)	34.0 (17.1)
	Median	29.0
	Min, max	10.0, 77.5
Change at OL Part A Week 96	n	63
	Mean (SD)	-7.2 (18.6)
	Median	-6.5
	Min, max	-83.0, 37.5

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.1.2c1a
MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	77
Mean (SD)	40.4 (20.9)
Absolute change at Day 15	
n	72
LS mean (SE)	-5.9 (1.3)
95% CI of LS mean	(-8.6, -3.3)
Absolute change at Week 4	
n	70
LS mean (SE)	-6.8 (1.3)
95% CI of LS mean	(-9.4, -4.2)
Absolute change at Week 16	
n	76
LS mean (SE)	-8.8 (1.6)
95% CI of LS mean	(-11.9, -5.6)
Absolute change at Week 24	
n	74
LS mean (SE)	-8.4 (1.2)
95% CI of LS mean	(-10.8, -6.1)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.1.2c1a
MMRM Analysis of Absolute Change from Baseline in Sweat Chloride (mmol/L) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	71
LS mean (SE)	-8.1 (1.8)
95% CI of LS mean	(-11.6, -4.6)
Absolute change at OL Part A Week 48	
n	70
LS mean (SE)	-6.2 (1.5)
95% CI of LS mean	(-9.1, -3.3)
Absolute change at OL Part A Week 72	
n	65
LS mean (SE)	-4.4 (1.9)
95% CI of LS mean	(-8.2, -0.7)
Absolute change at OL Part A Week 96	
n	63
LS mean (SE)	-6.2 (1.8)
95% CI of LS mean	(-9.9, -2.6)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline sweat chloride as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Forced Expiratory Volume in 1 Second (Absolute changes have a unit of L)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	74
	Mean (SD)	1.76 (0.43)
	Median	1.67
	Min, max	0.53, 2.68
OL Part A Week 8	n	66
	Mean (SD)	1.93 (0.46)
	Median	1.82
	Min, max	1.07, 2.93
Absolute Change at OL Part A Week 8	n	65
	Mean (SD)	0.14 (0.19)
	Median	0.15
	Min, max	-0.33, 0.93
OL Part A Week 16	n	70
	Mean (SD)	1.90 (0.43)
	Median	1.80
	Min, max	0.79, 2.94
Absolute Change at OL Part A Week 16	n	69
	Mean (SD)	0.15 (0.20)
	Median	0.15
	Min, max	-0.21, 1.17

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Forced Expiratory Volume in 1 Second (Absolute changes have a unit of L)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 24	n	65
	Mean (SD)	1.92 (0.43)
	Median	1.77
	Min, max	1.19, 2.98
Absolute Change at OL Part A Week 24	n	65
	Mean (SD)	0.17 (0.21)
	Median	0.18
	Min, max	-0.40, 1.16
OL Part A Week 36	n	68
	Mean (SD)	2.02 (0.47)
	Median	1.94
	Min, max	1.03, 3.08
Absolute Change at OL Part A Week 36	n	67
	Mean (SD)	0.23 (0.16)
	Median	0.23
	Min, max	-0.28, 0.57
OL Part A Week 48	n	64
	Mean (SD)	2.08 (0.48)
	Median	1.98
	Min, max	1.19, 3.07
Absolute Change at OL Part A Week 48	n	63
	Mean (SD)	0.30 (0.21)
	Median	0.27
	Min, max	-0.20, 1.21

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Forced Expiratory Volume in 1 Second (Absolute changes have a unit of L)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 60	n	63
	Mean (SD)	2.10 (0.49)
	Median	2.09
	Min, max	1.25, 3.10
Absolute Change at OL Part A Week 60	n	62
	Mean (SD)	0.35 (0.27)
	Median	0.30
	Min, max	-0.38, 1.55
OL Part A Week 72	n	63
	Mean (SD)	2.16 (0.50)
	Median	2.09
	Min, max	1.29, 3.21
Absolute Change at OL Part A Week 72	n	62
	Mean (SD)	0.40 (0.26)
	Median	0.36
	Min, max	-0.29, 1.41
OL Part A Week 84	n	63
	Mean (SD)	2.27 (0.54)
	Median	2.15
	Min, max	1.14, 3.43
Absolute Change at OL Part A Week 84	n	62
	Mean (SD)	0.49 (0.28)
	Median	0.47
	Min, max	-0.17, 1.56

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Forced Expiratory Volume in 1 Second (Absolute changes have a unit of L)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	62
	Mean (SD)	2.32 (0.58)
	Median	2.14
	Min, max	1.48, 3.70
Absolute Change at OL Part A Week 96	n	62
	Mean (SD)	0.54 (0.27)
	Median	0.47
	Min, max	0.11, 1.35

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Ratio of FEV1/FVC (Absolute changes have a unit of RATIO)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	74
	Mean (SD)	0.84 (0.08)
	Median	0.85
	Min, max	0.47, 0.96
OL Part A Week 8	n	63
	Mean (SD)	0.84 (0.08)
	Median	0.86
	Min, max	0.64, 1.00
Absolute Change at OL Part A Week 8	n	63
	Mean (SD)	0.00 (0.06)
	Median	0.00
	Min, max	-0.20, 0.18
OL Part A Week 16	n	69
	Mean (SD)	0.84 (0.08)
	Median	0.85
	Min, max	0.56, 0.96
Absolute Change at OL Part A Week 16	n	68
	Mean (SD)	0.00 (0.06)
	Median	0.00
	Min, max	-0.24, 0.25

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Ratio of FEV1/FVC (Absolute changes have a unit of RATIO)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 24	n	65
	Mean (SD)	0.83 (0.08)
	Median	0.85
	Min, max	0.66, 0.97
Absolute Change at OL Part A Week 24	n	65
	Mean (SD)	0.00 (0.06)
	Median	0.00
	Min, max	-0.22, 0.22
OL Part A Week 36	n	68
	Mean (SD)	0.84 (0.08)
	Median	0.84
	Min, max	0.65, 0.97
Absolute Change at OL Part A Week 36	n	67
	Mean (SD)	0.00 (0.04)
	Median	0.00
	Min, max	-0.15, 0.11
OL Part A Week 48	n	60
	Mean (SD)	0.84 (0.07)
	Median	0.84
	Min, max	0.68, 0.95
Absolute Change at OL Part A Week 48	n	59
	Mean (SD)	-0.01 (0.04)
	Median	-0.01
	Min, max	-0.17, 0.13

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Ratio of FEV1/FVC (Absolute changes have a unit of RATIO)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 60	n	60
	Mean (SD)	0.84 (0.07)
	Median	0.85
	Min, max	0.58, 0.95
Absolute Change at OL Part A Week 60	n	59
	Mean (SD)	0.01 (0.06)
	Median	0.00
	Min, max	-0.20, 0.33
OL Part A Week 72	n	61
	Mean (SD)	0.83 (0.08)
	Median	0.85
	Min, max	0.65, 0.95
Absolute Change at OL Part A Week 72	n	60
	Mean (SD)	-0.01 (0.05)
	Median	-0.01
	Min, max	-0.20, 0.26
OL Part A Week 84	n	60
	Mean (SD)	0.84 (0.07)
	Median	0.85
	Min, max	0.68, 0.96
Absolute Change at OL Part A Week 84	n	59
	Mean (SD)	0.00 (0.06)
	Median	0.00
	Min, max	-0.12, 0.31

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Ratio of FEV1/FVC (Absolute changes have a unit of RATIO)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	58
	Mean (SD)	0.84 (0.07)
	Median	0.85
	Min, max	0.63, 0.95
Absolute Change at OL Part A Week 96	n	58
	Mean (SD)	0.01 (0.04)
	Median	0.00
	Min, max	-0.12, 0.16

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Forced Vital Capacity (Absolute changes have a unit of L)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	74
	Mean (SD)	2.09 (0.49)
	Median	2.04
	Min, max	1.14, 3.57
OL Part A Week 8	n	68
	Mean (SD)	2.25 (0.51)
	Median	2.16
	Min, max	1.34, 3.60
Absolute Change at OL Part A Week 8	n	68
	Mean (SD)	0.14 (0.18)
	Median	0.12
	Min, max	-0.38, 1.11
OL Part A Week 16	n	72
	Mean (SD)	2.26 (0.49)
	Median	2.21
	Min, max	1.39, 3.65
Absolute Change at OL Part A Week 16	n	71
	Mean (SD)	0.18 (0.19)
	Median	0.17
	Min, max	-0.21, 1.23

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Forced Vital Capacity (Absolute changes have a unit of L)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 24	n	70
	Mean (SD)	2.28 (0.51)
	Median	2.24
	Min, max	1.35, 3.73
Absolute Change at OL Part A Week 24	n	70
	Mean (SD)	0.22 (0.19)
	Median	0.18
	Min, max	-0.12, 1.30
OL Part A Week 36	n	70
	Mean (SD)	2.39 (0.54)
	Median	2.29
	Min, max	1.34, 3.75
Absolute Change at OL Part A Week 36	n	69
	Mean (SD)	0.28 (0.15)
	Median	0.26
	Min, max	0.02, 0.65
OL Part A Week 48	n	68
	Mean (SD)	2.45 (0.58)
	Median	2.32
	Min, max	1.42, 3.95
Absolute Change at OL Part A Week 48	n	67
	Mean (SD)	0.34 (0.16)
	Median	0.31
	Min, max	0.09, 0.89

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Forced Vital Capacity (Absolute changes have a unit of L)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 60	n	65
	Mean (SD)	2.47 (0.57)
	Median	2.30
	Min, max	1.54, 4.03
Absolute Change at OL Part A Week 60	n	64
	Mean (SD)	0.42 (0.25)
	Median	0.38
	Min, max	0.07, 1.49
OL Part A Week 72	n	68
	Mean (SD)	2.57 (0.61)
	Median	2.44
	Min, max	1.50, 4.29
Absolute Change at OL Part A Week 72	n	67
	Mean (SD)	0.48 (0.27)
	Median	0.39
	Min, max	0.06, 1.51
OL Part A Week 84	n	65
	Mean (SD)	2.67 (0.64)
	Median	2.60
	Min, max	1.64, 4.53
Absolute Change at OL Part A Week 84	n	64
	Mean (SD)	0.58 (0.30)
	Median	0.52
	Min, max	-0.04, 1.55

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Forced Vital Capacity (Absolute changes have a unit of L)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	62
	Mean (SD)	2.71 (0.67)
	Median	2.49
	Min, max	1.67, 4.91
Absolute Change at OL Part A Week 96	n	61
	Mean (SD)	0.63 (0.33)
	Median	0.55
	Min, max	0.17, 1.66

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Percent Predicted Forced Expiratory Volume in 1 Second (Absolute changes have a unit of %)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	74
	Mean (SD)	99.9 (15.3)
	Median	101.3
	Min, max	29.3, 146.0
OL Part A Week 8	n	66
	Mean (SD)	100.4 (15.0)
	Median	102.8
	Min, max	49.6, 140.0
Absolute Change at OL Part A Week 8	n	65
	Mean (SD)	0.4 (10.7)
	Median	0.1
	Min, max	-24.4, 41.9
OL Part A Week 16	n	70
	Mean (SD)	99.2 (13.2)
	Median	101.9
	Min, max	60.7, 138.6
Absolute Change at OL Part A Week 16	n	69
	Mean (SD)	-0.4 (10.9)
	Median	-1.1
	Min, max	-21.2, 50.9

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Percent Predicted Forced Expiratory Volume in 1 Second (Absolute changes have a unit of %)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 24	n	65
	Mean (SD)	98.1 (14.0)
	Median	98.5
	Min, max	57.2, 140.5
Absolute Change at OL Part A Week 24	n	65
	Mean (SD)	-1.3 (11.5)
	Median	-1.7
	Min, max	-31.1, 48.6
OL Part A Week 36	n	68
	Mean (SD)	99.4 (13.4)
	Median	101.0
	Min, max	68.4, 140.1
Absolute Change at OL Part A Week 36	n	67
	Mean (SD)	-2.0 (8.0)
	Median	-1.2
	Min, max	-29.4, 12.8
OL Part A Week 48	n	64
	Mean (SD)	98.1 (13.1)
	Median	98.4
	Min, max	65.3, 145.6
Absolute Change at OL Part A Week 48	n	63
	Mean (SD)	-1.0 (10.7)
	Median	-1.7
	Min, max	-24.0, 47.3

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Percent Predicted Forced Expiratory Volume in 1 Second (Absolute changes have a unit of %)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 60	n	63
	Mean (SD)	97.2 (12.1)
	Median	98.7
	Min, max	52.5, 119.0
Absolute Change at OL Part A Week 60	n	62
	Mean (SD)	-1.6 (12.6)
	Median	-2.9
	Min, max	-32.1, 59.3
OL Part A Week 72	n	63
	Mean (SD)	96.9 (12.6)
	Median	97.9
	Min, max	64.9, 137.7
Absolute Change at OL Part A Week 72	n	62
	Mean (SD)	-2.4 (11.3)
	Median	-4.7
	Min, max	-32.8, 50.0
OL Part A Week 84	n	63
	Mean (SD)	98.6 (13.3)
	Median	99.0
	Min, max	62.0, 136.5
Absolute Change at OL Part A Week 84	n	62
	Mean (SD)	-1.0 (11.7)
	Median	-2.5
	Min, max	-29.2, 54.0

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Percent Predicted Forced Expiratory Volume in 1 Second (Absolute changes have a unit of %)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	62
	Mean (SD)	98.0 (13.5)
	Median	100.1
	Min, max	61.4, 138.5
Absolute Change at OL Part A Week 96	n	62
	Mean (SD)	-1.7 (9.8)
	Median	-3.6
	Min, max	-19.4, 40.4

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Percent Predicted Ratio of FEV1/FVC (Absolute changes have a unit of %)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	74
	Mean (SD)	94.7 (8.6)
	Median	95.9
	Min, max	52.7, 108.1
OL Part A Week 8	n	63
	Mean (SD)	95.8 (8.8)
	Median	96.4
	Min, max	73.0, 111.8
Absolute Change at OL Part A Week 8	n	63
	Mean (SD)	0.9 (6.5)
	Median	0.3
	Min, max	-22.4, 21.4
OL Part A Week 16	n	69
	Mean (SD)	94.9 (8.2)
	Median	95.6
	Min, max	61.6, 107.5
Absolute Change at OL Part A Week 16	n	68
	Mean (SD)	0.4 (6.6)
	Median	0.3
	Min, max	-25.8, 28.5

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Percent Predicted Ratio of FEV1/FVC (Absolute changes have a unit of %)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 24	n	65
	Mean (SD)	94.6 (8.4)
	Median	96.3
	Min, max	74.7, 108.6
Absolute Change at OL Part A Week 24	n	65
	Mean (SD)	0.3 (6.7)
	Median	0.2
	Min, max	-24.3, 25.6
OL Part A Week 36	n	68
	Mean (SD)	95.3 (8.4)
	Median	95.9
	Min, max	75.0, 108.5
Absolute Change at OL Part A Week 36	n	67
	Mean (SD)	0.1 (4.7)
	Median	0.4
	Min, max	-15.6, 14.0
OL Part A Week 48	n	60
	Mean (SD)	95.0 (7.8)
	Median	95.5
	Min, max	77.7, 108.4
Absolute Change at OL Part A Week 48	n	59
	Mean (SD)	0.1 (4.7)
	Median	0.3
	Min, max	-17.8, 16.1

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Percent Predicted Ratio of FEV1/FVC (Absolute changes have a unit of %)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 60	n	60
	Mean (SD)	95.5 (7.9)
	Median	96.4
	Min, max	64.6, 108.2
Absolute Change at OL Part A Week 60	n	59
	Mean (SD)	1.5 (6.8)
	Median	1.1
	Min, max	-22.3, 36.7
OL Part A Week 72	n	61
	Mean (SD)	94.6 (8.4)
	Median	96.1
	Min, max	76.6, 107.9
Absolute Change at OL Part A Week 72	n	60
	Mean (SD)	0.3 (6.1)
	Median	0.1
	Min, max	-20.8, 29.9
OL Part A Week 84	n	60
	Mean (SD)	95.5 (7.9)
	Median	96.4
	Min, max	75.8, 111.7
Absolute Change at OL Part A Week 84	n	59
	Mean (SD)	1.3 (6.9)
	Median	0.7
	Min, max	-11.6, 34.7

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Percent Predicted Ratio of FEV1/FVC (Absolute changes have a unit of %)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	58
	Mean (SD)	95.6 (7.6)
	Median	96.2
	Min, max	70.4, 107.2
Absolute Change at OL Part A Week 96	n	58
	Mean (SD)	1.6 (4.8)
	Median	1.1
	Min, max	-11.0, 17.9

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Percent Predicted Forced Vital Capacity (Absolute changes have a unit of %)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	74
	Mean (SD)	104.4 (13.5)
	Median	105.3
	Min, max	55.2, 140.0
OL Part A Week 8	n	68
	Mean (SD)	102.8 (12.4)
	Median	103.4
	Min, max	66.2, 132.2
Absolute Change at OL Part A Week 8	n	68
	Mean (SD)	-1.5 (8.2)
	Median	-1.4
	Min, max	-32.2, 39.9
OL Part A Week 16	n	72
	Mean (SD)	103.5 (12.0)
	Median	103.3
	Min, max	66.5, 132.8
Absolute Change at OL Part A Week 16	n	71
	Mean (SD)	-0.5 (9.3)
	Median	-2.0
	Min, max	-20.0, 42.8

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Percent Predicted Forced Vital Capacity (Absolute changes have a unit of %)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 24	n	70
	Mean (SD)	103.1 (12.4)
	Median	103.3
	Min, max	70.3, 137.8
Absolute Change at OL Part A Week 24	n	70
	Mean (SD)	-1.3 (9.1)
	Median	-2.3
	Min, max	-17.5, 43.6
OL Part A Week 36	n	70
	Mean (SD)	103.5 (12.5)
	Median	102.5
	Min, max	76.6, 133.6
Absolute Change at OL Part A Week 36	n	69
	Mean (SD)	-1.9 (6.5)
	Median	-1.2
	Min, max	-18.2, 12.1
OL Part A Week 48	n	68
	Mean (SD)	103.0 (11.6)
	Median	102.2
	Min, max	74.2, 136.8
Absolute Change at OL Part A Week 48	n	67
	Mean (SD)	-2.4 (5.2)
	Median	-2.7
	Min, max	-15.7, 12.4

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Percent Predicted Forced Vital Capacity (Absolute changes have a unit of %)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 60	n	65
	Mean (SD)	101.9 (11.9)
	Median	101.0
	Min, max	76.6, 144.3
Absolute Change at OL Part A Week 60	n	64
	Mean (SD)	-1.6 (9.5)
	Median	-3.0
	Min, max	-15.9, 43.2
OL Part A Week 72	n	68
	Mean (SD)	101.5 (11.7)
	Median	100.8
	Min, max	69.7, 131.5
Absolute Change at OL Part A Week 72	n	67
	Mean (SD)	-3.0 (8.1)
	Median	-4.3
	Min, max	-16.3, 40.2
OL Part A Week 84	n	65
	Mean (SD)	102.6 (12.6)
	Median	102.1
	Min, max	71.4, 134.5
Absolute Change at OL Part A Week 84	n	64
	Mean (SD)	-2.0 (9.3)
	Median	-3.5
	Min, max	-28.8, 39.5

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.2.1c1a
Summary of Spirometry Assessments and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Percent Predicted Forced Vital Capacity (Absolute changes have a unit of %)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	62
	Mean (SD)	101.5 (12.8)
	Median	99.9
	Min, max	78.3, 133.4
Absolute Change at OL Part A Week 96	n	61
	Mean (SD)	-3.0 (9.2)
	Median	-4.8
	Min, max	-15.3, 37.0

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

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Table 14.2.2.2c1a
MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	77
Mean (SD)	99.7 (15.1)
Absolute change at Day 15	
n	71
LS mean (SE)	-1.6 (0.9)
95% CI of LS mean	(-3.5, 0.2)
Absolute change at Week 4	
n	64
LS mean (SE)	-1.1 (0.8)
95% CI of LS mean	(-2.7, 0.6)
Absolute change at Week 8	
n	72
LS mean (SE)	-1.5 (1.3)
95% CI of LS mean	(-4.1, 1.1)
Absolute change at Week 12	
n	72
LS mean (SE)	0.1 (1.0)
95% CI of LS mean	(-1.9, 2.1)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline ppFEV1 as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.2.2c1a
MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	73
LS mean (SE)	0.2 (1.1)
95% CI of LS mean	(-2.0, 2.5)
Absolute change at Week 24	
n	69
LS mean (SE)	-0.3 (1.1)
95% CI of LS mean	(-2.4, 1.8)
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 8	
n	65
LS mean (SE)	-0.2 (1.2)
95% CI of LS mean	(-2.6, 2.3)
Absolute change at OL Part A Week 16	
n	69
LS mean (SE)	-0.8 (1.1)
95% CI of LS mean	(-3.1, 1.4)
Absolute change at OL Part A Week 24	
n	65
LS mean (SE)	-2.0 (1.2)
95% CI of LS mean	(-4.5, 0.4)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline ppFEV1 as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.2.2c1a
MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 36	
n	67
LS mean (SE)	-0.8 (1.2)
95% CI of LS mean	(-3.1, 1.5)
Absolute change at OL Part A Week 48	
n	63
LS mean (SE)	-1.3 (1.1)
95% CI of LS mean	(-3.5, 0.9)
Absolute change at OL Part A Week 60	
n	62
LS mean (SE)	-2.3 (1.3)
95% CI of LS mean	(-4.9, 0.4)
Absolute change at OL Part A Week 72	
n	62
LS mean (SE)	-2.6 (1.1)
95% CI of LS mean	(-4.9, -0.4)
Absolute change at OL Part A Week 84	
n	62
LS mean (SE)	-1.3 (1.2)
95% CI of LS mean	(-3.6, 1.1)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline ppFEV1 as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.2.2c1a
MMRM Analysis of Absolute Change from Baseline in $ppFEV_1$ (percentage points) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 96	
n	62
LS mean (SE)	-2.2 (1.1)
95% CI of LS mean	(-4.3, -0.1)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline ppFEV1 as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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Table 14.2.3.1c1a
Summary of Pulmonary Exacerbations During the Cumulative Efficacy Period for Part A
Cumulative Efficacy Set

	VNZ/TEZ/D-IVA N = 78
Total number of days (years) in the Cumulative Efficacy Period for Part A	61503 (183.0)
Pulmonary exacerbations (PEx)	
Number of subjects with events, n (%)	19 (24.4)
Total number of events	45
Observed event rate per year	0.25
PEx requiring hospitalization	
Number of subjects with events, n (%)	6 (7.7)
Total number of events	10
Observed event rate per year	0.05
PEx requiring IV antibiotic therapy	
Number of subjects with events, n (%)	6 (7.7)
Total number of events	10
Observed event rate per year	0.05
PEx requiring hospitalization or IV antibiotic therapy	
Number of subjects with events, n (%)	6 (7.7)
Total number of events	10
Observed event rate per year	0.05

- Pulmonary exacerbation (PEx): new or change in antibiotic therapy (intravenous (IV), inhaled, or oral) for ≥4 sinopulmonary signs/symptoms
- Total number of days = sum of the individual duration (actual number of days) in the Cumulative Efficacy Period for Part A across all subjects in the analysis set. Total number of years = total number of days / 336; for analysis purposes, 1 year is defined as 48 weeks or 336 days.
- Observed event rate per year = total number of events * 336 / total number of days in the Cumulative Efficacy Period for Part A

Table 14.2.4.1c1a
Summary of CFQ-R Respiratory Domain Score (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	72
	Mean (SD)	84.7 (16.4)
	Median	91.7
	Min, max	16.7, 100.0
OL Part A Week 24	n	71
	Mean (SD)	85.2 (13.0)
	Median	83.3
	Min, max	33.3, 100.0
Change at OL Part A Week 24	n	68
	Mean (SD)	0.6 (20.0)
	Median	0.0
	Min, max	-66.7, 75.0
OL Part A Week 48	n	69
	Mean (SD)	90.9 (12.4)
	Median	91.7
	Min, max	41.7, 100.0
Change at OL Part A Week 48	n	68
	Mean (SD)	6.6 (17.8)
	Median	8.3
	Min, max	-41.7, 66.7

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.1c1a
Summary of CFQ-R Respiratory Domain Score (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	87.9 (11.8)
	Median	91.7
	Min, max	50.0, 100.0
Change at OL Part A Week 72	n	68
	Mean (SD)	2.6 (17.9)
	Median	0.0
	Min, max	-33.3, 83.3
OL Part A Week 96	n	66
	Mean (SD)	91.4 (11.4)
	Median	91.7
	Min, max	58.3, 100.0
Change at OL Part A Week 96	n	63
	Mean (SD)	6.4 (17.7)
	Median	8.3
	Min, max	-33.3, 83.3

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.2c1a
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	75
Mean (SD)	84.8 (16.1)
Absolute change at Week 4	
n	75
LS mean (SE)	0.6 (1.7)
95% CI of LS mean	(-2.7, 4.0)
Absolute change at Week 8	
n	75
LS mean (SE)	1.6 (1.8)
95% CI of LS mean	(-1.9, 5.1)
Absolute change at Week 12	
n	74
LS mean (SE)	5.6 (1.3)
95% CI of LS mean	(3.0, 8.2)
Absolute change at Week 16	
n	75
LS mean (SE)	6.1 (1.3)
95% CI of LS mean	(3.4, 8.8)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.4.2c1a
MMRM Analysis of Absolute Change from Baseline in CFQ-R Respiratory Domain Score (Child's Version) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at Week 24	
n	75
LS mean (SE)	1.8 (1.7)
95% CI of LS mean	(-1.5, 5.1)
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	68
LS mean (SE)	0.3 (1.6)
95% CI of LS mean	(-2.9, 3.5)
Absolute change at OL Part A Week 48	
n	68
LS mean (SE)	6.2 (1.5)
95% CI of LS mean	(3.3, 9.2)
Absolute change at OL Part A Week 72	
n	68
LS mean (SE)	2.9 (1.4)
95% CI of LS mean	(0.0, 5.7)
Absolute change at OL Part A Week 96	
n	63
LS mean (SE)	6.3 (1.4)
95% CI of LS mean	(3.5, 9.2)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.4.3.1c1a.ph

MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Respiratory Domain Score (Parent's Version) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Parent study baseline	
n	78
Mean (SD)	87.4 (15.8)
Absolute change at Week 4	
n	78
LS mean (SE)	-2.8 (2.0)
95% CI of LS mean	(-6.7, 1.1)
Absolute change at Week 8	
n	78
LS mean (SE)	-0.6 (1.8)
95% CI of LS mean	(-4.3, 3.0)
Absolute change at Week 12	
n	77
LS mean (SE)	4.8 (1.3)
95% CI of LS mean	(2.3, 7.3)
Absolute change at Week 16	
n	78
LS mean (SE)	4.0 (1.5)
95% CI of LS mean	(0.9, 7.0)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.4.3.1c1a.ph

MMRM Analysis of Absolute Change from Parent Study Baseline in CFQ-R Respiratory Domain Score (Parent's Version) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at Week 24	
n	78
LS mean (SE)	-0.4 (1.8)
95% CI of LS mean	(-3.9, 3.2)
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	74
LS mean (SE)	-1.4 (1.6)
95% CI of LS mean	(-4.7, 1.8)
Absolute change at OL Part A Week 48	
n	72
LS mean (SE)	6.1 (1.4)
95% CI of LS mean	(3.4, 8.9)
Absolute change at OL Part A Week 72	
n	70
LS mean (SE)	-0.2 (2.1)
95% CI of LS mean	(-4.4, 3.9)
Absolute change at OL Part A Week 96	
n	65
LS mean (SE)	4.6 (1.8)
95% CI of LS mean	(1.0, 8.2)

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R RD score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.4.3c1a
Summary of CFQ-R Respiratory Domain Score (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	87.0 (16.0)
	Median	93.3
	Min, max	16.7, 100.0
OL Part A Week 24	n	74
	Mean (SD)	85.6 (14.8)
	Median	88.9
	Min, max	33.3, 100.0
Change at OL Part A Week 24	n	74
	Mean (SD)	-1.4 (19.1)
	Median	0.0
	Min, max	-66.7, 50.0
OL Part A Week 48	n	72
	Mean (SD)	93.0 (11.3)
	Median	94.4
	Min, max	38.9, 100.0
Change at OL Part A Week 48	n	72
	Mean (SD)	6.4 (19.7)
	Median	5.6
	Min, max	-50.0, 77.8

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.3c1a
Summary of CFQ-R Respiratory Domain Score (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	87.1 (17.3)
	Median	94.4
	Min, max	33.3, 100.0
Change at OL Part A Week 72	n	70
	Mean (SD)	-0.6 (21.0)
	Median	0.0
	Min, max	-66.7, 77.8
OL Part A Week 96	n	65
	Mean (SD)	91.8 (15.0)
	Median	100.0
	Min, max	22.2, 100.0
Change at OL Part A Week 96	n	65
	Mean (SD)	4.1 (18.8)
	Median	0.0
	Min, max	-61.1, 83.3

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Physical

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	72
	Mean (SD)	87.4 (12.8)
	Median	88.9
	Min, max	50.0, 100.0
OL Part A Week 24	n	72
	Mean (SD)	85.9 (17.8)
	Median	94.4
	Min, max	27.8, 100.0
Change at OL Part A Week 24	n	69
	Mean (SD)	-1.6 (17.3)
	Median	0.0
	Min, max	-72.2, 33.3
OL Part A Week 48	n	69
	Mean (SD)	89.9 (13.8)
	Median	94.4
	Min, max	44.4, 100.0
Change at OL Part A Week 48	n	68
	Mean (SD)	2.6 (14.5)
	Median	0.0
	Min, max	-33.3, 38.9

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Physical

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	92.9 (11.2)
	Median	100.0
	Min, max	55.6, 100.0
Change at OL Part A Week 72	n	68
	Mean (SD)	4.9 (13.7)
	Median	0.0
	Min, max	-44.4, 38.9
OL Part A Week 96	n	66
	Mean (SD)	92.6 (14.4)
	Median	100.0
	Min, max	22.2, 100.0
Change at OL Part A Week 96	n	63
	Mean (SD)	4.0 (15.0)
	Median	0.0
	Min, max	-55.6, 33.3

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Vitality

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	1
	Mean (SD)	50.0 (--)
	Median	50.0
	Min, max	50.0, 50.0
Change at OL Part A Week 96	n	0
	Mean (SD)	--
	Median	--
	Min, max	--

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Emotion

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	72
	Mean (SD)	76.4 (14.9)
	Median	79.2
	Min, max	45.8, 100.0
OL Part A Week 24	n	72
	Mean (SD)	77.8 (16.2)
	Median	77.1
	Min, max	29.2, 100.0
Change at OL Part A Week 24	n	69
	Mean (SD)	2.1 (15.0)
	Median	4.2
	Min, max	-41.7, 29.2
OL Part A Week 48	n	69
	Mean (SD)	79.5 (15.0)
	Median	79.2
	Min, max	37.5, 100.0
Change at OL Part A Week 48	n	68
	Mean (SD)	3.6 (14.4)
	Median	4.2
	Min, max	-37.5, 45.8

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Emotion

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	79.2 (15.9)
	Median	81.3
	Min, max	20.8, 100.0
Change at OL Part A Week 72	n	68
	Mean (SD)	2.0 (13.4)
	Median	2.1
	Min, max	-37.5, 37.5
OL Part A Week 96	n	66
	Mean (SD)	81.6 (13.7)
	Median	83.3
	Min, max	37.5, 100.0
Change at OL Part A Week 96	n	63
	Mean (SD)	4.3 (14.5)
	Median	4.2
	Min, max	-50.0, 37.5

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Body

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	72
	Mean (SD)	82.7 (23.9)
	Median	100.0
	Min, max	0.0, 100.0
OL Part A Week 24	n	72
	Mean (SD)	89.4 (14.4)
	Median	100.0
	Min, max	33.3, 100.0
Change at OL Part A Week 24	n	69
	Mean (SD)	7.1 (17.9)
	Median	0.0
	Min, max	-33.3, 77.8
OL Part A Week 48	n	69
	Mean (SD)	87.9 (20.7)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 48	n	68
	Mean (SD)	4.7 (22.7)
	Median	0.0
	Min, max	-77.8, 66.7

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Body

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	90.3 (16.4)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 72	n	68
	Mean (SD)	5.9 (19.3)
	Median	0.0
	Min, max	-33.3, 66.7
OL Part A Week 96	n	66
	Mean (SD)	88.4 (19.9)
	Median	100.0
	Min, max	22.2, 100.0
Change at OL Part A Week 96	n	63
	Mean (SD)	2.5 (18.6)
	Median	0.0
	Min, max	-55.6, 55.6

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Eat

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	72
	Mean (SD)	81.2 (21.7)
	Median	88.9
	Min, max	11.1, 100.0
OL Part A Week 24	n	72
	Mean (SD)	83.8 (21.7)
	Median	88.9
	Min, max	22.2, 100.0
Change at OL Part A Week 24	n	69
	Mean (SD)	2.3 (19.6)
	Median	0.0
	Min, max	-55.6, 55.6
OL Part A Week 48	n	69
	Mean (SD)	87.0 (19.8)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 48	n	68
	Mean (SD)	5.9 (14.7)
	Median	0.0
	Min, max	-22.2, 55.6

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Eat

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	89.8 (18.2)
	Median	100.0
	Min, max	33.3, 100.0
Change at OL Part A Week 72	n	68
	Mean (SD)	8.2 (15.8)
	Median	0.0
	Min, max	-33.3, 44.4
OL Part A Week 96	n	66
	Mean (SD)	87.5 (20.9)
	Median	100.0
	Min, max	11.1, 100.0
Change at OL Part A Week 96	n	63
	Mean (SD)	7.1 (18.5)
	Median	0.0
	Min, max	-33.3, 66.7

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Treatment Burden

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	72
	Mean (SD)	76.5 (21.1)
	Median	77.8
	Min, max	33.3, 100.0
OL Part A Week 24	n	72
	Mean (SD)	81.8 (18.2)
	Median	88.9
	Min, max	33.3, 100.0
Change at OL Part A Week 24	n	69
	Mean (SD)	5.6 (17.3)
	Median	0.0
	Min, max	-33.3, 44.4
OL Part A Week 48	n	69
	Mean (SD)	80.5 (20.4)
	Median	88.9
	Min, max	22.2, 100.0
Change at OL Part A Week 48	n	68
	Mean (SD)	3.3 (21.3)
	Median	0.0
	Min, max	-55.6, 55.6

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Treatment Burden

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	81.9 (16.9)
	Median	88.9
	Min, max	33.3, 100.0
Change at OL Part A Week 72	n	68
	Mean (SD)	4.2 (19.2)
	Median	0.0
	Min, max	-55.6, 44.4
OL Part A Week 96	n	66
	Mean (SD)	82.0 (16.6)
	Median	88.9
	Min, max	44.4, 100.0
Change at OL Part A Week 96	n	63
	Mean (SD)	5.0 (22.1)
	Median	0.0
	Min, max	-55.6, 55.6

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Health Perceptions

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	1
	Mean (SD)	77.8 (--)
	Median	77.8
	Min, max	77.8, 77.8
Change at OL Part A Week 96	n	0
	Mean (SD)	--
	Median	--
	Min, max	--

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Weight

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	1
	Mean (SD)	33.3 (--)
	Median	33.3
	Min, max	33.3, 33.3
Change at OL Part A Week 96	n	0
	Mean (SD)	--
	Median	--
	Min, max	--

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Digestion

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	71
	Mean (SD)	79.3 (21.4)
	Median	66.7
	Min, max	33.3, 100.0
OL Part A Week 24	n	71
	Mean (SD)	80.8 (23.7)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 24	n	67
	Mean (SD)	1.0 (27.8)
	Median	0.0
	Min, max	-100.0, 66.7
OL Part A Week 48	n	69
	Mean (SD)	79.7 (23.7)
	Median	100.0
	Min, max	33.3, 100.0
Change at OL Part A Week 48	n	67
	Mean (SD)	0.5 (23.6)
	Median	0.0
	Min, max	-66.7, 33.3

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Digestion

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	81.0 (25.7)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 72	n	67
	Mean (SD)	0.5 (30.4)
	Median	0.0
	Min, max	-100.0, 66.7
OL Part A Week 96	n	66
	Mean (SD)	81.0 (26.1)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 96	n	62
	Mean (SD)	1.3 (28.3)
	Median	0.0
	Min, max	-66.7, 33.3

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Role

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	1
	Mean (SD)	66.7 (--)
	Median	66.7
	Min, max	66.7, 66.7
Change at OL Part A Week 96	n	0
	Mean (SD)	--
	Median	--
	Min, max	--

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Social

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	72
	Mean (SD)	66.8 (19.6)
	Median	66.7
	Min, max	0.0, 100.0
OL Part A Week 24	n	72
	Mean (SD)	72.8 (17.3)
	Median	71.4
	Min, max	28.6, 100.0
Change at OL Part A Week 24	n	69
	Mean (SD)	5.8 (19.9)
	Median	4.8
	Min, max	-38.1, 61.9
OL Part A Week 48	n	69
	Mean (SD)	75.5 (16.7)
	Median	76.2
	Min, max	28.6, 100.0
Change at OL Part A Week 48	n	68
	Mean (SD)	8.8 (18.4)
	Median	9.5
	Min, max	-33.3, 57.1

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.4c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Child's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Social

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	74.0 (18.9)
	Median	76.2
	Min, max	33.3, 100.0
Change at OL Part A Week 72	n	68
	Mean (SD)	6.8 (20.4)
	Median	4.8
	Min, max	-38.1, 61.9
OL Part A Week 96	n	66
	Mean (SD)	74.4 (16.1)
	Median	76.2
	Min, max	38.1, 100.0
Change at OL Part A Week 96	n	63
	Mean (SD)	5.2 (17.3)
	Median	4.8
	Min, max	-38.1, 47.6

- Child's Version includes three different CFQ-R forms: Children Ages 6 to 11, Children Ages 12 and 13, and Adolescents and Adults.
- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Physical (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	91.7 (13.5)
	Median	95.8
	Min, max	41.7, 100.0
OL Part A Week 24	n	74
	Mean (SD)	91.8 (14.6)
	Median	100.0
	Min, max	29.2, 100.0
Change at OL Part A Week 24	n	74
	Mean (SD)	0.2 (14.9)
	Median	0.0
	Min, max	-66.7, 50.0
OL Part A Week 48	n	72
	Mean (SD)	92.7 (12.1)
	Median	100.0
	Min, max	50.0, 100.0
Change at OL Part A Week 48	n	72
	Mean (SD)	0.9 (11.5)
	Median	0.0
	Min, max	-37.5, 50.0

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Physical (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	91.8 (15.8)
	Median	100.0
	Min, max	16.7, 100.0
Change at OL Part A Week 72	n	70
	Mean (SD)	-0.7 (18.0)
	Median	0.0
	Min, max	-62.5, 54.2
OL Part A Week 96	n	65
	Mean (SD)	93.2 (13.8)
	Median	100.0
	Min, max	16.7, 100.0
Change at OL Part A Week 96	n	65
	Mean (SD)	0.4 (13.1)
	Median	0.0
	Min, max	-54.2, 45.8

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Vitality (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	76.4 (12.4)
	Median	73.3
	Min, max	40.0, 100.0
OL Part A Week 24	n	74
	Mean (SD)	74.6 (15.2)
	Median	73.3
	Min, max	33.3, 100.0
Change at OL Part A Week 24	n	74
	Mean (SD)	-1.9 (15.2)
	Median	0.0
	Min, max	-40.0, 40.0
OL Part A Week 48	n	72
	Mean (SD)	78.1 (13.1)
	Median	80.0
	Min, max	33.3, 100.0
Change at OL Part A Week 48	n	72
	Mean (SD)	1.4 (11.8)
	Median	0.0
	Min, max	-20.0, 40.0

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Vitality (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	76.5 (15.8)
	Median	76.7
	Min, max	26.7, 100.0
Change at OL Part A Week 72	n	70
	Mean (SD)	-0.3 (15.1)
	Median	0.0
	Min, max	-46.7, 33.3
OL Part A Week 96	n	65
	Mean (SD)	78.9 (14.3)
	Median	80.0
	Min, max	33.3, 100.0
Change at OL Part A Week 96	n	65
	Mean (SD)	1.4 (15.2)
	Median	0.0
	Min, max	-46.7, 33.3

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Emotion (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	86.3 (13.1)
	Median	86.7
	Min, max	40.0, 100.0
OL Part A Week 24	n	74
	Mean (SD)	88.1 (12.3)
	Median	93.3
	Min, max	46.7, 100.0
Change at OL Part A Week 24	n	74
	Mean (SD)	1.5 (15.4)
	Median	0.0
	Min, max	-46.7, 46.7
OL Part A Week 48	n	72
	Mean (SD)	87.6 (12.1)
	Median	86.7
	Min, max	40.0, 100.0
Change at OL Part A Week 48	n	72
	Mean (SD)	0.6 (11.9)
	Median	0.0
	Min, max	-46.7, 33.3

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Emotion (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	87.4 (13.8)
	Median	93.3
	Min, max	40.0, 100.0
Change at OL Part A Week 72	n	70
	Mean (SD)	0.5 (13.8)
	Median	0.0
	Min, max	-46.7, 46.7
OL Part A Week 96	n	65
	Mean (SD)	88.7 (12.0)
	Median	93.3
	Min, max	46.7, 100.0
Change at OL Part A Week 96	n	65
	Mean (SD)	1.2 (12.3)
	Median	0.0
	Min, max	-33.3, 26.7

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: School (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	80.0 (17.4)
	Median	83.3
	Min, max	16.7, 100.0
OL Part A Week 24	n	74
	Mean (SD)	80.6 (17.5)
	Median	83.3
	Min, max	33.3, 100.0
Change at OL Part A Week 24	n	74
	Mean (SD)	0.8 (15.8)
	Median	0.0
	Min, max	-41.7, 50.0
OL Part A Week 48	n	72
	Mean (SD)	82.5 (16.4)
	Median	83.3
	Min, max	41.7, 100.0
Change at OL Part A Week 48	n	72
	Mean (SD)	2.5 (15.9)
	Median	0.0
	Min, max	-41.7, 41.7

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: School (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	80.0 (18.8)
	Median	83.3
	Min, max	25.0, 100.0
Change at OL Part A Week 72	n	70
	Mean (SD)	-0.6 (18.2)
	Median	0.0
	Min, max	-58.3, 41.7
OL Part A Week 96	n	65
	Mean (SD)	81.8 (15.6)
	Median	83.3
	Min, max	25.0, 100.0
Change at OL Part A Week 96	n	65
	Mean (SD)	0.6 (16.4)
	Median	0.0
	Min, max	-41.7, 41.7

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Body (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	79.6 (26.4)
	Median	88.9
	Min, max	0.0, 100.0
OL Part A Week 24	n	74
	Mean (SD)	85.6 (20.6)
	Median	100.0
	Min, max	22.2, 100.0
Change at OL Part A Week 24	n	74
	Mean (SD)	5.6 (19.2)
	Median	0.0
	Min, max	-33.3, 100.0
OL Part A Week 48	n	72
	Mean (SD)	83.5 (21.7)
	Median	94.4
	Min, max	22.2, 100.0
Change at OL Part A Week 48	n	72
	Mean (SD)	2.9 (20.5)
	Median	0.0
	Min, max	-66.7, 66.7

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Body (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	82.5 (25.1)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 72	n	70
	Mean (SD)	0.2 (23.2)
	Median	0.0
	Min, max	-77.8, 100.0
OL Part A Week 96	n	65
	Mean (SD)	84.6 (22.5)
	Median	88.9
	Min, max	11.1, 100.0
Change at OL Part A Week 96	n	65
	Mean (SD)	1.6 (22.1)
	Median	0.0
	Min, max	-66.7, 66.7

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Eat (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	78.9 (25.9)
	Median	83.3
	Min, max	0.0, 100.0
OL Part A Week 24	n	74
	Mean (SD)	81.3 (26.0)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 24	n	74
	Mean (SD)	2.0 (22.6)
	Median	0.0
	Min, max	-83.3, 50.0
OL Part A Week 48	n	72
	Mean (SD)	84.3 (21.3)
	Median	100.0
	Min, max	16.7, 100.0
Change at OL Part A Week 48	n	72
	Mean (SD)	5.3 (20.7)
	Median	0.0
	Min, max	-50.0, 66.7

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Eat (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	82.9 (20.5)
	Median	83.3
	Min, max	16.7, 100.0
Change at OL Part A Week 72	n	70
	Mean (SD)	3.3 (24.0)
	Median	0.0
	Min, max	-83.3, 50.0
OL Part A Week 96	n	65
	Mean (SD)	86.4 (21.0)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 96	n	65
	Mean (SD)	5.4 (22.5)
	Median	0.0
	Min, max	-50.0, 66.7

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Treatment Burden (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	68.9 (21.3)
	Median	66.7
	Min, max	11.1, 100.0
OL Part A Week 24	n	74
	Mean (SD)	77.2 (20.5)
	Median	77.8
	Min, max	33.3, 100.0
Change at OL Part A Week 24	n	74
	Mean (SD)	8.0 (20.0)
	Median	11.1
	Min, max	-33.3, 55.6
OL Part A Week 48	n	72
	Mean (SD)	78.5 (20.1)
	Median	77.8
	Min, max	33.3, 100.0
Change at OL Part A Week 48	n	72
	Mean (SD)	10.0 (18.7)
	Median	11.1
	Min, max	-33.3, 55.6

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Treatment Burden (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	77.0 (20.9)
	Median	77.8
	Min, max	33.3, 100.0
Change at OL Part A Week 72	n	70
	Mean (SD)	7.9 (21.3)
	Median	11.1
	Min, max	-44.4, 66.7
OL Part A Week 96	n	65
	Mean (SD)	80.9 (19.2)
	Median	88.9
	Min, max	33.3, 100.0
Change at OL Part A Week 96	n	65
	Mean (SD)	11.3 (20.0)
	Median	11.1
	Min, max	-55.6, 55.6

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Health Perceptions (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	86.8 (13.4)
	Median	88.9
	Min, max	55.6, 100.0
OL Part A Week 24	n	74
	Mean (SD)	83.5 (17.3)
	Median	88.9
	Min, max	44.4, 100.0
Change at OL Part A Week 24	n	74
	Mean (SD)	-3.5 (17.5)
	Median	0.0
	Min, max	-44.4, 44.4
OL Part A Week 48	n	72
	Mean (SD)	84.6 (16.5)
	Median	88.9
	Min, max	44.4, 100.0
Change at OL Part A Week 48	n	72
	Mean (SD)	-2.6 (16.2)
	Median	0.0
	Min, max	-44.4, 33.3

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Health Perceptions (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	84.3 (17.5)
	Median	88.9
	Min, max	33.3, 100.0
Change at OL Part A Week 72	n	70
	Mean (SD)	-3.3 (16.9)
	Median	0.0
	Min, max	-55.6, 33.3
OL Part A Week 96	n	65
	Mean (SD)	86.0 (17.8)
	Median	100.0
	Min, max	22.2, 100.0
Change at OL Part A Week 96	n	65
	Mean (SD)	-2.1 (16.1)
	Median	0.0
	Min, max	-33.3, 33.3

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Weight (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	68.4 (35.9)
	Median	66.7
	Min, max	0.0, 100.0
OL Part A Week 24	n	74
	Mean (SD)	73.9 (32.8)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 24	n	74
	Mean (SD)	5.0 (31.5)
	Median	0.0
	Min, max	-66.7, 100.0
OL Part A Week 48	n	72
	Mean (SD)	71.3 (36.4)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 48	n	72
	Mean (SD)	2.3 (34.2)
	Median	0.0
	Min, max	-100.0, 100.0

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Weight (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	77.6 (33.9)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 72	n	70
	Mean (SD)	8.1 (29.7)
	Median	0.0
	Min, max	-100.0, 100.0
OL Part A Week 96	n	65
	Mean (SD)	77.4 (32.3)
	Median	100.0
	Min, max	0.0, 100.0
Change at OL Part A Week 96	n	65
	Mean (SD)	5.6 (28.0)
	Median	0.0
	Min, max	-100.0, 66.7

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Digestion (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	81.9 (17.6)
	Median	88.9
	Min, max	22.2, 100.0
OL Part A Week 24	n	74
	Mean (SD)	81.4 (17.9)
	Median	88.9
	Min, max	22.2, 100.0
Change at OL Part A Week 24	n	74
	Mean (SD)	-0.8 (18.2)
	Median	0.0
	Min, max	-55.6, 44.4
OL Part A Week 48	n	72
	Mean (SD)	81.0 (17.2)
	Median	88.9
	Min, max	33.3, 100.0
Change at OL Part A Week 48	n	72
	Mean (SD)	-0.6 (18.4)
	Median	0.0
	Min, max	-44.4, 66.7

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.4.5c1a
Summary of CFQ-R Non-Respiratory Domain Scores (Parent's Version) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Domain: Digestion (Parents/Caregivers Form)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	70
	Mean (SD)	81.1 (17.4)
	Median	88.9
	Min, max	22.2, 100.0
Change at OL Part A Week 72	n	70
	Mean (SD)	-1.3 (17.6)
	Median	0.0
	Min, max	-55.6, 66.7
OL Part A Week 96	n	65
	Mean (SD)	81.7 (17.5)
	Median	88.9
	Min, max	33.3, 100.0
Change at OL Part A Week 96	n	65
	Mean (SD)	-0.3 (18.0)
	Median	0.0
	Min, max	-44.4, 55.6

- Baseline is defined as the pre-dose Day 1 value in the parent study.

Table 14.2.5.1c1a
Summary of BMI (kg/m^2) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	16.80 (2.02)
	Median	16.39
	Min, max	13.40, 23.43
OL Part A Week 8	n	75
	Mean (SD)	17.12 (2.23)
	Median	16.68
	Min, max	13.18, 24.21
Change at OL Part A Week 8	n	75
	Mean (SD)	0.32 (0.80)
	Median	0.14
	Min, max	-1.19, 3.00
OL Part A Week 16	n	74
	Mean (SD)	17.20 (2.38)
	Median	16.54
	Min, max	13.55, 25.73
Change at OL Part A Week 16	n	74
	Mean (SD)	0.41 (0.89)
	Median	0.22
	Min, max	-1.12, 3.02

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.5.1c1a
Summary of BMI (kg/m^2) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 24	n	73
	Mean (SD)	17.32 (2.40)
	Median	16.58
	Min, max	13.38, 25.94
Change at OL Part A Week 24	n	73
	Mean (SD)	0.49 (1.05)
	Median	0.30
	Min, max	-1.34, 3.85
OL Part A Week 36	n	73
	Mean (SD)	17.46 (2.53)
	Median	16.91
	Min, max	13.28, 26.07
Change at OL Part A Week 36	n	73
	Mean (SD)	0.63 (1.24)
	Median	0.50
	Min, max	-3.06, 3.90
OL Part A Week 48	n	73
	Mean (SD)	17.54 (2.55)
	Median	17.38
	Min, max	13.50, 27.43
Change at OL Part A Week 48	n	73
	Mean (SD)	0.71 (1.25)
	Median	0.47
	Min, max	-2.54, 5.10

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.5.1c1a
Summary of BMI (kg/m^2) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 60	n	71
	Mean (SD)	17.58 (2.55)
	Median	17.36
	Min, max	13.32, 26.32
Change at OL Part A Week 60	n	71
	Mean (SD)	0.76 (1.28)
	Median	0.79
	Min, max	-2.28, 5.78
OL Part A Week 72	n	71
	Mean (SD)	17.75 (2.64)
	Median	17.34
	Min, max	13.06, 26.23
Change at OL Part A Week 72	n	71
	Mean (SD)	0.92 (1.30)
	Median	0.76
	Min, max	-2.47, 5.98
OL Part A Week 84	n	69
	Mean (SD)	17.98 (2.59)
	Median	17.71
	Min, max	13.67, 25.03
Change at OL Part A Week 84	n	69
	Mean (SD)	1.15 (1.38)
	Median	0.82
	Min, max	-2.06, 6.31

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.5.1c1a
Summary of BMI (kg/m^2) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	68
	Mean (SD)	18.18 (2.80)
	Median	17.65
	Min, max	13.72, 25.79
Change at OL Part A Week 96	n	68
	Mean (SD)	1.34 (1.55)
	Median	1.06
	Min, max	-1.66, 7.11
OL Safety Follow-up	n	1
	Mean (SD)	18.11 (--)
	Median	18.11
	Min, max	18.11, 18.11
Change at OL Safety Follow-up	n	1
	Mean (SD)	2.27 (--)
	Median	2.27
	Min, max	2.27, 2.27

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

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Table 14.2.5.2c1a

MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A

Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	16.83 (2.13)
Absolute change at Day 15	
n	78
LS mean (SE)	-0.04 (0.04)
95% CI of LS mean	(-0.12, 0.04)
Absolute change at Week 4	
n	76
LS mean (SE)	0.01 (0.05)
95% CI of LS mean	(-0.09, 0.10)
Absolute change at Week 8	
n	78
LS mean (SE)	0.09 (0.05)
95% CI of LS mean	(-0.02, 0.19)
Absolute change at Week 12	
n	77
LS mean (SE)	0.06 (0.07)
95% CI of LS mean	(-0.08, 0.20)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.5.2c1a

MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A

Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	0.14 (0.07)
95% CI of LS mean	(0.00, 0.28)
Absolute change at Week 24	
n	78
LS mean (SE)	0.22 (0.08)
95% CI of LS mean	(0.05, 0.38)
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 8	
n	75
LS mean (SE)	0.32 (0.09)
95% CI of LS mean	(0.13, 0.50)
Absolute change at OL Part A Week 16	
n	74
LS mean (SE)	0.42 (0.10)
95% CI of LS mean	(0.22, 0.63)
Absolute change at OL Part A Week 24	
n	73
LS mean (SE)	0.50 (0.12)
95% CI of LS mean	(0.26, 0.75)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.5.2c1a

MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A

Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 36	
n	73
LS mean (SE)	0.64 (0.14)
95% CI of LS mean	(0.35, 0.93)
Absolute change at OL Part A Week 48	
n	73
LS mean (SE)	0.73 (0.14)
95% CI of LS mean	(0.44, 1.01)
Absolute change at OL Part A Week 60	
n	71
LS mean (SE)	0.76 (0.15)
95% CI of LS mean	(0.47, 1.05)
Absolute change at OL Part A Week 72	
n	71
LS mean (SE)	0.92 (0.15)
95% CI of LS mean	(0.62, 1.22)
Absolute change at OL Part A Week 84	
n	69
LS mean (SE)	1.15 (0.16)
95% CI of LS mean	(0.83, 1.47)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.5.2c1a
MMRM Analysis of Absolute Change from Baseline in BMI (kg/m^2) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 96	
n	68
LS mean (SE)	1.36 (0.18)
95% CI of LS mean	(1.00, 1.72)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline BMI as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.5.3c1a
Summary of BMI-for-Age z-score and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	0.07 (0.86)
	Median	0.09
	Min, max	-1.75, 1.84
OL Part A Week 8	n	75
	Mean (SD)	0.04 (0.89)
	Median	0.12
	Min, max	-2.06, 1.91
Change at OL Part A Week 8	n	75
	Mean (SD)	-0.03 (0.32)
	Median	-0.08
	Min, max	-0.67, 0.74
OL Part A Week 16	n	74
	Mean (SD)	0.03 (0.93)
	Median	0.01
	Min, max	-1.97, 2.07
Change at OL Part A Week 16	n	74
	Mean (SD)	-0.04 (0.35)
	Median	-0.05
	Min, max	-0.72, 0.69

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.5.3c1a
Summary of BMI-for-Age z-score and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 24	n	73
	Mean (SD)	0.05 (0.91)
	Median	0.05
	Min, max	-1.92, 2.22
Change at OL Part A Week 24	n	73
	Mean (SD)	-0.04 (0.38)
	Median	-0.06
	Min, max	-0.82, 0.78
OL Part A Week 36	n	73
	Mean (SD)	0.03 (0.96)
	Median	0.11
	Min, max	-2.05, 2.08
Change at OL Part A Week 36	n	73
	Mean (SD)	-0.05 (0.48)
	Median	-0.02
	Min, max	-1.69, 0.95
OL Part A Week 48	n	73
	Mean (SD)	0.01 (0.97)
	Median	0.05
	Min, max	-2.40, 2.26
Change at OL Part A Week 48	n	73
	Mean (SD)	-0.07 (0.48)
	Median	-0.08
	Min, max	-2.08, 0.85

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.5.3c1a
Summary of BMI-for-Age z-score and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 60	n	71
	Mean (SD)	-0.02 (0.98)
	Median	0.05
	Min, max	-2.60, 2.30
Change at OL Part A Week 60	n	71
	Mean (SD)	-0.10 (0.49)
	Median	-0.07
	Min, max	-1.49, 0.83
OL Part A Week 72	n	71
	Mean (SD)	-0.02 (1.02)
	Median	0.02
	Min, max	-3.07, 2.27
Change at OL Part A Week 72	n	71
	Mean (SD)	-0.10 (0.54)
	Median	-0.09
	Min, max	-2.74, 0.97
OL Part A Week 84	n	69
	Mean (SD)	0.04 (0.95)
	Median	0.03
	Min, max	-2.42, 2.26
Change at OL Part A Week 84	n	69
	Mean (SD)	-0.04 (0.51)
	Median	0.08
	Min, max	-2.10, 1.02

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.5.3c1a
Summary of BMI-for-Age z-score and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	68
	Mean (SD)	0.02 (1.04)
	Median	-0.03
	Min, max	-2.30, 2.29
Change at OL Part A Week 96	n	68
	Mean (SD)	-0.06 (0.53)
	Median	-0.03
	Min, max	-1.98, 1.17
OL Safety Follow-up	n	1
	Mean (SD)	0.67 (--)
	Median	0.67
	Min, max	0.67, 0.67
Change at OL Safety Follow-up	n	1
	Mean (SD)	0.42 (--)
	Median	0.42
	Min, max	0.42, 0.42

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.5.4c1a
MMRM Analysis of Absolute Change from Baseline in BMI-for-Age z-score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	0.07 (0.87)
Absolute change at Day 15	
n	78
LS mean (SE)	-0.04 (0.02)
95% CI of LS mean	(-0.09, 0.00)
Absolute change at Week 4	
n	76
LS mean (SE)	-0.04 (0.02)
95% CI of LS mean	(-0.09, 0.00)
Absolute change at Week 8	
n	78
LS mean (SE)	-0.02 (0.03)
95% CI of LS mean	(-0.07, 0.03)
Absolute change at Week 12	
n	77
LS mean (SE)	-0.07 (0.04)
95% CI of LS mean	(-0.14, 0.01)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline BMI-for-age z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.5.4c1a
MMRM Analysis of Absolute Change from Baseline in BMI-for-Age z-score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	-0.04 (0.03)
95% CI of LS mean	(-0.10, 0.03)
Absolute change at Week 24	
n	78
LS mean (SE)	-0.05 (0.03)
95% CI of LS mean	(-0.12, 0.02)
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 8	
n	75
LS mean (SE)	-0.03 (0.04)
95% CI of LS mean	(-0.10, 0.05)
Absolute change at OL Part A Week 16	
n	74
LS mean (SE)	-0.03 (0.04)
95% CI of LS mean	(-0.11, 0.05)
Absolute change at OL Part A Week 24	
n	73
LS mean (SE)	-0.03 (0.04)
95% CI of LS mean	(-0.12, 0.06)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline BMI-for-age z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.5.4c1a
MMRM Analysis of Absolute Change from Baseline in BMI-for-Age z-score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 36	
n	73
LS mean (SE)	-0.04 (0.06)
95% CI of LS mean	(-0.16, 0.07)
Absolute change at OL Part A Week 48	
n	73
LS mean (SE)	-0.07 (0.06)
95% CI of LS mean	(-0.18, 0.05)
Absolute change at OL Part A Week 60	
n	71
LS mean (SE)	-0.10 (0.06)
95% CI of LS mean	(-0.22, 0.01)
Absolute change at OL Part A Week 72	
n	71
LS mean (SE)	-0.11 (0.06)
95% CI of LS mean	(-0.23, 0.02)
Absolute change at OL Part A Week 84	
n	69
LS mean (SE)	-0.04 (0.06)
95% CI of LS mean	(-0.16, 0.08)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline BMI-for-age z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.5.4c1a
MMRM Analysis of Absolute Change from Baseline in BMI-for-Age z-score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 96	
n	68
LS mean (SE)	-0.05 (0.06)
95% CI of LS mean	(-0.17, 0.07)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline BMI-for-age z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.1c1a
Summary of Weight (kg) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	30.08 (7.01)
	Median	29.00
	Min, max	19.30, 47.50
OL Part A Week 8	n	75
	Mean (SD)	32.37 (7.78)
	Median	32.00
	Min, max	19.70, 48.90
Change at OL Part A Week 8	n	75
	Mean (SD)	2.29 (1.70)
	Median	1.70
	Min, max	-0.40, 7.20
OL Part A Week 16	n	74
	Mean (SD)	32.80 (8.01)
	Median	32.55
	Min, max	20.00, 49.70
Change at OL Part A Week 16	n	74
	Mean (SD)	2.77 (1.95)
	Median	2.20
	Min, max	-0.30, 7.44

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.6.1c1a
Summary of Weight (kg) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 24	n	73
	Mean (SD)	33.53 (8.17)
	Median	33.10
	Min, max	21.80, 51.20
Change at OL Part A Week 24	n	73
	Mean (SD)	3.44 (2.35)
	Median	2.60
	Min, max	0.30, 9.56
OL Part A Week 36	n	73
	Mean (SD)	34.46 (8.43)
	Median	34.60
	Min, max	22.00, 52.34
Change at OL Part A Week 36	n	73
	Mean (SD)	4.37 (2.69)
	Median	3.60
	Min, max	-1.70, 10.90
OL Part A Week 48	n	73
	Mean (SD)	35.39 (8.75)
	Median	35.60
	Min, max	22.40, 56.79
Change at OL Part A Week 48	n	73
	Mean (SD)	5.30 (3.02)
	Median	4.40
	Min, max	-0.20, 15.15

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.6.1c1a
Summary of Weight (kg) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 60	n	71
	Mean (SD)	36.29 (8.98)
	Median	35.60
	Min, max	23.00, 55.79
Change at OL Part A Week 60	n	71
	Mean (SD)	6.13 (3.21)
	Median	5.20
	Min, max	0.70, 16.00
OL Part A Week 72	n	71
	Mean (SD)	37.40 (9.56)
	Median	37.30
	Min, max	22.80, 58.20
Change at OL Part A Week 72	n	71
	Mean (SD)	7.24 (3.61)
	Median	6.20
	Min, max	0.00, 16.50
OL Part A Week 84	n	69
	Mean (SD)	38.66 (9.80)
	Median	38.60
	Min, max	23.90, 59.30
Change at OL Part A Week 84	n	69
	Mean (SD)	8.42 (3.86)
	Median	7.10
	Min, max	1.90, 17.90

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.6.1c1a
Summary of Weight (kg) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	68
	Mean (SD)	40.02 (10.12)
	Median	39.95
	Min, max	24.10, 60.30
Change at OL Part A Week 96	n	68
	Mean (SD)	9.62 (4.41)
	Median	8.35
	Min, max	2.80, 20.00
OL Safety Follow-up	n	1
	Mean (SD)	29.40 (--)
	Median	29.40
	Min, max	29.40, 29.40
Change at OL Safety Follow-up	n	1
	Mean (SD)	9.70 (--)
	Median	9.70
	Min, max	9.70, 9.70

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.6.2c1a

MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A

Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	30.21 (7.48)
Absolute change at Day 15	
n	78
LS mean (SE)	0.04 (0.06)
95% CI of LS mean	(-0.08, 0.17)
Absolute change at Week 4	
n	76
LS mean (SE)	0.23 (0.08)
95% CI of LS mean	(0.06, 0.39)
Absolute change at Week 8	
n	78
LS mean (SE)	0.58 (0.10)
95% CI of LS mean	(0.38, 0.78)
Absolute change at Week 12	
n	77
LS mean (SE)	0.74 (0.12)
95% CI of LS mean	(0.50, 0.99)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.2c1a
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	1.13 (0.13)
95% CI of LS mean	(0.88, 1.39)
Absolute change at Week 24	
n	78
LS mean (SE)	1.67 (0.17)
95% CI of LS mean	(1.34, 2.00)
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 8	
n	75
LS mean (SE)	2.29 (0.19)
95% CI of LS mean	(1.92, 2.66)
Absolute change at OL Part A Week 16	
n	74
LS mean (SE)	2.81 (0.21)
95% CI of LS mean	(2.38, 3.24)
Absolute change at OL Part A Week 24	
n	73
LS mean (SE)	3.46 (0.26)
95% CI of LS mean	(2.94, 3.99)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.2c1a
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 36	
n	73
LS mean (SE)	4.40 (0.30)
95% CI of LS mean	(3.80, 4.99)
Absolute change at OL Part A Week 48	
n	73
LS mean (SE)	5.32 (0.33)
95% CI of LS mean	(4.65, 5.98)
Absolute change at OL Part A Week 60	
n	71
LS mean (SE)	6.11 (0.35)
95% CI of LS mean	(5.40, 6.81)
Absolute change at OL Part A Week 72	
n	71
LS mean (SE)	7.22 (0.39)
95% CI of LS mean	(6.44, 8.01)
Absolute change at OL Part A Week 84	
n	69
LS mean (SE)	8.42 (0.42)
95% CI of LS mean	(7.58, 9.26)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.2c1a
MMRM Analysis of Absolute Change from Baseline in Weight (kg) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 96	
n	68
LS mean (SE)	9.63 (0.49)
95% CI of LS mean	(8.65, 10.60)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline weight as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.3c1a
Summary of Weight-for-Age z-score and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	-0.01 (0.88)
	Median	0.00
	Min, max	-1.89, 1.48
OL Part A Week 8	n	75
	Mean (SD)	-0.02 (0.94)
	Median	0.07
	Min, max	-1.87, 1.88
Change at OL Part A Week 8	n	75
	Mean (SD)	-0.01 (0.25)
	Median	-0.07
	Min, max	-0.51, 0.65
OL Part A Week 16	n	74
	Mean (SD)	-0.05 (0.96)
	Median	0.01
	Min, max	-1.89, 1.98
Change at OL Part A Week 16	n	74
	Mean (SD)	-0.04 (0.27)
	Median	-0.06
	Min, max	-0.61, 0.58

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.6.3c1a
Summary of Weight-for-Age z-score and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 24	n	73
	Mean (SD)	-0.03 (0.95)
	Median	-0.01
	Min, max	-1.78, 2.21
Change at OL Part A Week 24	n	73
	Mean (SD)	-0.02 (0.30)
	Median	-0.08
	Min, max	-0.57, 0.74
OL Part A Week 36	n	73
	Mean (SD)	-0.03 (0.97)
	Median	-0.02
	Min, max	-2.22, 2.07
Change at OL Part A Week 36	n	73
	Mean (SD)	-0.01 (0.33)
	Median	-0.04
	Min, max	-0.83, 0.77
OL Part A Week 48	n	73
	Mean (SD)	-0.03 (1.00)
	Median	0.00
	Min, max	-2.20, 2.27
Change at OL Part A Week 48	n	73
	Mean (SD)	-0.02 (0.37)
	Median	-0.07
	Min, max	-1.11, 0.80

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.6.3c1a
Summary of Weight-for-Age z-score and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 60	n	71
	Mean (SD)	-0.03 (0.99)
	Median	0.00
	Min, max	-2.54, 2.40
Change at OL Part A Week 60	n	71
	Mean (SD)	-0.04 (0.38)
	Median	-0.08
	Min, max	-0.94, 0.92
OL Part A Week 72	n	71
	Mean (SD)	-0.02 (1.04)
	Median	0.12
	Min, max	-2.54, 2.31
Change at OL Part A Week 72	n	71
	Mean (SD)	-0.03 (0.41)
	Median	-0.12
	Min, max	-1.40, 0.83
OL Part A Week 84	n	69
	Mean (SD)	0.02 (1.00)
	Median	0.12
	Min, max	-2.40, 2.29
Change at OL Part A Week 84	n	69
	Mean (SD)	0.00 (0.40)
	Median	-0.08
	Min, max	-0.93, 0.81

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.6.3c1a
Summary of Weight-for-Age z-score and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	68
	Mean (SD)	0.04 (1.07)
	Median	0.13
	Min, max	-2.40, 2.31
Change at OL Part A Week 96	n	68
	Mean (SD)	0.01 (0.43)
	Median	-0.07
	Min, max	-0.85, 1.04
OL Safety Follow-up	n	1
	Mean (SD)	-0.12 (--)
	Median	-0.12
	Min, max	-0.12, -0.12
Change at OL Safety Follow-up	n	1
	Mean (SD)	0.84 (--)
	Median	0.84
	Min, max	0.84, 0.84

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.6.4c1a
MMRM Analysis of Absolute Change from Baseline in Weight-for-Age z-score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	0.00 (0.89)
Absolute change at Day 15	
n	78
LS mean (SE)	-0.03 (0.01)
95% CI of LS mean	(-0.05, 0.00)
Absolute change at Week 4	
n	76
LS mean (SE)	-0.03 (0.02)
95% CI of LS mean	(-0.07, 0.00)
Absolute change at Week 8	
n	78
LS mean (SE)	-0.01 (0.02)
95% CI of LS mean	(-0.04, 0.03)
Absolute change at Week 12	
n	77
LS mean (SE)	-0.03 (0.02)
95% CI of LS mean	(-0.08, 0.01)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline weight-for-age z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.4c1a
MMRM Analysis of Absolute Change from Baseline in Weight-for-Age z-score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	-0.01 (0.02)
95% CI of LS mean	(-0.06, 0.03)
Absolute change at Week 24	
n	78
LS mean (SE)	-0.02 (0.03)
95% CI of LS mean	(-0.07, 0.03)
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 8	
n	75
LS mean (SE)	-0.01 (0.03)
95% CI of LS mean	(-0.07, 0.04)
Absolute change at OL Part A Week 16	
n	74
LS mean (SE)	-0.03 (0.03)
95% CI of LS mean	(-0.09, 0.03)
Absolute change at OL Part A Week 24	
n	73
LS mean (SE)	-0.02 (0.04)
95% CI of LS mean	(-0.09, 0.06)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline weight-for-age z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.4c1a
MMRM Analysis of Absolute Change from Baseline in Weight-for-Age z-score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 36	
n	73
LS mean (SE)	-0.01 (0.04)
95% CI of LS mean	(-0.09, 0.07)
Absolute change at OL Part A Week 48	
n	73
LS mean (SE)	-0.02 (0.04)
95% CI of LS mean	(-0.10, 0.07)
Absolute change at OL Part A Week 60	
n	71
LS mean (SE)	-0.04 (0.04)
95% CI of LS mean	(-0.13, 0.05)
Absolute change at OL Part A Week 72	
n	71
LS mean (SE)	-0.04 (0.05)
95% CI of LS mean	(-0.13, 0.06)
Absolute change at OL Part A Week 84	
n	69
LS mean (SE)	0.00 (0.05)
95% CI of LS mean	(-0.09, 0.10)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline weight-for-age z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.6.4c1a
MMRM Analysis of Absolute Change from Baseline in Weight-for-Age z-score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 96	
n	68
LS mean (SE)	0.02 (0.05)
95% CI of LS mean	(-0.08, 0.12)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline weight-for-age z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.1c1a
Summary of Height (cm) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	132.9 (10.4)
	Median	133.1
	Min, max	111.5, 153.7
OL Part A Week 8	n	75
	Mean (SD)	136.5 (10.6)
	Median	135.0
	Min, max	113.5, 158.3
Change at OL Part A Week 8	n	75
	Mean (SD)	3.6 (1.2)
	Median	3.5
	Min, max	1.3, 7.3
OL Part A Week 16	n	74
	Mean (SD)	137.1 (10.7)
	Median	136.0
	Min, max	114.2, 159.1
Change at OL Part A Week 16	n	74
	Mean (SD)	4.3 (1.3)
	Median	4.2
	Min, max	1.4, 8.4

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.7.1c1a
Summary of Height (cm) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 24	n	73
	Mean (SD)	138.2 (10.9)
	Median	137.5
	Min, max	114.6, 160.7
Change at OL Part A Week 24	n	73
	Mean (SD)	5.4 (1.6)
	Median	5.0
	Min, max	0.9, 9.4
OL Part A Week 36	n	73
	Mean (SD)	139.6 (11.2)
	Median	138.4
	Min, max	116.8, 162.2
Change at OL Part A Week 36	n	73
	Mean (SD)	6.8 (2.5)
	Median	6.0
	Min, max	3.2, 17.2
OL Part A Week 48	n	73
	Mean (SD)	141.0 (10.9)
	Median	139.4
	Min, max	120.4, 163.8
Change at OL Part A Week 48	n	73
	Mean (SD)	8.2 (2.0)
	Median	8.2
	Min, max	4.2, 14.2

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.7.1c1a
Summary of Height (cm) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 60	n	71
	Mean (SD)	142.6 (11.1)
	Median	141.8
	Min, max	121.5, 166.0
Change at OL Part A Week 60	n	71
	Mean (SD)	9.7 (2.4)
	Median	9.7
	Min, max	3.8, 15.6
OL Part A Week 72	n	71
	Mean (SD)	144.0 (11.4)
	Median	142.2
	Min, max	124.0, 167.6
Change at OL Part A Week 72	n	71
	Mean (SD)	11.1 (2.9)
	Median	10.6
	Min, max	3.9, 19.6
OL Part A Week 84	n	69
	Mean (SD)	145.5 (11.5)
	Median	143.4
	Min, max	125.3, 170.4
Change at OL Part A Week 84	n	69
	Mean (SD)	12.4 (3.2)
	Median	11.9
	Min, max	5.5, 19.4

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.7.1c1a
Summary of Height (cm) and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	68
	Mean (SD)	147.2 (11.3)
	Median	145.9
	Min, max	126.8, 170.4
Change at OL Part A Week 96	n	68
	Mean (SD)	13.8 (3.5)
	Median	13.3
	Min, max	5.0, 22.9
OL Safety Follow-up	n	1
	Mean (SD)	127.4 (--)
	Median	127.4
	Min, max	127.4, 127.4
Change at OL Safety Follow-up	n	1
	Mean (SD)	15.9 (--)
	Median	15.9
	Min, max	15.9, 15.9

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

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Table 14.2.7.2c1a

MMRM Analysis of Absolute Change from Baseline in Height (cm) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A

Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	133.0 (10.5)
Absolute change at Day 15	
n	78
LS mean (SE)	0.2 (0.1)
95% CI of LS mean	(0.1, 0.3)
Absolute change at Week 4	
n	76
LS mean (SE)	0.4 (0.1)
95% CI of LS mean	(0.3, 0.6)
Absolute change at Week 8	
n	78
LS mean (SE)	0.9 (0.1)
95% CI of LS mean	(0.7, 1.0)
Absolute change at Week 12	
n	77
LS mean (SE)	1.3 (0.1)
95% CI of LS mean	(1.1, 1.6)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.2c1a
MMRM Analysis of Absolute Change from Baseline in Height (cm) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	1.9 (0.1)
95% CI of LS mean	(1.7, 2.1)
Absolute change at Week 24	
n	78
LS mean (SE)	2.7 (0.1)
95% CI of LS mean	(2.5, 3.0)
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 8	
n	75
LS mean (SE)	3.6 (0.1)
95% CI of LS mean	(3.3, 3.9)
Absolute change at OL Part A Week 16	
n	74
LS mean (SE)	4.3 (0.2)
95% CI of LS mean	(4.0, 4.6)
Absolute change at OL Part A Week 24	
n	73
LS mean (SE)	5.4 (0.2)
95% CI of LS mean	(5.0, 5.7)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.2c1a
MMRM Analysis of Absolute Change from Baseline in Height (cm) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 36	
n	73
LS mean (SE)	6.8 (0.3)
95% CI of LS mean	(6.2, 7.3)
Absolute change at OL Part A Week 48	
n	73
LS mean (SE)	8.2 (0.2)
95% CI of LS mean	(7.7, 8.7)
Absolute change at OL Part A Week 60	
n	71
LS mean (SE)	9.6 (0.3)
95% CI of LS mean	(9.1, 10.2)
Absolute change at OL Part A Week 72	
n	71
LS mean (SE)	11.0 (0.3)
95% CI of LS mean	(10.3, 11.7)
Absolute change at OL Part A Week 84	
n	69
LS mean (SE)	12.4 (0.4)
95% CI of LS mean	(11.6, 13.1)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.2c1a
MMRM Analysis of Absolute Change from Baseline in Height (cm) at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 96	
n	68
LS mean (SE)	13.8 (0.4)
95% CI of LS mean	(13.0, 14.6)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline height as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.3c1a
Summary of Height-for-Age z-score and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	75
	Mean (SD)	-0.05 (0.95)
	Median	-0.06
	Min, max	-2.18, 2.06
OL Part A Week 8	n	75
	Mean (SD)	-0.04 (0.97)
	Median	-0.09
	Min, max	-2.11, 2.19
Change at OL Part A Week 8	n	75
	Mean (SD)	0.00 (0.18)
	Median	-0.02
	Min, max	-0.37, 0.51
OL Part A Week 16	n	74
	Mean (SD)	-0.08 (0.98)
	Median	-0.17
	Min, max	-2.14, 2.21
Change at OL Part A Week 16	n	74
	Mean (SD)	-0.03 (0.20)
	Median	-0.03
	Min, max	-0.54, 0.51

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.7.3c1a
Summary of Height-for-Age z-score and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 24	n	73
	Mean (SD)	-0.07 (0.99)
	Median	-0.18
	Min, max	-2.15, 2.39
Change at OL Part A Week 24	n	73
	Mean (SD)	0.00 (0.25)
	Median	-0.01
	Min, max	-0.55, 0.62
OL Part A Week 36	n	73
	Mean (SD)	-0.05 (1.07)
	Median	-0.22
	Min, max	-2.16, 3.39
Change at OL Part A Week 36	n	73
	Mean (SD)	0.02 (0.35)
	Median	-0.06
	Min, max	-0.53, 1.45
OL Part A Week 48	n	73
	Mean (SD)	-0.03 (0.96)
	Median	-0.11
	Min, max	-2.02, 2.38
Change at OL Part A Week 48	n	73
	Mean (SD)	0.03 (0.29)
	Median	0.01
	Min, max	-0.74, 0.92

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.7.3c1a
Summary of Height-for-Age z-score and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 60	n	71
	Mean (SD)	0.02 (0.95)
	Median	-0.10
	Min, max	-2.06, 2.30
Change at OL Part A Week 60	n	71
	Mean (SD)	0.04 (0.34)
	Median	0.02
	Min, max	-0.98, 0.96
OL Part A Week 72	n	71
	Mean (SD)	0.03 (0.97)
	Median	-0.02
	Min, max	-1.84, 2.61
Change at OL Part A Week 72	n	71
	Mean (SD)	0.05 (0.40)
	Median	0.03
	Min, max	-0.99, 1.25
OL Part A Week 84	n	69
	Mean (SD)	0.04 (0.96)
	Median	-0.03
	Min, max	-1.65, 2.56
Change at OL Part A Week 84	n	69
	Mean (SD)	0.05 (0.42)
	Median	0.02
	Min, max	-0.99, 0.93

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.7.3c1a
Summary of Height-for-Age z-score and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 96	n	68
	Mean (SD)	0.09 (0.97)
	Median	0.01
	Min, max	-1.65, 2.67
Change at OL Part A Week 96	n	68
	Mean (SD)	0.07 (0.44)
	Median	0.04
	Min, max	-1.19, 1.21
OL Safety Follow-up	n	1
	Mean (SD)	-1.13 (--)
	Median	-1.13
	Min, max	-1.13, -1.13
Change at OL Safety Follow-up	n	1
	Mean (SD)	0.73 (--)
	Median	0.73
	Min, max	0.73, 0.73

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.7.4c1a
MMRM Analysis of Absolute Change from Baseline in Height-for-Age z-score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	78
Mean (SD)	-0.03 (0.94)
Absolute change at Day 15	
n	78
LS mean (SE)	0.00 (0.01)
95% CI of LS mean	(-0.02, 0.02)
Absolute change at Week 4	
n	76
LS mean (SE)	-0.01 (0.01)
95% CI of LS mean	(-0.03, 0.02)
Absolute change at Week 8	
n	78
LS mean (SE)	0.00 (0.01)
95% CI of LS mean	(-0.03, 0.03)
Absolute change at Week 12	
n	77
LS mean (SE)	0.01 (0.02)
95% CI of LS mean	(-0.03, 0.04)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline height-for-age z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.4c1a
MMRM Analysis of Absolute Change from Baseline in Height-for-Age z-score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at Week 16	
n	78
LS mean (SE)	0.02 (0.02)
95% CI of LS mean	(-0.02, 0.05)
Absolute change at Week 24	
n	78
LS mean (SE)	0.01 (0.02)
95% CI of LS mean	(-0.03, 0.05)
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 8	
n	75
LS mean (SE)	0.00 (0.02)
95% CI of LS mean	(-0.04, 0.05)
Absolute change at OL Part A Week 16	
n	74
LS mean (SE)	-0.03 (0.02)
95% CI of LS mean	(-0.07, 0.02)
Absolute change at OL Part A Week 24	
n	73
LS mean (SE)	0.00 (0.03)
95% CI of LS mean	(-0.06, 0.05)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline height-for-age z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.4c1a
MMRM Analysis of Absolute Change from Baseline in Height-for-Age z-score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 36	
n	73
LS mean (SE)	0.01 (0.04)
95% CI of LS mean	(-0.07, 0.09)
Absolute change at OL Part A Week 48	
n	73
LS mean (SE)	0.03 (0.03)
95% CI of LS mean	(-0.04, 0.10)
Absolute change at OL Part A Week 60	
n	71
LS mean (SE)	0.04 (0.04)
95% CI of LS mean	(-0.04, 0.12)
Absolute change at OL Part A Week 72	
n	71
LS mean (SE)	0.05 (0.05)
95% CI of LS mean	(-0.04, 0.15)
Absolute change at OL Part A Week 84	
n	69
LS mean (SE)	0.05 (0.05)
95% CI of LS mean	(-0.05, 0.15)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline height-for-age z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.7.4c1a
MMRM Analysis of Absolute Change from Baseline in Height-for-Age z-score at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Absolute change at OL Part A Week 96	
n	68
LS mean (SE)	0.08 (0.05)
95% CI of LS mean	(-0.02, 0.19)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline height-for-age z-score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.8.1c1a
Proportion of Subjects with Sweat Chloride <60 mmol/L at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	VNZ/TEZ/D-IVA N = 75
Baseline	
N1	74
n	62
Proportion, n/N1 (%)	83.8
OL Part A Week 24	
N1	71
n	65
Proportion, n/N1 (%)	91.5
95% CI for the proportion	(82.5, 96.8)
OL Part A Week 48	
N1	71
n	65
Proportion, n/N1 (%)	91.5
95% CI for the proportion	(82.5, 96.8)
OL Part A Week 72	
N1	65
n	57
Proportion, n/N1 (%)	87.7
95% CI for the proportion	(77.2, 94.5)
OL Part A Week 96	
N1	63
n	56
Proportion, n/N1 (%)	88.9
95% CI for the proportion	(78.4, 95.4)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- N1: number of subjects with non-missing SwCl at the given visit
- n: number of subjects at a given visit with SwCl <60 mmol/L
- 95% CI is based on the Clopper-Pearson method.

Table 14.2.8.2c1a
Proportion of Subjects with Sweat Chloride <30 mmol/L at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Visit	VNZ/TEZ/D-IVA N = 75
Baseline	
N1	74
n	29
Proportion, n/N1 (%)	39.2
OL Part A Week 24	
N1	71
n	38
Proportion, n/N1 (%)	53.5
95% CI for the proportion	(41.3, 65.5)
OL Part A Week 48	
N1	71
n	29
Proportion, n/N1 (%)	40.8
95% CI for the proportion	(29.3, 53.2)
OL Part A Week 72	
N1	65
n	25
Proportion, n/N1 (%)	38.5
95% CI for the proportion	(26.7, 51.4)
OL Part A Week 96	
N1	63
n	32
Proportion, n/N1 (%)	50.8
95% CI for the proportion	(37.9, 63.6)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- N1: number of subjects with non-missing SwCl at the given visit
- n: number of subjects at a given visit with SwCl <30 mmol/L
- 95% CI is based on the Clopper-Pearson method.

Table 14.2.12.1c1a
Summary of LCI Parameters and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

LCI to 2.5% Initial Concentration

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	69
	Mean (SD)	6.64 (0.75)
	Median	6.51
	Min, max	5.30, 9.37
OL Part A Week 24	n	63
	Mean (SD)	6.49 (0.92)
	Median	6.38
	Min, max	5.19, 12.29
Change at OL Part A Week 24	n	61
	Mean (SD)	-0.14 (0.77)
	Median	-0.16
	Min, max	-2.03, 2.92
OL Part A Week 48	n	62
	Mean (SD)	6.48 (0.88)
	Median	6.31
	Min, max	5.15, 9.65
Change at OL Part A Week 48	n	59
	Mean (SD)	-0.15 (0.87)
	Median	-0.20
	Min, max	-1.69, 3.08

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.12.1c1a
Summary of LCI Parameters and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

LCI to 2.5% Initial Concentration

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	54
	Mean (SD)	6.42 (0.70)
	Median	6.38
	Min, max	5.48, 9.97
Change at OL Part A Week 72	n	53
	Mean (SD)	-0.24 (0.59)
	Median	-0.24
	Min, max	-1.63, 1.06
OL Part A Week 96	n	56
	Mean (SD)	6.49 (0.64)
	Median	6.35
	Min, max	5.40, 9.13
Change at OL Part A Week 96	n	52
	Mean (SD)	-0.12 (0.59)
	Median	-0.11
	Min, max	-1.58, 1.44

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.12.1c1a
Summary of LCI Parameters and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

LCI to 5% Initial Concentration

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	69
	Mean (SD)	5.15 (0.50)
	Median	4.99
	Min, max	4.38, 6.81
OL Part A Week 24	n	63
	Mean (SD)	5.02 (0.50)
	Median	4.94
	Min, max	4.16, 8.01
Change at OL Part A Week 24	n	61
	Mean (SD)	-0.12 (0.46)
	Median	-0.09
	Min, max	-1.42, 1.39
OL Part A Week 48	n	62
	Mean (SD)	5.01 (0.47)
	Median	4.91
	Min, max	4.08, 6.62
Change at OL Part A Week 48	n	59
	Mean (SD)	-0.13 (0.51)
	Median	-0.14
	Min, max	-1.18, 1.24

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.12.1c1a
Summary of LCI Parameters and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

LCI to 5% Initial Concentration

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	54
	Mean (SD)	4.96 (0.37)
	Median	4.94
	Min, max	4.21, 6.16
Change at OL Part A Week 72	n	53
	Mean (SD)	-0.20 (0.40)
	Median	-0.13
	Min, max	-1.24, 0.58
OL Part A Week 96	n	56
	Mean (SD)	5.06 (0.38)
	Median	5.04
	Min, max	4.22, 6.06
Change at OL Part A Week 96	n	52
	Mean (SD)	-0.07 (0.44)
	Median	-0.06
	Min, max	-1.21, 1.05

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.12.1c1a
Summary of LCI Parameters and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Functional Residual Capacity (L)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
Baseline	n	69
	Mean (SD)	1.14 (0.28)
	Median	1.10
	Min, max	0.62, 1.87
OL Part A Week 24	n	63
	Mean (SD)	1.30 (0.38)
	Median	1.25
	Min, max	0.69, 2.49
Change at OL Part A Week 24	n	61
	Mean (SD)	0.15 (0.21)
	Median	0.15
	Min, max	-0.58, 0.68
OL Part A Week 48	n	62
	Mean (SD)	1.33 (0.40)
	Median	1.26
	Min, max	0.62, 2.47
Change at OL Part A Week 48	n	59
	Mean (SD)	0.20 (0.24)
	Median	0.23
	Min, max	-0.59, 0.65

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.

Table 14.2.12.1c1a
Summary of LCI Parameters and Change from Baseline at Each Visit - OL Efficacy Period for Part A
OL Full Analysis Set - Cohort 1

Functional Residual Capacity (L)

Visit	Statistic	VNZ/TEZ/D-IVA N = 75
OL Part A Week 72	n	54
	Mean (SD)	1.45 (0.43)
	Median	1.40
	Min, max	0.70, 2.62
Change at OL Part A Week 72	n	53
	Mean (SD)	0.33 (0.24)
	Median	0.30
	Min, max	-0.39, 0.84
OL Part A Week 96	n	56
	Mean (SD)	1.43 (0.47)
	Median	1.29
	Min, max	0.79, 3.26
Change at OL Part A Week 96	n	52
	Mean (SD)	0.31 (0.27)
	Median	0.28
	Min, max	-0.21, 1.38

Table 14.2.12.2c1a
MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
Parent Study Efficacy Period	
N	78
Baseline	
n	72
Mean (SD)	6.63 (0.74)
Absolute change at Day 15	
n	65
LS mean (SE)	0.11 (0.07)
95% CI of LS mean	(-0.04, 0.26)
Absolute change at Week 4	
n	64
LS mean (SE)	-0.01 (0.07)
95% CI of LS mean	(-0.16, 0.13)
Absolute change at Week 12	
n	63
LS mean (SE)	0.00 (0.06)
95% CI of LS mean	(-0.13, 0.12)
Absolute change at Week 24	
n	58
LS mean (SE)	-0.16 (0.06)
95% CI of LS mean	(-0.28, -0.04)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline LCI2.5 as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.2.12.2c1a
MMRM Analysis of Absolute Change from Baseline in $LCI_{2.5}$ at Each Visit - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

	VNZ/TEZ/D-IVA
OL Efficacy Period for Part A	
N	75
Absolute change at OL Part A Week 24	
n	61
LS mean (SE)	-0.15 (0.10)
95% CI of LS mean	(-0.34, 0.04)
Absolute change at OL Part A Week 48	
n	59
LS mean (SE)	-0.14 (0.11)
95% CI of LS mean	(-0.35, 0.08)
Absolute change at OL Part A Week 72	
n	53
LS mean (SE)	-0.24 (0.07)
95% CI of LS mean	(-0.38, -0.10)
Absolute change at OL Part A Week 96	
n	52
LS mean (SE)	-0.15 (0.07)
95% CI of LS mean	(-0.28, -0.02)

- Baseline is defined as the pre-dose Day 1 value in the parent study. For subjects who are on stable ELX/TEZ/IVA prior to the parent study, if the pre-dose Day 1 value in the parent study is missing, parent study screening assessments will be used as baseline.
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline LCI2.5 as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78		OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Total duration of safety analysis period in 100 PY	--	0.39	--	1.44
Subjects with any TEAEs	75 (96.2)	1101.01	74 (98.7)	709.32
Infections and infestations	42 (53.8)	184.78	64 (85.3)	192.31
Infective pulmonary exacerbation of cystic fibrosis	13 (16.7)	41.06	23 (30.7)	36.93
Influenza	0	0	16 (21.3)	13.94
Upper respiratory tract infection	6 (7.7)	20.53	13 (17.3)	16.03
Nasopharyngitis	3 (3.8)	10.27	12 (16.0)	16.03
Pharyngitis streptococcal	7 (9.0)	20.53	11 (14.7)	9.06
Rhinitis	7 (9.0)	20.53	9 (12.0)	16.72
Sinusitis	0	0	7 (9.3)	6.27
COVID-19	3 (3.8)	7.70	5 (6.7)	3.48
Conjunctivitis	0	0	5 (6.7)	3.48
Ear infection	4 (5.1)	10.27	5 (6.7)	4.18
Otitis media	1 (1.3)	2.57	5 (6.7)	3.48
Viral upper respiratory tract infection	2 (2.6)	5.13	5 (6.7)	5.57
Bronchitis	0	0	4 (5.3)	3.48
Gastroenteritis	1 (1.3)	2.57	4 (5.3)	2.79
Gastroenteritis viral	0	0	4 (5.3)	2.79
Pharyngitis	0	0	4 (5.3)	4.18
Respiratory tract infection	1 (1.3)	2.57	4 (5.3)	3.48
Bacterial disease carrier	0	0	3 (4.0)	6.27
Impetigo	1 (1.3)	2.57	3 (4.0)	2.09
Otitis externa	3 (3.8)	7.70	3 (4.0)	2.79

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1)		OL study (121-106 Cohort 1 Part A)	
	VNZ/TEZ/D-IVA N = 78		VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Respiratory tract infection viral	0	0	3 (4.0)	2.09
Tonsillitis	0	0	3 (4.0)	2.79
Gastrointestinal viral infection	0	0	2 (2.7)	1.39
Lower respiratory tract infection	1 (1.3)	2.57	2 (2.7)	1.39
Lower respiratory tract infection bacterial	0	0	2 (2.7)	1.39
Molluscum contagiosum	0	0	2 (2.7)	1.39
Parainfluenzae virus infection	0	0	2 (2.7)	1.39
Pneumonia	0	0	2 (2.7)	1.39
Pneumonia bacterial	0	0	2 (2.7)	1.39
Acute sinusitis	0	0	1 (1.3)	0.70
Campylobacter gastroenteritis	0	0	1 (1.3)	0.70
Croup infectious	2 (2.6)	5.13	1 (1.3)	0.70
Eczema herpeticum	1 (1.3)	2.57	1 (1.3)	1.39
Escherichia urinary tract infection	0	0	1 (1.3)	0.70
Gastroenteritis norovirus	0	0	1 (1.3)	0.70
Gastrointestinal infection	0	0	1 (1.3)	0.70
Genital infection fungal	0	0	1 (1.3)	0.70
Human ehrlichiosis	0	0	1 (1.3)	0.70
Lice infestation	0	0	1 (1.3)	0.70
Localised infection	0	0	1 (1.3)	0.70
Oral herpes	0	0	1 (1.3)	0.70
Peritonsillar abscess	0	0	1 (1.3)	0.70
Pneumonia haemophilus	0	0	1 (1.3)	0.70
Pneumonia mycoplasmal	0	0	1 (1.3)	0.70
Pneumonia pseudomonal	1 (1.3)	2.57	1 (1.3)	0.70

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78		OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Rhinovirus infection	0	0	1 (1.3)	0.70
Scarlet fever	0	0	1 (1.3)	0.70
Tinea cruris	0	0	1 (1.3)	0.70
Viral rash	0	0	1 (1.3)	0.70
Adenovirus infection	1 (1.3)	5.13	0	0
Eye infection	1 (1.3)	2.57	0	0
Hordeolum	1 (1.3)	2.57	0	0
Pseudomonas bronchitis	1 (1.3)	2.57	0	0
Respiratory tract infection bacterial	1 (1.3)	2.57	0	0
Skin bacterial infection	1 (1.3)	2.57	0	0
Respiratory, thoracic and mediastinal disorders	51 (65.4)	313.11	60 (80.0)	227.15
Cough	36 (46.2)	138.59	54 (72.0)	110.09
Oropharyngeal pain	13 (16.7)	41.06	21 (28.0)	25.08
Nasal congestion	9 (11.5)	28.23	20 (26.7)	34.84
Productive cough	6 (7.7)	15.40	12 (16.0)	15.33
Rhinorrhoea	9 (11.5)	30.80	10 (13.3)	11.15
Dyspnoea	2 (2.6)	5.13	4 (5.3)	4.18
Sinus pain	0	0	3 (4.0)	3.48
Sputum increased	2 (2.6)	7.70	3 (4.0)	2.09
Asthma	1 (1.3)	2.57	2 (2.7)	1.39
Epistaxis	2 (2.6)	5.13	2 (2.7)	9.06
Sneezing	1 (1.3)	2.57	2 (2.7)	1.39
Wheezing	3 (3.8)	7.70	2 (2.7)	1.39
Allergic cough	0	0	1 (1.3)	0.70

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78		OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Haemoptysis	1 (1.3)	2.57	1 (1.3)	0.70
Nasal dryness	0	0	1 (1.3)	0.70
Nasal obstruction	0	0	1 (1.3)	0.70
Obstructive sleep apnoea syndrome	0	0	1 (1.3)	0.70
Sinus congestion	2 (2.6)	5.13	1 (1.3)	0.70
Stridor	0	0	1 (1.3)	0.70
Tonsillar hypertrophy	0	0	1 (1.3)	0.70
Upper respiratory tract congestion	0	0	1 (1.3)	1.39
Upper-airway cough syndrome	1 (1.3)	2.57	1 (1.3)	0.70
Dysphonia	1 (1.3)	2.57	0	0
Dyspnoea exertional	1 (1.3)	2.57	0	0
Lower respiratory tract congestion	1 (1.3)	5.13	0	0
Pleurisy	1 (1.3)	2.57	0	0
Sputum discoloured	1 (1.3)	2.57	0	0
Throat clearing	1 (1.3)	2.57	0	0
Gastrointestinal disorders	25 (32.1)	151.42	38 (50.7)	64.10
Abdominal pain	9 (11.5)	46.20	13 (17.3)	18.12
Vomiting	8 (10.3)	35.93	11 (14.7)	11.15
Abdominal pain upper	6 (7.7)	23.10	10 (13.3)	7.66
Diarrhoea	6 (7.7)	15.40	10 (13.3)	7.66
Constipation	2 (2.6)	5.13	8 (10.7)	5.57
Nausea	3 (3.8)	7.70	7 (9.3)	4.88
Distal intestinal obstruction syndrome	0	0	2 (2.7)	1.39
Gastrooesophageal reflux disease	0	0	2 (2.7)	1.39

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78		OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Abdominal discomfort	0	0	1 (1.3)	0.70
Angular cheilitis	0	0	1 (1.3)	0.70
Cheilitis	0	0	1 (1.3)	0.70
Dyspepsia	0	0	1 (1.3)	0.70
Faecaloma	0	0	1 (1.3)	0.70
Gastritis	0	0	1 (1.3)	0.70
Odynophagia	0	0	1 (1.3)	0.70
Salivary gland calculus	0	0	1 (1.3)	0.70
Toothache	0	0	1 (1.3)	0.70
Abdominal distension	1 (1.3)	2.57	0	0
Dysphagia	1 (1.3)	2.57	0	0
Flatulence	1 (1.3)	2.57	0	0
Gastrointestinal pain	1 (1.3)	2.57	0	0
Overflow diarrhoea	1 (1.3)	2.57	0	0
Steatorrhoea	1 (1.3)	2.57	0	0
Stomatitis	1 (1.3)	2.57	0	0
General disorders and administration site conditions	22 (28.2)	92.39	36 (48.0)	46.68
Pyrexia	16 (20.5)	64.16	29 (38.7)	34.14
Fatigue	7 (9.0)	17.97	9 (12.0)	6.27
Ill-defined disorder	0	0	2 (2.7)	1.39
Pain	1 (1.3)	2.57	2 (2.7)	1.39
Asthenia	0	0	1 (1.3)	0.70
Chest pain	1 (1.3)	2.57	1 (1.3)	0.70
Chills	1 (1.3)	2.57	1 (1.3)	0.70

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78		OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Influenza like illness	1 (1.3)	2.57	1 (1.3)	0.70
Malaise	0	0	1 (1.3)	0.70
Investigations	22 (28.2)	146.29	32 (42.7)	53.65
Pulmonary function test decreased	3 (3.8)	10.27	7 (9.3)	5.57
Bacterial test positive	3 (3.8)	10.27	6 (8.0)	4.88
Alanine aminotransferase increased	4 (5.1)	10.27	4 (5.3)	2.79
Blood creatine phosphokinase increased	2 (2.6)	5.13	3 (4.0)	2.79
Streptococcus test positive	1 (1.3)	2.57	3 (4.0)	2.09
Aspartate aminotransferase increased	2 (2.6)	5.13	2 (2.7)	1.39
Escherichia test positive	0	0	2 (2.7)	1.39
Monocyte count decreased	2 (2.6)	5.13	2 (2.7)	2.09
Mycoplasma test positive	0	0	2 (2.7)	1.39
Neutrophil count decreased	6 (7.7)	25.66	2 (2.7)	4.88
White blood cell count decreased	4 (5.1)	10.27	2 (2.7)	4.18
Amylase increased	0	0	1 (1.3)	0.70
Blood glucose increased	1 (1.3)	2.57	1 (1.3)	0.70
Blood lactate dehydrogenase increased	0	0	1 (1.3)	0.70
Bordetella test positive	0	0	1 (1.3)	0.70
Burkholderia test positive	0	0	1 (1.3)	2.79
Enterovirus test positive	1 (1.3)	2.57	1 (1.3)	0.70
Forced expiratory volume decreased	0	0	1 (1.3)	0.70
Gamma-glutamyltransferase increased	0	0	1 (1.3)	0.70
Haemoglobin increased	1 (1.3)	2.57	1 (1.3)	0.70
Haemophilus test positive	2 (2.6)	5.13	1 (1.3)	0.70

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1)		OL study (121-106 Cohort 1 Part A)	
	VNZ/TEZ/D-IVA N = 78		VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Human metapneumovirus test positive	0	0	1 (1.3)	0.70
Human rhinovirus test positive	1 (1.3)	2.57	1 (1.3)	0.70
Influenza A virus test positive	0	0	1 (1.3)	0.70
Influenza virus test positive	0	0	1 (1.3)	0.70
International normalised ratio increased	1 (1.3)	2.57	1 (1.3)	0.70
Neutrophil percentage decreased	0	0	1 (1.3)	0.70
Pseudomonas test positive	0	0	1 (1.3)	1.39
Respiratory syncytial virus test positive	0	0	1 (1.3)	0.70
SARS-CoV-2 test positive	3 (3.8)	7.70	1 (1.3)	0.70
Specific gravity urine increased	0	0	1 (1.3)	0.70
Staphylococcus test positive	1 (1.3)	2.57	1 (1.3)	0.70
Viral test positive	0	0	1 (1.3)	0.70
Vitamin A increased	0	0	1 (1.3)	0.70
Vitamin D decreased	0	0	1 (1.3)	0.70
Weight decreased	1 (1.3)	2.57	1 (1.3)	0.70
Activated partial thromboplastin time prolonged	1 (1.3)	2.57	0	0
Blood bilirubin increased	1 (1.3)	2.57	0	0
Blood bilirubin unconjugated increased	1 (1.3)	2.57	0	0
Blood potassium increased	1 (1.3)	2.57	0	0
Eosinophil count increased	1 (1.3)	5.13	0	0
Haemoglobin decreased	1 (1.3)	2.57	0	0
Influenza B virus test positive	1 (1.3)	2.57	0	0
Monocyte count increased	1 (1.3)	2.57	0	0
Platelet count decreased	1 (1.3)	2.57	0	0
Prothrombin time prolonged	1 (1.3)	2.57	0	0

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78		OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Red blood cells urine positive	1 (1.3)	2.57	0	0
Nervous system disorders	17 (21.8)	64.16	27 (36.0)	39.72
Headache	14 (17.9)	43.63	21 (28.0)	27.87
Lethargy	3 (3.8)	7.70	5 (6.7)	4.18
Dizziness	3 (3.8)	7.70	3 (4.0)	2.09
Epilepsy	0	0	1 (1.3)	0.70
Febrile convulsion	0	0	1 (1.3)	0.70
Presyncope	0	0	1 (1.3)	0.70
Seizure	1 (1.3)	2.57	1 (1.3)	2.79
Syncope	0	0	1 (1.3)	0.70
Loss of consciousness	1 (1.3)	2.57	0	0
Injury, poisoning and procedural complications	11 (14.1)	35.93	19 (25.3)	19.51
Skin laceration	1 (1.3)	5.13	4 (5.3)	2.79
Fall	0	0	2 (2.7)	1.39
Hand fracture	1 (1.3)	2.57	2 (2.7)	1.39
Joint injury	0	0	2 (2.7)	1.39
Chest injury	0	0	1 (1.3)	0.70
Concussion	1 (1.3)	2.57	1 (1.3)	0.70
Eye contusion	0	0	1 (1.3)	0.70
Humerus fracture	0	0	1 (1.3)	0.70
Ligament sprain	1 (1.3)	2.57	1 (1.3)	0.70
Limb injury	0	0	1 (1.3)	0.70
Procedural pain	0	0	1 (1.3)	0.70

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78		OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Radius fracture	0	0	1 (1.3)	0.70
Skin abrasion	0	0	1 (1.3)	0.70
Stoma site hypergranulation	0	0	1 (1.3)	0.70
Stoma site irritation	0	0	1 (1.3)	0.70
Sunburn	0	0	1 (1.3)	0.70
Thermal burn	0	0	1 (1.3)	0.70
Torus fracture	0	0	1 (1.3)	0.70
Upper limb fracture	0	0	1 (1.3)	0.70
Vascular access site pain	0	0	1 (1.3)	0.70
Vascular access site thrombosis	0	0	1 (1.3)	0.70
Wrist fracture	1 (1.3)	2.57	1 (1.3)	0.70
Arthropod sting	1 (1.3)	2.57	0	0
Exposure to allergen	1 (1.3)	2.57	0	0
Foot fracture	1 (1.3)	2.57	0	0
Incorrect dose administered	2 (2.6)	5.13	0	0
Tooth fracture	1 (1.3)	2.57	0	0
Wound	2 (2.6)	5.13	0	0
Musculoskeletal and connective tissue disorders	4 (5.1)	15.40	12 (16.0)	13.94
Pain in extremity	2 (2.6)	7.70	4 (5.3)	2.79
Arthralgia	1 (1.3)	2.57	3 (4.0)	2.09
Back pain	0	0	3 (4.0)	2.09
Musculoskeletal chest pain	0	0	3 (4.0)	2.79
Growing pains	0	0	1 (1.3)	2.09
Juvenile idiopathic arthritis	0	0	1 (1.3)	0.70

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78		OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Muscle spasms	0	0	1 (1.3)	0.70
Scoliosis	0	0	1 (1.3)	0.70
Myalgia	1 (1.3)	2.57	0	0
Neck pain	1 (1.3)	2.57	0	0
Psychiatric disorders	5 (6.4)	12.83	10 (13.3)	10.45
Anger	0	0	2 (2.7)	1.39
Insomnia	0	0	2 (2.7)	1.39
Affective disorder	0	0	1 (1.3)	1.39
Aggression	1 (1.3)	2.57	1 (1.3)	0.70
Anxiety	1 (1.3)	2.57	1 (1.3)	0.70
Attention deficit hyperactivity disorder	0	0	1 (1.3)	0.70
Depressed mood	0	0	1 (1.3)	0.70
Major depression	0	0	1 (1.3)	0.70
Nightmare	0	0	1 (1.3)	0.70
Personality change	0	0	1 (1.3)	0.70
Somnambulism	0	0	1 (1.3)	1.39
Affect lability	1 (1.3)	2.57	0	0
Initial insomnia	2 (2.6)	5.13	0	0
Eye disorders	4 (5.1)	12.83	8 (10.7)	9.06
Cataract cortical	1 (1.3)	2.57	2 (2.7)	1.39
Eye pain	1 (1.3)	5.13	2 (2.7)	2.79
Lacrimation increased	0	0	2 (2.7)	1.39
Ocular hyperaemia	0	0	2 (2.7)	1.39

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78		OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Hypermetropia	0	0	1 (1.3)	0.70
Mydriasis	0	0	1 (1.3)	0.70
Vision blurred	0	0	1 (1.3)	0.70
Conjunctivitis allergic	1 (1.3)	2.57	0	0
Dry eye	1 (1.3)	2.57	0	0
Metabolism and nutrition disorders	3 (3.8)	10.27	8 (10.7)	6.97
Decreased appetite	2 (2.6)	5.13	2 (2.7)	2.09
Vitamin D deficiency	0	0	2 (2.7)	1.39
Glucose tolerance impaired	1 (1.3)	2.57	1 (1.3)	0.70
Hypoglycaemia	0	0	1 (1.3)	0.70
Lactose intolerance	0	0	1 (1.3)	0.70
Vitamin K deficiency	0	0	1 (1.3)	0.70
Weight gain poor	0	0	1 (1.3)	0.70
Failure to thrive	1 (1.3)	2.57	0	0
Skin and subcutaneous tissue disorders	9 (11.5)	25.66	8 (10.7)	6.97
Dermatitis contact	0	0	2 (2.7)	1.39
Pruritus	0	0	2 (2.7)	1.39
Rash	4 (5.1)	10.27	2 (2.7)	1.39
Drug eruption	0	0	1 (1.3)	0.70
Dry skin	0	0	1 (1.3)	0.70
Yellow skin	0	0	1 (1.3)	1.39
Acne	1 (1.3)	2.57	0	0
Eczema asteatotic	1 (1.3)	2.57	0	0

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78		OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Erythema	1 (1.3)	2.57	0	0
Night sweats	1 (1.3)	2.57	0	0
Pigmentation disorder	1 (1.3)	5.13	0	0
Immune system disorders	4 (5.1)	10.27	6 (8.0)	5.57
Seasonal allergy	3 (3.8)	7.70	3 (4.0)	3.48
Allergy to arthropod bite	0	0	1 (1.3)	0.70
Drug hypersensitivity	0	0	1 (1.3)	0.70
Food allergy	1 (1.3)	2.57	1 (1.3)	0.70
Ear and labyrinth disorders	2 (2.6)	7.70	4 (5.3)	3.48
Ear pain	1 (1.3)	5.13	3 (4.0)	2.09
External ear disorder	0	0	1 (1.3)	0.70
Vertigo	0	0	1 (1.3)	0.70
Middle ear effusion	1 (1.3)	2.57	0	0
Reproductive system and breast disorders	2 (2.6)	5.13	3 (4.0)	4.18
Dysmenorrhoea	1 (1.3)	2.57	1 (1.3)	2.09
Gynaecomastia	0	0	1 (1.3)	0.70
Penile erythema	1 (1.3)	2.57	1 (1.3)	0.70
Testicular disorder	0	0	1 (1.3)	0.70
Hepatobiliary disorders	0	0	2 (2.7)	1.39
Cholelithiasis	0	0	1 (1.3)	0.70
Hepatic mass	0	0	1 (1.3)	0.70

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.2c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78		OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Blood and lymphatic system disorders	2 (2.6)	5.13	1 (1.3)	0.70
Mesenteric lymphadenitis	0	0	1 (1.3)	0.70
Lymphadenitis	1 (1.3)	2.57	0	0
Lymphadenopathy	1 (1.3)	2.57	0	0
Congenital, familial and genetic disorders	0	0	1 (1.3)	0.70
Cystic fibrosis related diabetes	0	0	1 (1.3)	0.70
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (1.3)	2.57	1 (1.3)	0.70
Skin papilloma	1 (1.3)	2.57	1 (1.3)	0.70
Renal and urinary disorders	1 (1.3)	5.13	1 (1.3)	1.39
Dysuria	1 (1.3)	2.57	1 (1.3)	0.70
Nephrocalcinosis	0	0	1 (1.3)	0.70
Micturition urgency	1 (1.3)	2.57	0	0
Vascular disorders	0	0	1 (1.3)	0.70
Pallor	0	0	1 (1.3)	0.70

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Subjects with any TEAEs	75 (96.2)	74 (98.7)
Grade 1/Mild	39 (50.0)	26 (34.7)
Grade 2/Moderate	36 (46.2)	41 (54.7)
Grade 3/Severe	0	7 (9.3)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Infections and infestations	42 (53.8)	64 (85.3)
Grade 1/Mild	25 (32.1)	32 (42.7)
Grade 2/Moderate	17 (21.8)	27 (36.0)
Grade 3/Severe	0	5 (6.7)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Infective pulmonary exacerbation of cystic fibrosis	13 (16.7)	23 (30.7)
Grade 1/Mild	6 (7.7)	9 (12.0)
Grade 2/Moderate	7 (9.0)	10 (13.3)
Grade 3/Severe	0	4 (5.3)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Influenza	0	16 (21.3)
Grade 1/Mild	0	7 (9.3)
Grade 2/Moderate	0	8 (10.7)
Grade 3/Severe	0	1 (1.3)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Upper respiratory tract infection	6 (7.7)	13 (17.3)
Grade 1/Mild	5 (6.4)	7 (9.3)
Grade 2/Moderate	1 (1.3)	6 (8.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Nasopharyngitis	3 (3.8)	12 (16.0)
Grade 1/Mild	3 (3.8)	11 (14.7)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pharyngitis streptococcal	7 (9.0)	11 (14.7)
Grade 1/Mild	6 (7.7)	8 (10.7)
Grade 2/Moderate	1 (1.3)	3 (4.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Rhinitis	7 (9.0)	9 (12.0)
Grade 1/Mild	7 (9.0)	6 (8.0)
Grade 2/Moderate	0	3 (4.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Sinusitis	0	7 (9.3)
Grade 1/Mild	0	6 (8.0)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
COVID-19	3 (3.8)	5 (6.7)
Grade 1/Mild	1 (1.3)	3 (4.0)
Grade 2/Moderate	2 (2.6)	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Conjunctivitis	0	5 (6.7)
Grade 1/Mild	0	4 (5.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Ear infection	4 (5.1)	5 (6.7)
Grade 1/Mild	3 (3.8)	2 (2.7)
Grade 2/Moderate	1 (1.3)	3 (4.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Otitis media	1 (1.3)	5 (6.7)
Grade 1/Mild	0	3 (4.0)
Grade 2/Moderate	1 (1.3)	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Viral upper respiratory tract infection	2 (2.6)	5 (6.7)
Grade 1/Mild	2 (2.6)	4 (5.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Bronchitis	0	4 (5.3)
Grade 1/Mild	0	3 (4.0)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Gastroenteritis	1 (1.3)	4 (5.3)
Grade 1/Mild	0	3 (4.0)
Grade 2/Moderate	1 (1.3)	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Gastroenteritis viral	0	4 (5.3)
Grade 1/Mild	0	3 (4.0)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pharyngitis	0	4 (5.3)
Grade 1/Mild	0	3 (4.0)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Respiratory tract infection	1 (1.3)	4 (5.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	3 (4.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Bacterial disease carrier	0	3 (4.0)
Grade 1/Mild	0	0
Grade 2/Moderate	0	3 (4.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Impetigo	1 (1.3)	3 (4.0)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Otitis externa	3 (3.8)	3 (4.0)
Grade 1/Mild	2 (2.6)	0
Grade 2/Moderate	1 (1.3)	3 (4.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Respiratory tract infection viral	0	3 (4.0)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Tonsillitis	0	3 (4.0)
Grade 1/Mild	0	3 (4.0)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Gastrointestinal viral infection	0	2 (2.7)
Grade 1/Mild	0	0
Grade 2/Moderate	0	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Lower respiratory tract infection	1 (1.3)	2 (2.7)
Grade 1/Mild	0	2 (2.7)
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Lower respiratory tract infection bacterial	0	2 (2.7)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Molluscum contagiosum	0	2 (2.7)
Grade 1/Mild	0	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Parainfluenzae virus infection	0	2 (2.7)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	1 (1.3)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pneumonia	0	2 (2.7)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pneumonia bacterial	0	2 (2.7)
Grade 1/Mild	0	0
Grade 2/Moderate	0	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Acute sinusitis	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Campylobacter gastroenteritis	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Croup infectious	2 (2.6)	1 (1.3)
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	1 (1.3)	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Eczema herpeticum	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Escherichia urinary tract infection	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Gastroenteritis norovirus	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Gastrointestinal infection	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Genital infection fungal	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Human ehrlichiosis	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Lice infestation	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Localised infection	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Oral herpes	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Peritonsillar abscess	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Pneumonia haemophilus	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pneumonia mycoplasmal	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pneumonia pseudomonal	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Rhinovirus infection	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Scarlet fever	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Tinea cruris	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Viral rash	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Adenovirus infection	1 (1.3)	0
Grade 1/Mild	0	0
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Eye infection	1 (1.3)	0
Grade 1/Mild	0	0
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Hordeolum	1 (1.3)	0
Grade 1/Mild	0	0
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pseudomonas bronchitis	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Respiratory tract infection bacterial	1 (1.3)	0
Grade 1/Mild	0	0
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Skin bacterial infection	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Respiratory, thoracic and mediastinal disorders	51 (65.4)	60 (80.0)
Grade 1/Mild	35 (44.9)	33 (44.0)
Grade 2/Moderate	16 (20.5)	26 (34.7)
Grade 3/Severe	0	1 (1.3)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Cough	36 (46.2)	54 (72.0)
Grade 1/Mild	24 (30.8)	31 (41.3)
Grade 2/Moderate	12 (15.4)	22 (29.3)
Grade 3/Severe	0	1 (1.3)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Oropharyngeal pain	13 (16.7)	21 (28.0)
Grade 1/Mild	13 (16.7)	18 (24.0)
Grade 2/Moderate	0	3 (4.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Nasal congestion	9 (11.5)	20 (26.7)
Grade 1/Mild	9 (11.5)	18 (24.0)
Grade 2/Moderate	0	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Productive cough	6 (7.7)	12 (16.0)
Grade 1/Mild	3 (3.8)	8 (10.7)
Grade 2/Moderate	3 (3.8)	4 (5.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Rhinorrhoea	9 (11.5)	10 (13.3)
Grade 1/Mild	9 (11.5)	9 (12.0)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Dyspnoea	2 (2.6)	4 (5.3)
Grade 1/Mild	2 (2.6)	1 (1.3)
Grade 2/Moderate	0	3 (4.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Sinus pain	0	3 (4.0)
Grade 1/Mild	0	3 (4.0)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Sputum increased	2 (2.6)	3 (4.0)
Grade 1/Mild	0	3 (4.0)
Grade 2/Moderate	2 (2.6)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Asthma	1 (1.3)	2 (2.7)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	1 (1.3)	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Epistaxis	2 (2.6)	2 (2.7)
Grade 1/Mild	2 (2.6)	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Sneezing	1 (1.3)	2 (2.7)
Grade 1/Mild	1 (1.3)	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Wheezing	3 (3.8)	2 (2.7)
Grade 1/Mild	3 (3.8)	1 (1.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Allergic cough	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Haemoptysis	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Nasal dryness	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Nasal obstruction	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Obstructive sleep apnoea syndrome	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Sinus congestion	2 (2.6)	1 (1.3)
Grade 1/Mild	2 (2.6)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Stridor	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Tonsillar hypertrophy	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Upper respiratory tract congestion	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Upper-airway cough syndrome	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Dysphonia	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Dyspnoea exertional	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Lower respiratory tract congestion	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pleurisy	1 (1.3)	0
Grade 1/Mild	0	0
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Sputum discoloured	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Throat clearing	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Gastrointestinal disorders	25 (32.1)	38 (50.7)
Grade 1/Mild	21 (26.9)	25 (33.3)
Grade 2/Moderate	4 (5.1)	13 (17.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Abdominal pain	9 (11.5)	13 (17.3)
Grade 1/Mild	8 (10.3)	9 (12.0)
Grade 2/Moderate	1 (1.3)	4 (5.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Vomiting	8 (10.3)	11 (14.7)
Grade 1/Mild	6 (7.7)	9 (12.0)
Grade 2/Moderate	2 (2.6)	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Abdominal pain upper	6 (7.7)	10 (13.3)
Grade 1/Mild	5 (6.4)	9 (12.0)
Grade 2/Moderate	1 (1.3)	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Diarrhoea	6 (7.7)	10 (13.3)
Grade 1/Mild	5 (6.4)	9 (12.0)
Grade 2/Moderate	1 (1.3)	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Constipation	2 (2.6)	8 (10.7)
Grade 1/Mild	2 (2.6)	2 (2.7)
Grade 2/Moderate	0	6 (8.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Nausea	3 (3.8)	7 (9.3)
Grade 1/Mild	3 (3.8)	7 (9.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Distal intestinal obstruction syndrome	0	2 (2.7)
Grade 1/Mild	0	0
Grade 2/Moderate	0	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Gastrooesophageal reflux disease	0	2 (2.7)
Grade 1/Mild	0	0
Grade 2/Moderate	0	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Abdominal discomfort	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Angular cheilitis	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Cheilitis	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Dyspepsia	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Faecaloma	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Gastritis	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Odynophagia	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Salivary gland calculus	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Toothache	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Abdominal distension	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Dysphagia	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Flatulence	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Gastrointestinal pain	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Overflow diarrhoea	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Steatorrhoea	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Stomatitis	1 (1.3)	0
Grade 1/Mild	0	0
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
General disorders and administration site conditions	22 (28.2)	36 (48.0)
Grade 1/Mild	19 (24.4)	24 (32.0)
Grade 2/Moderate	3 (3.8)	12 (16.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Pyrexia	16 (20.5)	29 (38.7)
Grade 1/Mild	14 (17.9)	19 (25.3)
Grade 2/Moderate	2 (2.6)	10 (13.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Fatigue	7 (9.0)	9 (12.0)
Grade 1/Mild	6 (7.7)	8 (10.7)
Grade 2/Moderate	1 (1.3)	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Ill-defined disorder	0	2 (2.7)
Grade 1/Mild	0	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pain	1 (1.3)	2 (2.7)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Asthenia	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Chest pain	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Chills	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Influenza like illness	1 (1.3)	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Malaise	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Investigations	22 (28.2)	32 (42.7)
Grade 1/Mild	17 (21.8)	18 (24.0)
Grade 2/Moderate	5 (6.4)	13 (17.3)
Grade 3/Severe	0	1 (1.3)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pulmonary function test decreased	3 (3.8)	7 (9.3)
Grade 1/Mild	2 (2.6)	3 (4.0)
Grade 2/Moderate	1 (1.3)	4 (5.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Bacterial test positive	3 (3.8)	6 (8.0)
Grade 1/Mild	3 (3.8)	4 (5.3)
Grade 2/Moderate	0	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Alanine aminotransferase increased	4 (5.1)	4 (5.3)
Grade 1/Mild	3 (3.8)	3 (4.0)
Grade 2/Moderate	1 (1.3)	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Blood creatine phosphokinase increased	2 (2.6)	3 (4.0)
Grade 1/Mild	2 (2.6)	1 (1.3)
Grade 2/Moderate	0	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Streptococcus test positive	1 (1.3)	3 (4.0)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	1 (1.3)	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Aspartate aminotransferase increased	2 (2.6)	2 (2.7)
Grade 1/Mild	1 (1.3)	2 (2.7)
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Escherichia test positive	0	2 (2.7)
Grade 1/Mild	0	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Monocyte count decreased	2 (2.6)	2 (2.7)
Grade 1/Mild	0	2 (2.7)
Grade 2/Moderate	2 (2.6)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Mycoplasma test positive	0	2 (2.7)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Neutrophil count decreased	6 (7.7)	2 (2.7)
Grade 1/Mild	4 (5.1)	2 (2.7)
Grade 2/Moderate	2 (2.6)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
White blood cell count decreased	4 (5.1)	2 (2.7)
Grade 1/Mild	4 (5.1)	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Amylase increased	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Blood glucose increased	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Blood lactate dehydrogenase increased	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Bordetella test positive	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Burkholderia test positive	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	1 (1.3)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Enterovirus test positive	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Forced expiratory volume decreased	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Gamma-glutamyltransferase increased	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Haemoglobin increased	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Haemophilus test positive	2 (2.6)	1 (1.3)
Grade 1/Mild	2 (2.6)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Human metapneumovirus test positive	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Human rhinovirus test positive	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Influenza A virus test positive	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Influenza virus test positive	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
International normalised ratio increased	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Neutrophil percentage decreased	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pseudomonas test positive	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Respiratory syncytial virus test positive	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
SARS-CoV-2 test positive	3 (3.8)	1 (1.3)
Grade 1/Mild	3 (3.8)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Specific gravity urine increased	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Staphylococcus test positive	1 (1.3)	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Viral test positive	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Vitamin A increased	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Vitamin D decreased	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Weight decreased	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Activated partial thromboplastin time prolonged	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Blood bilirubin increased	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Blood bilirubin unconjugated increased	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Blood potassium increased	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Eosinophil count increased	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Haemoglobin decreased	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Influenza B virus test positive	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Monocyte count increased	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Platelet count decreased	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Prothrombin time prolonged	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Red blood cells urine positive	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Nervous system disorders	17 (21.8)	27 (36.0)
Grade 1/Mild	13 (16.7)	20 (26.7)
Grade 2/Moderate	4 (5.1)	6 (8.0)
Grade 3/Severe	0	1 (1.3)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Headache	14 (17.9)	21 (28.0)
Grade 1/Mild	12 (15.4)	15 (20.0)
Grade 2/Moderate	2 (2.6)	6 (8.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Lethargy	3 (3.8)	5 (6.7)
Grade 1/Mild	3 (3.8)	5 (6.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Dizziness	3 (3.8)	3 (4.0)
Grade 1/Mild	2 (2.6)	3 (4.0)
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Epilepsy	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Febrile convulsion	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Presyncope	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Seizure	1 (1.3)	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	1 (1.3)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Syncope	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Loss of consciousness	1 (1.3)	0
Grade 1/Mild	0	0
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Injury, poisoning and procedural complications	11 (14.1)	19 (25.3)
Grade 1/Mild	10 (12.8)	12 (16.0)
Grade 2/Moderate	1 (1.3)	7 (9.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Skin laceration	1 (1.3)	4 (5.3)
Grade 1/Mild	0	2 (2.7)
Grade 2/Moderate	1 (1.3)	2 (2.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Fall	0	2 (2.7)
Grade 1/Mild	0	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Hand fracture	1 (1.3)	2 (2.7)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Joint injury	0	2 (2.7)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Chest injury	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Concussion	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Eye contusion	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Humerus fracture	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Ligament sprain	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Limb injury	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Procedural pain	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Radius fracture	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Skin abrasion	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Stoma site hypergranulation	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Stoma site irritation	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Sunburn	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Thermal burn	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Torus fracture	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Upper limb fracture	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Vascular access site pain	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Vascular access site thrombosis	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Wrist fracture	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Arthropod sting	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Exposure to allergen	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Foot fracture	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Incorrect dose administered	2 (2.6)	0
Grade 1/Mild	2 (2.6)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Tooth fracture	1 (1.3)	0
Grade 1/Mild	0	0
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Wound	2 (2.6)	0
Grade 1/Mild	2 (2.6)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Musculoskeletal and connective tissue disorders	4 (5.1)	12 (16.0)
Grade 1/Mild	4 (5.1)	7 (9.3)
Grade 2/Moderate	0	5 (6.7)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pain in extremity	2 (2.6)	4 (5.3)
Grade 1/Mild	2 (2.6)	1 (1.3)
Grade 2/Moderate	0	3 (4.0)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Arthralgia	1 (1.3)	3 (4.0)
Grade 1/Mild	1 (1.3)	2 (2.7)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Back pain	0	3 (4.0)
Grade 1/Mild	0	3 (4.0)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Musculoskeletal chest pain	0	3 (4.0)
Grade 1/Mild	0	3 (4.0)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Growing pains	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Juvenile idiopathic arthritis	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Muscle spasms	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Scoliosis	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Myalgia	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Neck pain	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Psychiatric disorders	5 (6.4)	10 (13.3)
Grade 1/Mild	5 (6.4)	6 (8.0)
Grade 2/Moderate	0	3 (4.0)
Grade 3/Severe	0	1 (1.3)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Anger	0	2 (2.7)
Grade 1/Mild	0	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Insomnia	0	2 (2.7)
Grade 1/Mild	0	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Affective disorder	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	1 (1.3)
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Aggression	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Anxiety	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Attention deficit hyperactivity disorder	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Depressed mood	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Major depression	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Nightmare	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Personality change	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Somnambulism	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Affect lability	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Initial insomnia	2 (2.6)	0
Grade 1/Mild	2 (2.6)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Eye disorders	4 (5.1)	8 (10.7)
Grade 1/Mild	4 (5.1)	7 (9.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Cataract cortical	1 (1.3)	2 (2.7)
Grade 1/Mild	1 (1.3)	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Eye pain	1 (1.3)	2 (2.7)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Lacrimation increased	0	2 (2.7)
Grade 1/Mild	0	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Ocular hyperaemia	0	2 (2.7)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Hypermetropia	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Mydriasis	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Vision blurred	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Conjunctivitis allergic	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Dry eye	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Metabolism and nutrition disorders	3 (3.8)	8 (10.7)
Grade 1/Mild	1 (1.3)	4 (5.3)
Grade 2/Moderate	2 (2.6)	4 (5.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Decreased appetite	2 (2.6)	2 (2.7)
Grade 1/Mild	2 (2.6)	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Vitamin D deficiency	0	2 (2.7)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Glucose tolerance impaired	1 (1.3)	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Hypoglycaemia	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Lactose intolerance	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Vitamin K deficiency	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Weight gain poor	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Failure to thrive	1 (1.3)	0
Grade 1/Mild	0	0
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Skin and subcutaneous tissue disorders	9 (11.5)	8 (10.7)
Grade 1/Mild	9 (11.5)	8 (10.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Dermatitis contact	0	2 (2.7)
Grade 1/Mild	0	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pruritus	0	2 (2.7)
Grade 1/Mild	0	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Rash	4 (5.1)	2 (2.7)
Grade 1/Mild	4 (5.1)	2 (2.7)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Drug eruption	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Dry skin	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Yellow skin	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Acne	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Eczema asteatotic	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Erythema	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Night sweats	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Pigmentation disorder	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Immune system disorders	4 (5.1)	6 (8.0)
Grade 1/Mild	3 (3.8)	5 (6.7)
Grade 2/Moderate	1 (1.3)	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Seasonal allergy	3 (3.8)	3 (4.0)
Grade 1/Mild	2 (2.6)	3 (4.0)
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Allergy to arthropod bite	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Drug hypersensitivity	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Food allergy	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Ear and labyrinth disorders	2 (2.6)	4 (5.3)
Grade 1/Mild	2 (2.6)	3 (4.0)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Ear pain	1 (1.3)	3 (4.0)
Grade 1/Mild	1 (1.3)	2 (2.7)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
External ear disorder	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Vertigo	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Middle ear effusion	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Reproductive system and breast disorders	2 (2.6)	3 (4.0)
Grade 1/Mild	2 (2.6)	3 (4.0)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Dysmenorrhoea	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Gynaecomastia	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Penile erythema	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Testicular disorder	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Hepatobiliary disorders	0	2 (2.7)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Cholelithiasis	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Hepatic mass	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Blood and lymphatic system disorders	2 (2.6)	1 (1.3)
Grade 1/Mild	2 (2.6)	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Mesenteric lymphadenitis	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Lymphadenitis	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Lymphadenopathy	1 (1.3)	0
Grade 1/Mild	1 (1.3)	0
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Congenital, familial and genetic disorders	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Cystic fibrosis related diabetes	0	1 (1.3)
Grade 1/Mild	0	0
Grade 2/Moderate	0	1 (1.3)
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

	Parent study (121-105 Part B1)	OL study (121-106 Cohort 1 Part A)
System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 78 n (%)	VNZ/TEZ/D-IVA N = 75 n (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Skin papilloma	1 (1.3)	1 (1.3)
Grade 1/Mild	1 (1.3)	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Renal and urinary disorders	1 (1.3)	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

System Organ Class Preferred Term Maximum Severity	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78 n (%)	OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75 n (%)
Dysuria	1 (1.3)	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Nephrocalcinosis	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Micturition urgency	1 (1.3)	0
Grade 1/Mild	0	0
Grade 2/Moderate	1 (1.3)	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0
Vascular disorders	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.1.5c1a
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term and by Maximum Severity - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set OL Safety Set - Cohort 1

	Parent study (121-105 Part B1)	OL study (121-106 Cohort 1 Part A)
System Organ Class Preferred Term Maximum Severity	VNZ/TEZ/D-IVA N = 78 n (%)	VNZ/TEZ/D-IVA N = 75 n (%)
Pallor	0	1 (1.3)
Grade 1/Mild	0	1 (1.3)
Grade 2/Moderate	0	0
Grade 3/Severe	0	0
Grade 4/Life-threatening	0	0
Grade 5/Death	0	0

- MedDRA version 28.0.
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted within the maximum severity in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

Table 14.3.2.1c1a
Treatment-Emergent Adverse Events Leading to Death by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1)		OL study (121-106 Cohort 1 Part A)	
	VNZ/TEZ/D-IVA N = 78		VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY

No data met the criteria for this table.

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.2.2c1a
Serious TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1) VNZ/TEZ/D-IVA N = 78		OL study (121-106 Cohort 1 Part A) VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Total duration of safety analysis period in 100 PY	--	0.39	--	1.44
Subjects with any serious TEAEs	6 (7.7)	17.97	15 (20.0)	15.33
Infections and infestations	3 (3.8)	7.70	9 (12.0)	10.45
Infective pulmonary exacerbation of cystic fibrosis	2 (2.6)	5.13	7 (9.3)	6.27
Gastrointestinal viral infection	0	0	1 (1.3)	0.70
Influenza	0	0	1 (1.3)	0.70
Parainfluenzae virus infection	0	0	1 (1.3)	0.70
Pneumonia	0	0	1 (1.3)	0.70
Pneumonia bacterial	0	0	1 (1.3)	0.70
Respiratory tract infection	0	0	1 (1.3)	0.70
Adenovirus infection	1 (1.3)	2.57	0	0
Investigations	1 (1.3)	2.57	3 (4.0)	2.09
Burkholderia test positive	0	0	1 (1.3)	0.70
Pseudomonas test positive	0	0	1 (1.3)	0.70
Pulmonary function test decreased	1 (1.3)	2.57	1 (1.3)	0.70
Gastrointestinal disorders	1 (1.3)	2.57	2 (2.7)	1.39
Abdominal pain	0	0	1 (1.3)	0.70
Distal intestinal obstruction syndrome	0	0	1 (1.3)	0.70

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.2.2c1a
Serious TEAEs by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1)		OL study (121-106 Cohort 1 Part A)	
	VNZ/TEZ/D-IVA N = 78		VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Constipation	1 (1.3)	2.57	0	0
Nervous system disorders	0	0	1 (1.3)	0.70
Seizure	0	0	1 (1.3)	0.70
Psychiatric disorders	0	0	1 (1.3)	0.70
Affective disorder	0	0	1 (1.3)	0.70
Metabolism and nutrition disorders	1 (1.3)	2.57	0	0
Failure to thrive	1 (1.3)	2.57	0	0
Respiratory, thoracic and mediastinal disorders	1 (1.3)	2.57	0	0
Cough	1 (1.3)	2.57	0	0

- MedDRA version 28.0.
- TEAE: treatment-emergent adverse event
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

Table 14.3.2.5c1a
Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1)		OL study (121-106 Cohort 1 Part A)	
	VNZ/TEZ/D-IVA N = 78		VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Total duration of safety analysis period in 100 PY	--	0.39	--	1.44
Subjects with TEAEs leading to treatment discontinuation	1 (1.3)	5.13	3 (4.0)	4.88
Investigations	0	0	1 (1.3)	2.79
Alanine aminotransferase increased	0	0	1 (1.3)	0.70
Aspartate aminotransferase increased	0	0	1 (1.3)	0.70
Blood lactate dehydrogenase increased	0	0	1 (1.3)	0.70
Gamma-glutamyltransferase increased	0	0	1 (1.3)	0.70
Nervous system disorders	0	0	1 (1.3)	1.39
Epilepsy	0	0	1 (1.3)	0.70
Seizure	0	0	1 (1.3)	0.70
Psychiatric disorders	0	0	1 (1.3)	0.70
Affective disorder	0	0	1 (1.3)	0.70
General disorders and administration site conditions	1 (1.3)	2.57	0	0
Fatigue	1 (1.3)	2.57	0	0

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Table 14.3.2.5c1a
Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1)		OL study (121-106 Cohort 1 Part A)	
	VNZ/TEZ/D-IVA N = 78		VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Respiratory, thoracic and mediastinal disorders	1 (1.3)	2.57	0	0
Cough	1 (1.3)	2.57	0	0

- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.

Zusatzanalysen zur Studie VX22-121-106

Table 14.3.2.7c1a
Grade 3+ Treatment-Emergent Adverse Events by System Organ Class and Preferred Term - Parent Study Safety Period and OL Safety Period for Part A
Parent Study Safety Set and OL Safety Set - Cohort 1

	Parent study (121-105 Part B1)		OL study (121-106 Cohort 1 Part A)	
	VNZ/TEZ/D-IVA N = 78		VNZ/TEZ/D-IVA N = 75	
System Organ Class Preferred Term	n (%)	Events/100PY	n (%)	Events/100PY
Total duration of safety analysis period in 100 PY	--	0.39	--	1.44
Subjects with any Grade 3+ TEAEs	0	0	7 (9.3)	6.97
Infections and infestations	0	0	5 (6.7)	4.18
Infective pulmonary exacerbation of cystic fibrosis	0	0	4 (5.3)	2.79
Influenza	0	0	1 (1.3)	0.70
Parainfluenzae virus infection	0	0	1 (1.3)	0.70
Investigations	0	0	1 (1.3)	0.70
Burkholderia test positive	0	0	1 (1.3)	0.70
Nervous system disorders	0	0	1 (1.3)	0.70
Seizure	0	0	1 (1.3)	0.70
Psychiatric disorders	0	0	1 (1.3)	0.70
Affective disorder	0	0	1 (1.3)	0.70
Respiratory, thoracic and mediastinal disorders	0	0	1 (1.3)	0.70
Cough	0	0	1 (1.3)	0.70

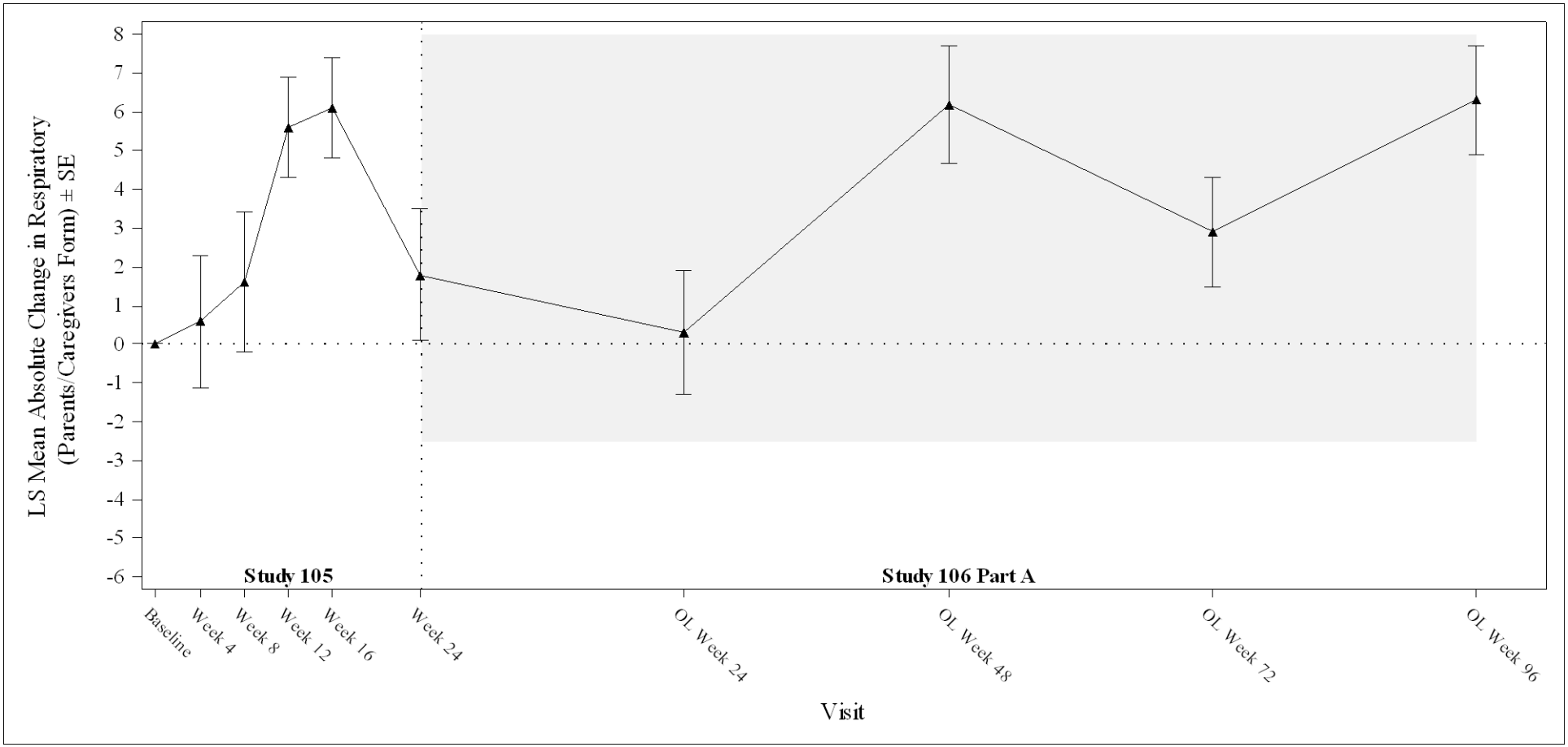
- MedDRA version 28.0.
- Events/100PY: number of events per 100 patient years (336 days = 48 weeks per year) = number of events/total duration of safety analysis period in 100PY
- A subject with multiple events within a category (Any, System Organ Class [SOC], or Preferred Term [PT]) is counted only once in that category.
- Table is sorted in descending order of frequency of the OL study (121-106 Cohort 1 Part A) column by SOC, and by PT within each SOC.
- Subjects with Grade 3+ TEAEs include the 'Severe', 'Life-threatening' and 'Death' categories.

Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Child's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Respiratory

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Respiratory score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX22-121-106



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Respiratory score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

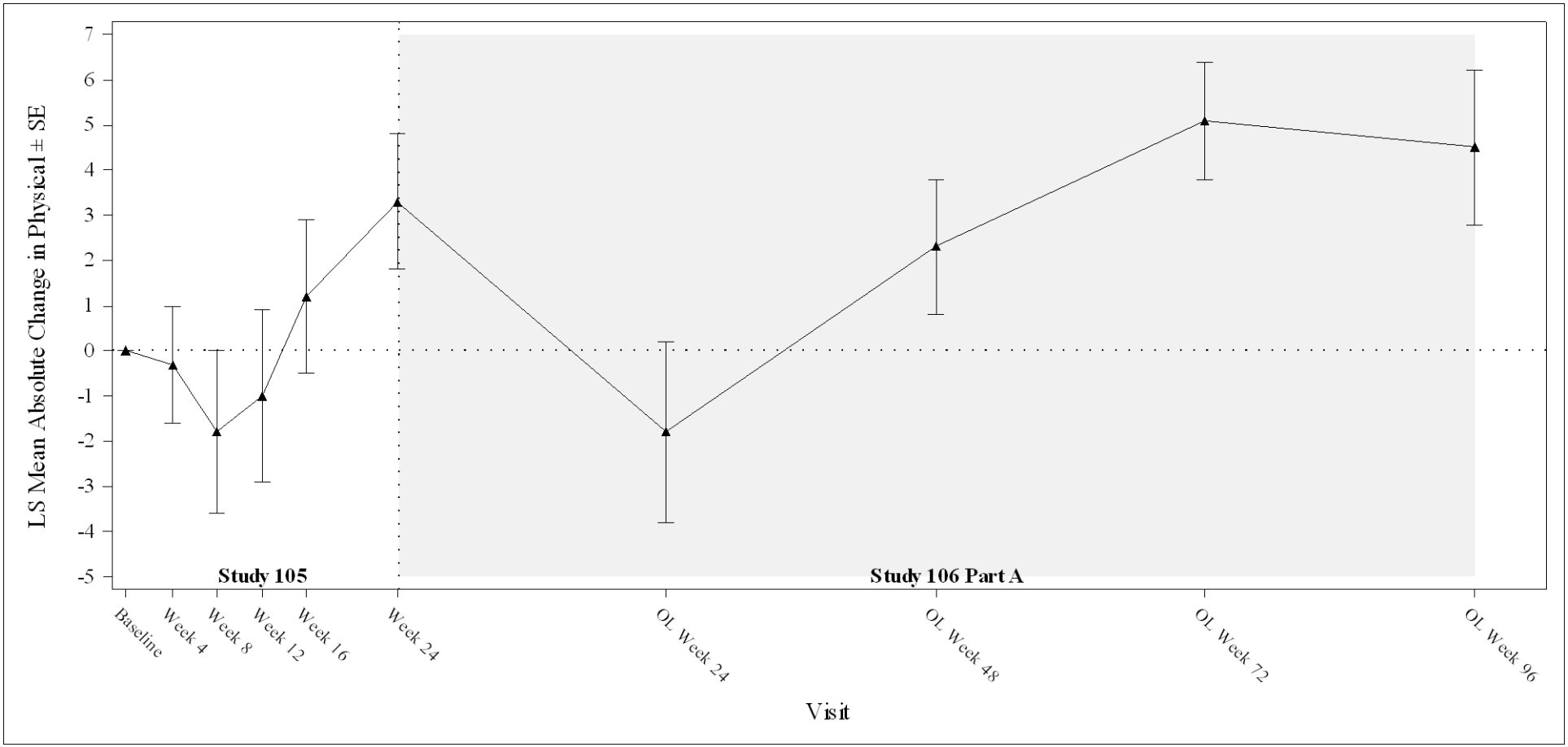
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Child's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Physical

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Physical score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX22-121-106



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Physical score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Child's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Vitality

No data met the criteria for this figure.

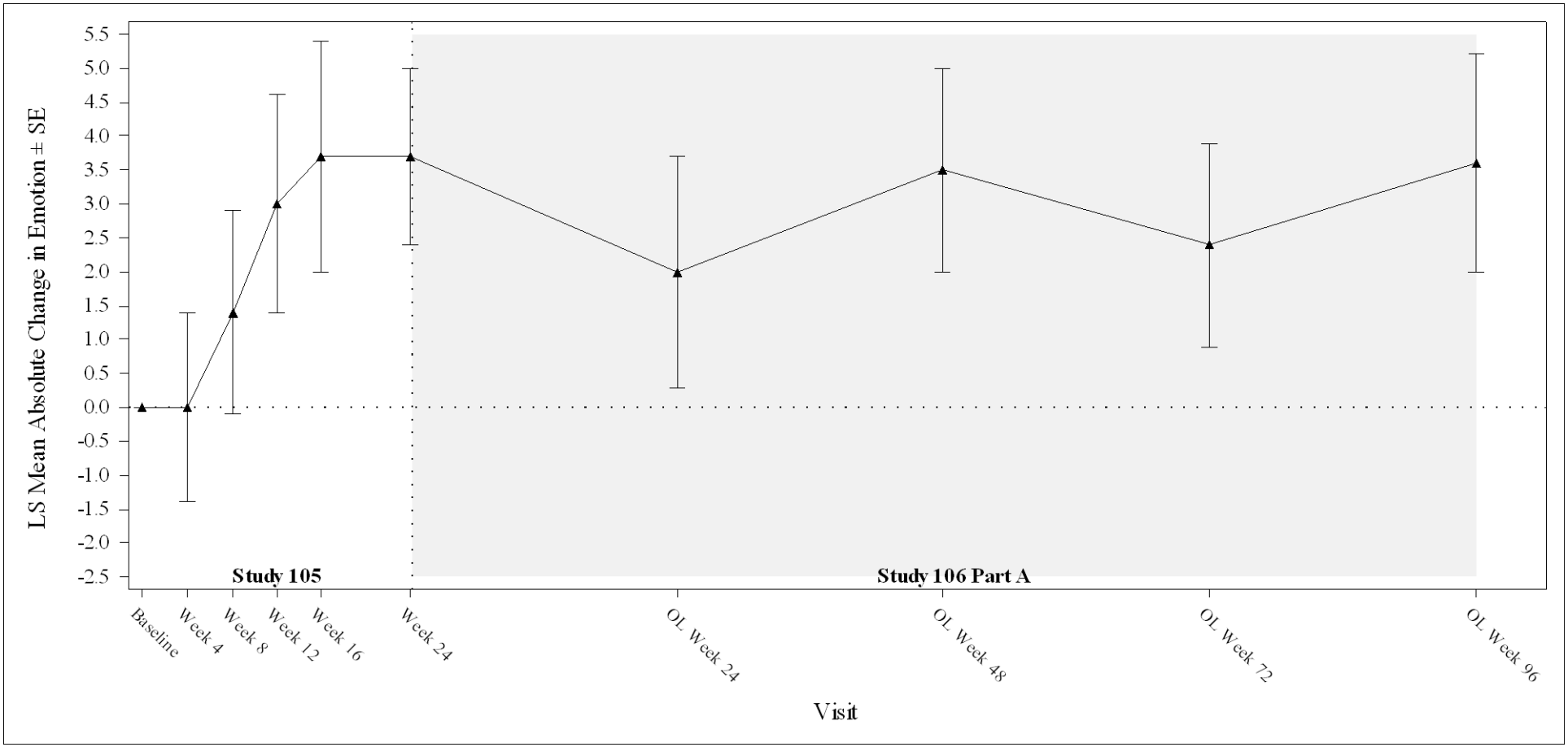
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Vitality score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Child's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Emotion

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Emotion score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Emotion score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

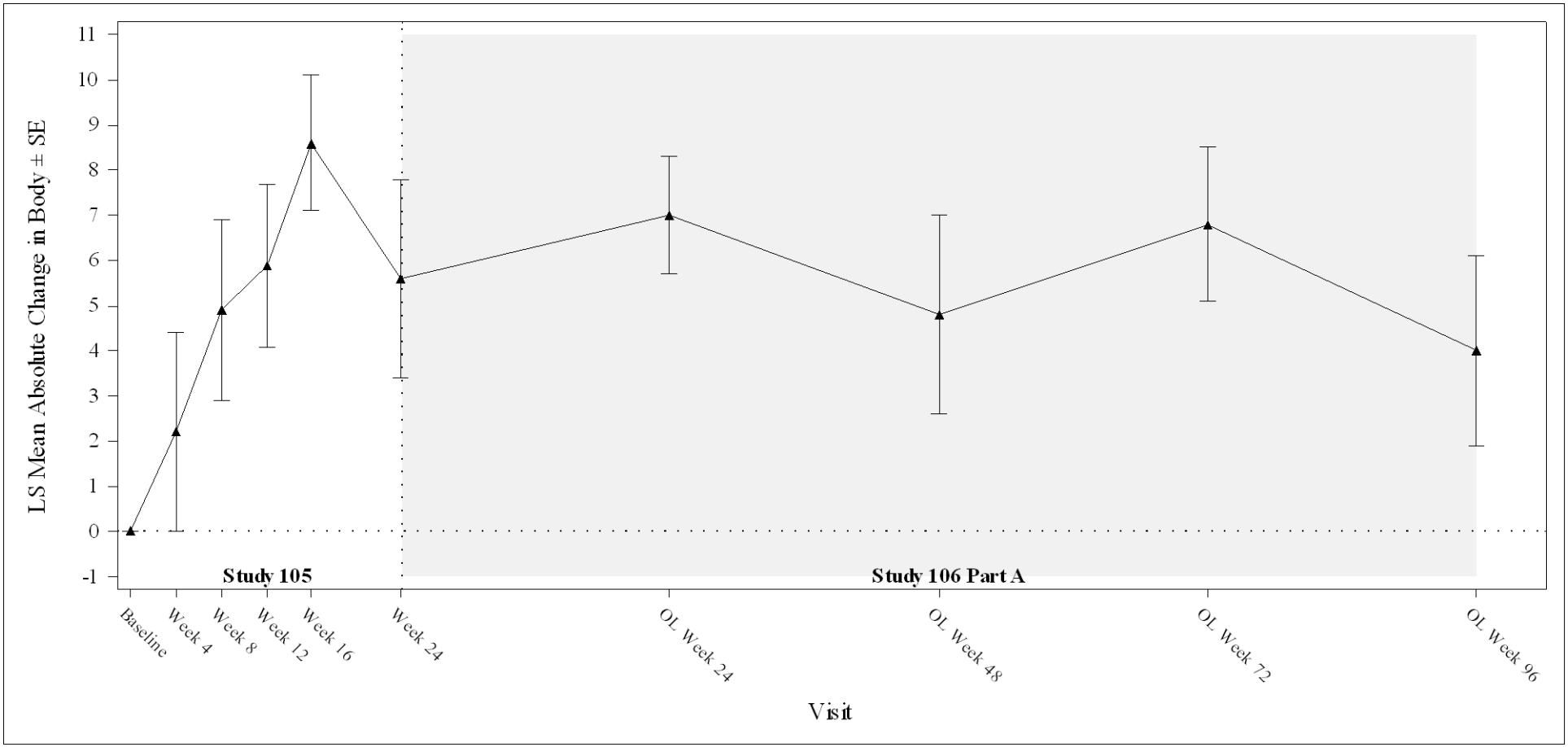
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Child's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Body

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Body score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Body score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

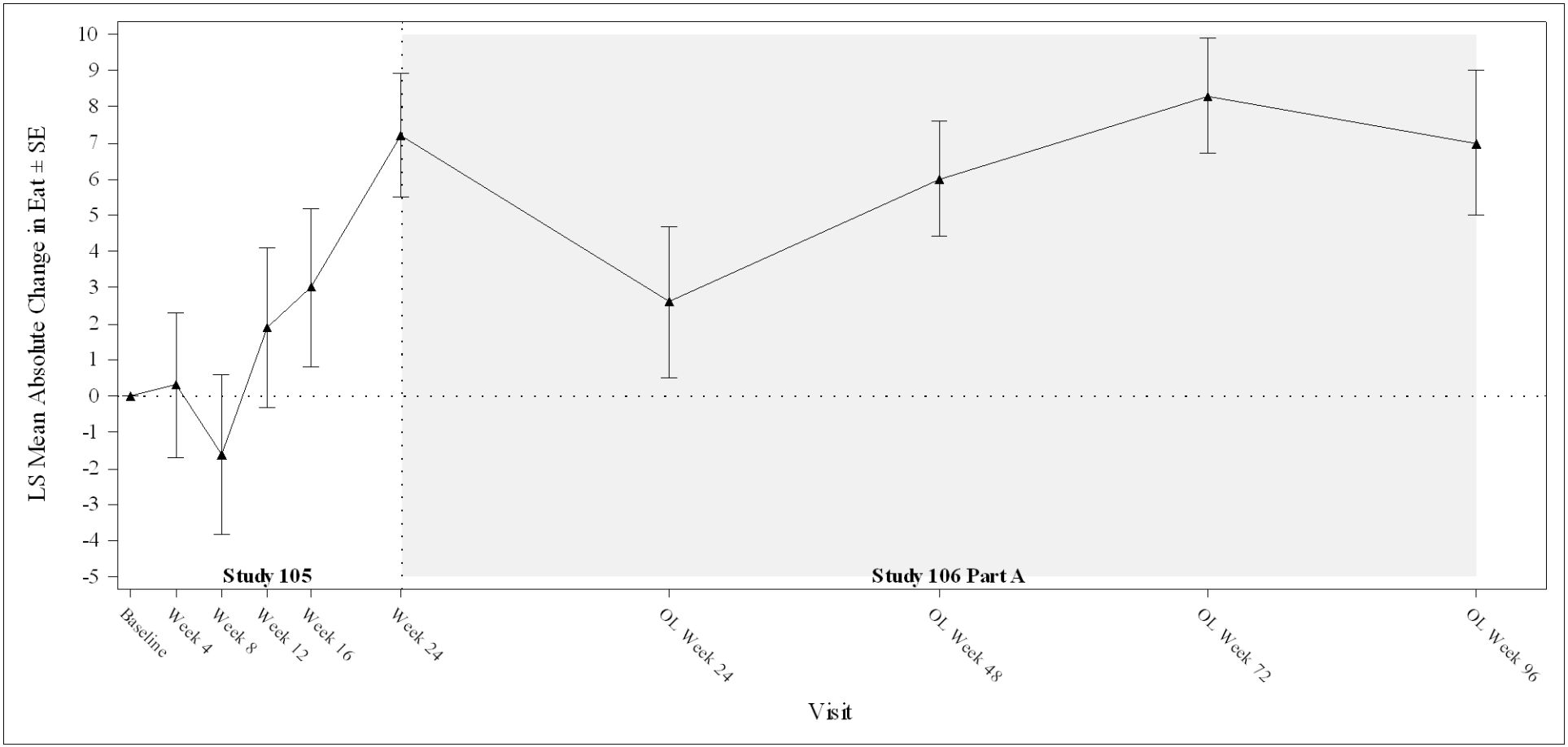
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Child's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Eat

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Eat score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Eat score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

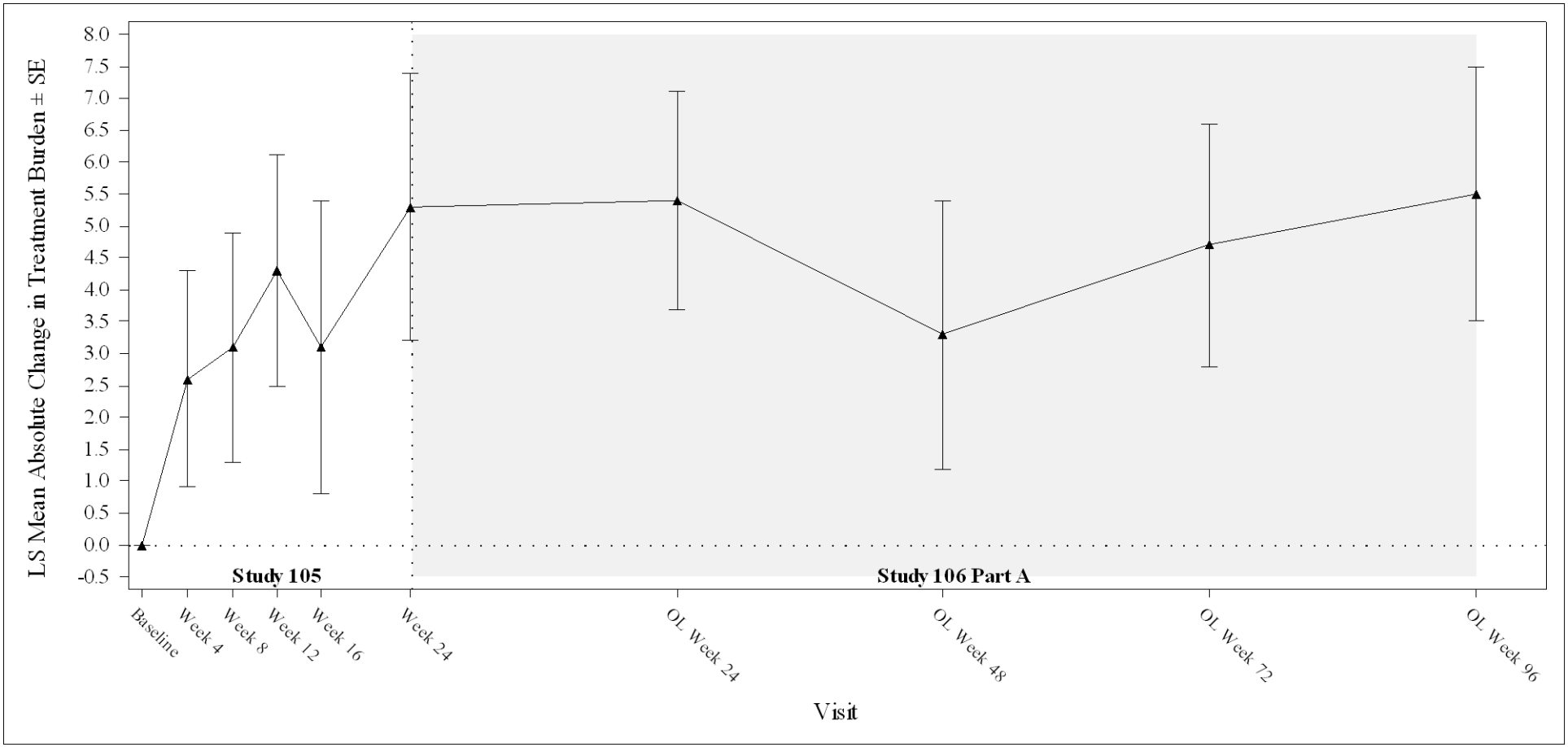
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Child's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Treatment Burden

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Treatment Burden score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Treatment Burden score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Child's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Health Perceptions

No data met the criteria for this figure.

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Health Perceptions score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Child's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Weight

No data met the criteria for this figure.

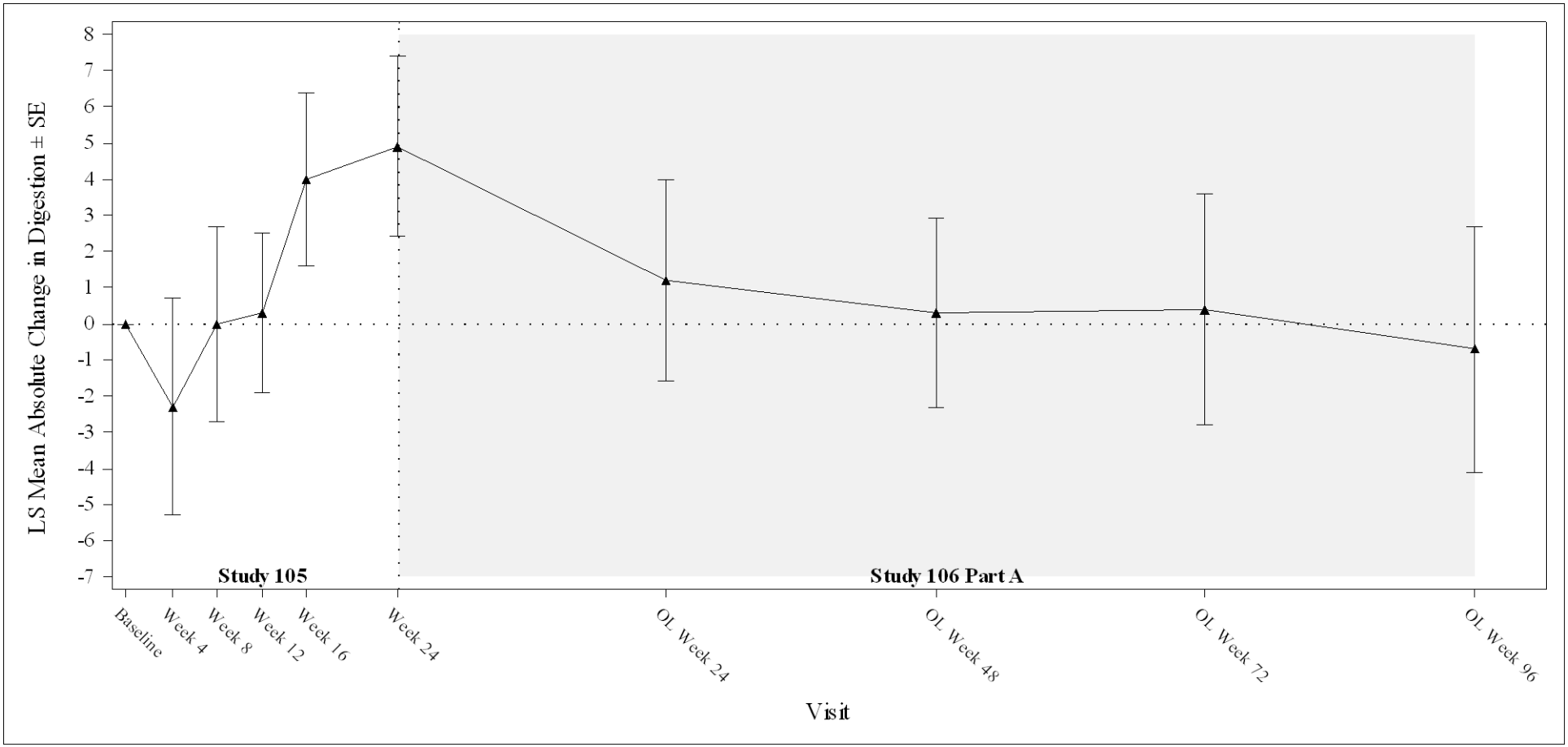
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Weight score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Child's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Digestion

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Digestion score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Digestion score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Child's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Role

No data met the criteria for this figure.

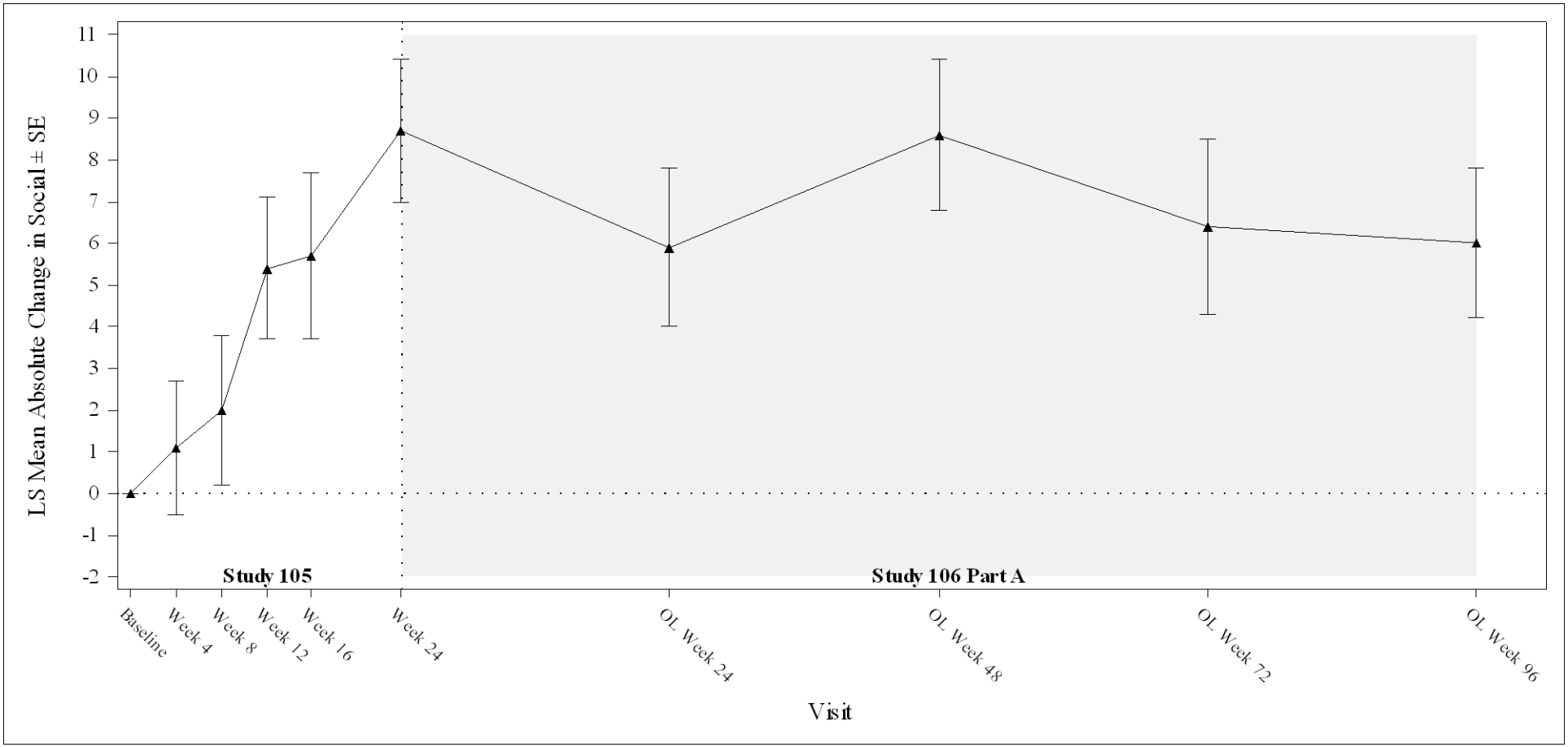
- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Role score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Child's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Social

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Social score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Social score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

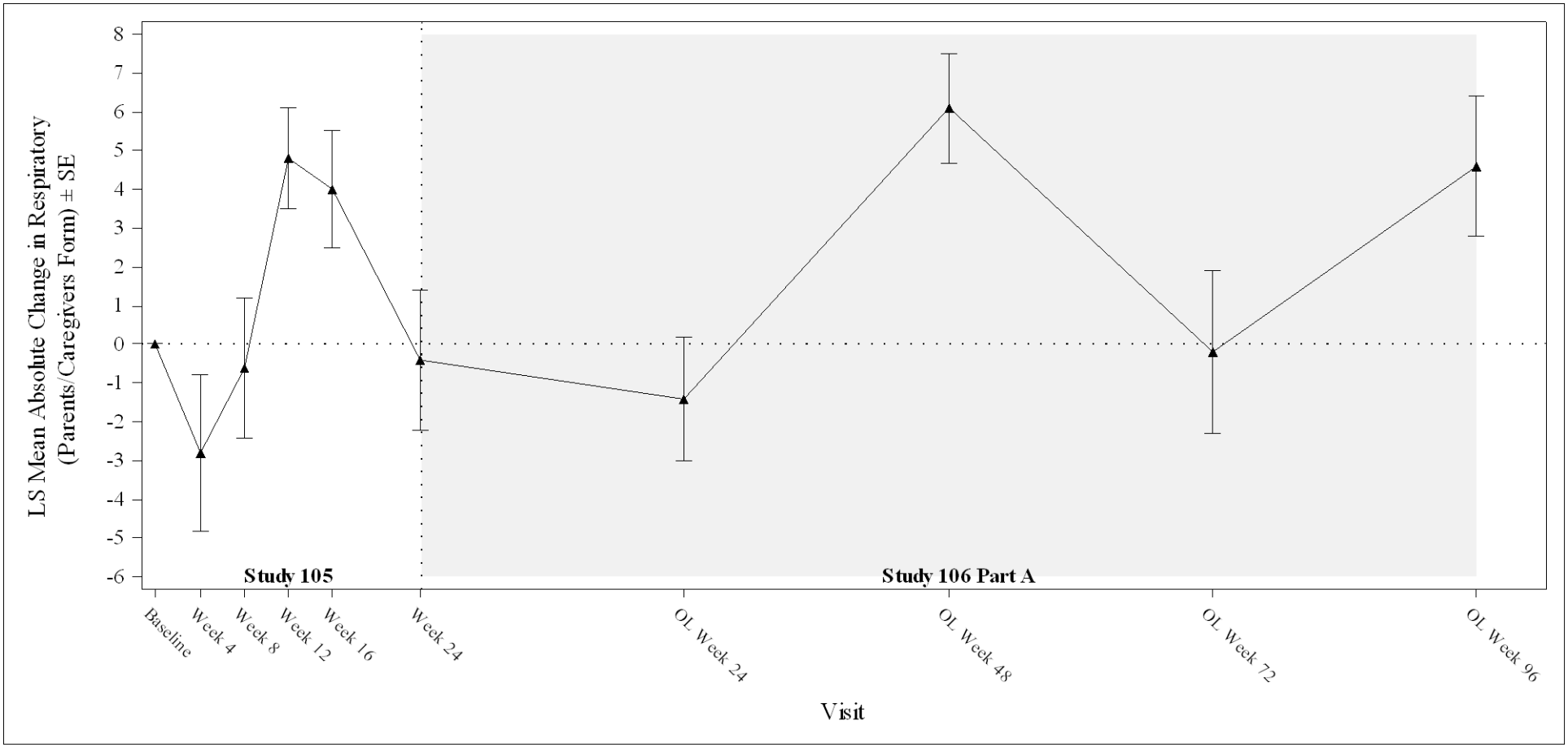
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Parent's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Respiratory (Parents/Caregivers Form)

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Respiratory (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX22-121-106



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Respiratory (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

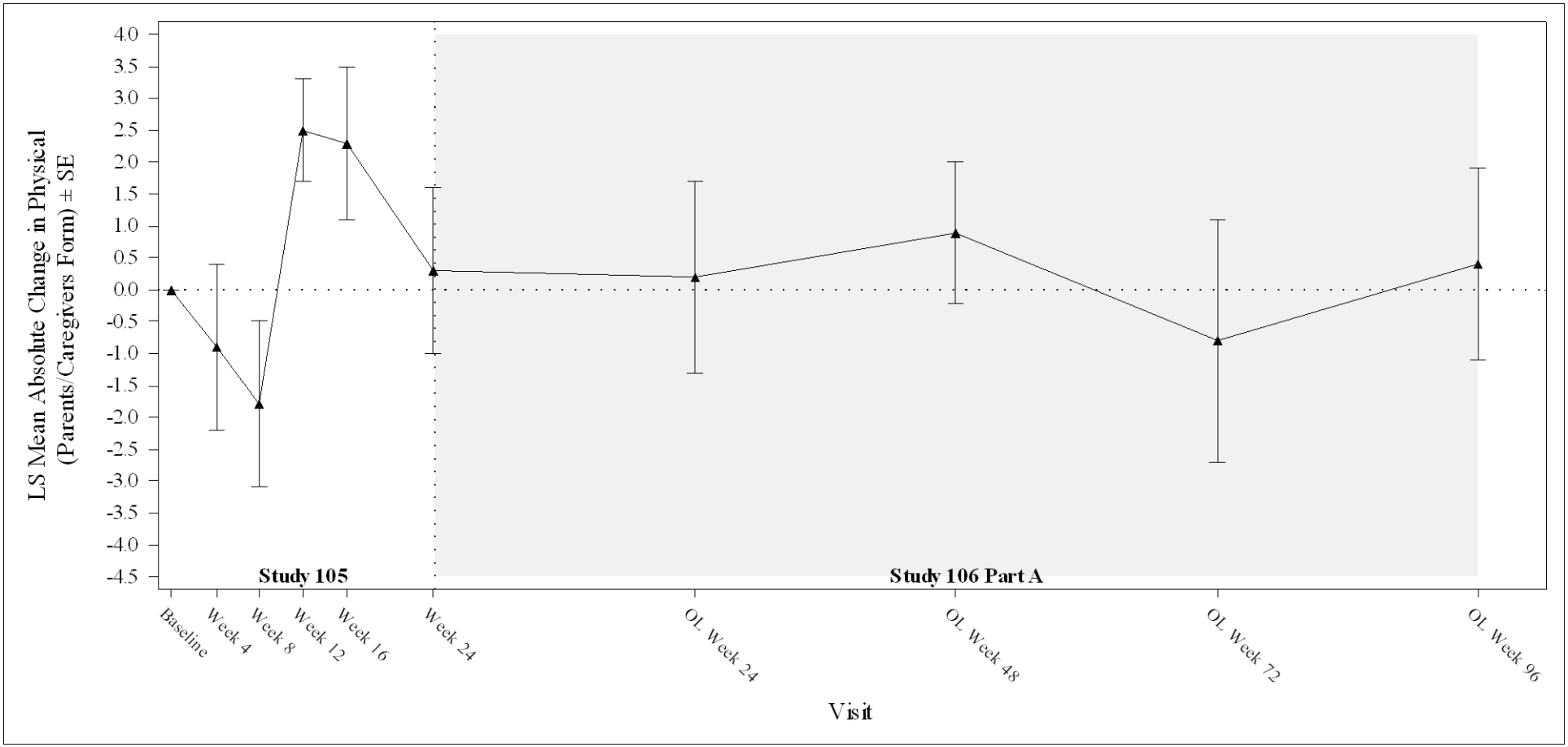
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Parent's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Physical (Parents/Caregivers Form)

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Physical (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX22-121-106



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Physical (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

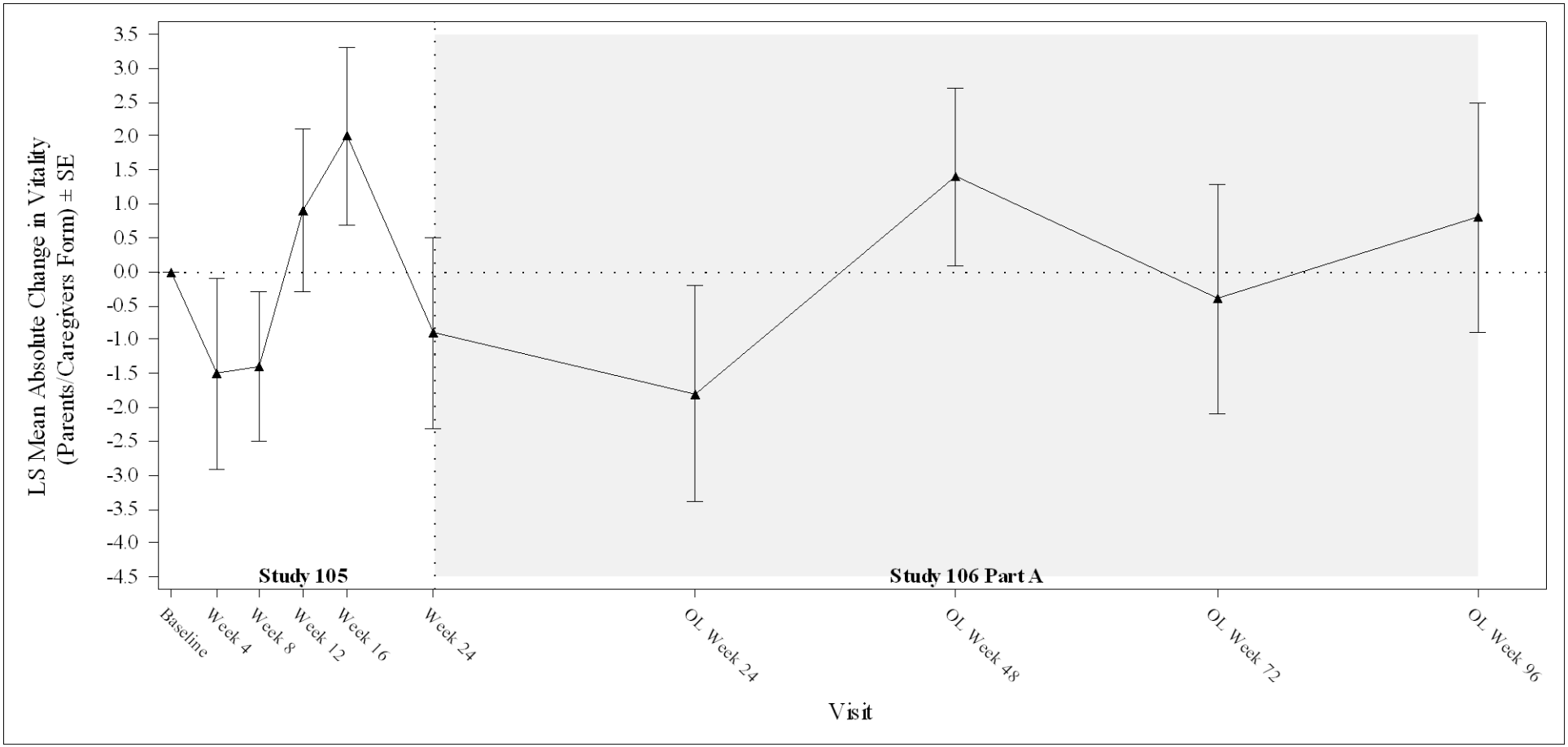
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Parent's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Vitality (Parents/Caregivers Form)

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX22-121-106



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Vitality (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

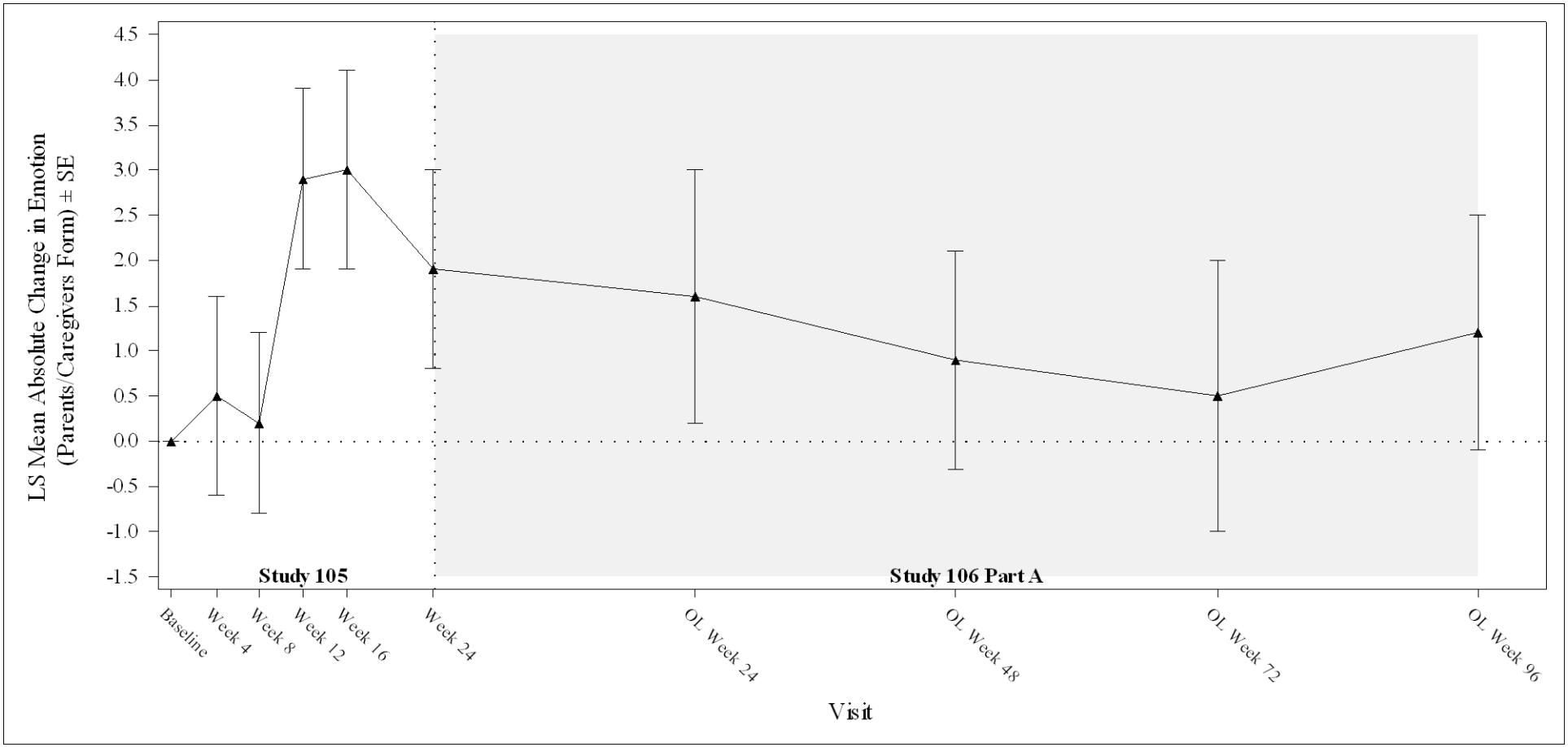
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Parent's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Emotion (Parents/Caregivers Form)

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX22-121-106



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Emotion (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

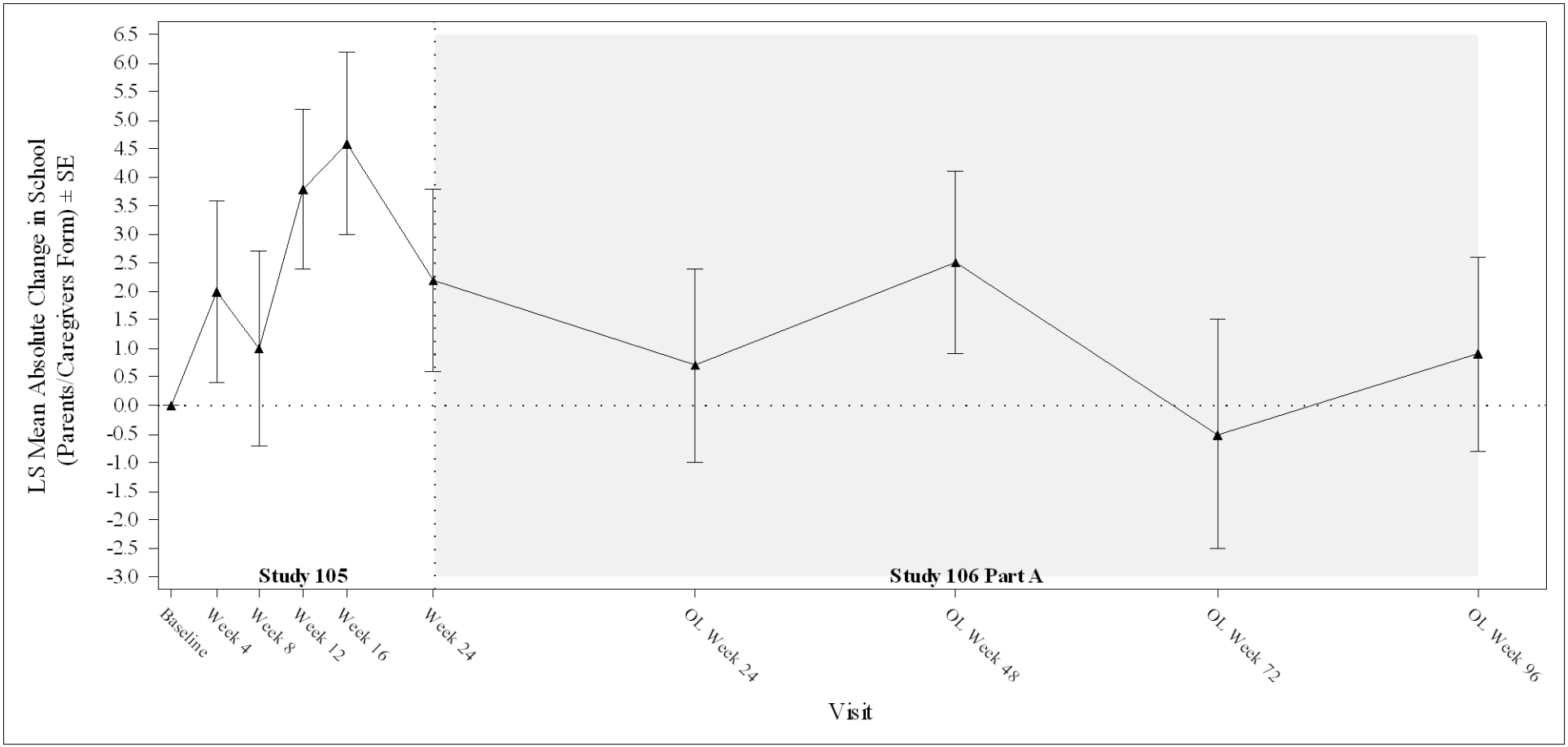
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Parent's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: School (Parents/Caregivers Form)

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R School (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX22-121-106



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R School (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

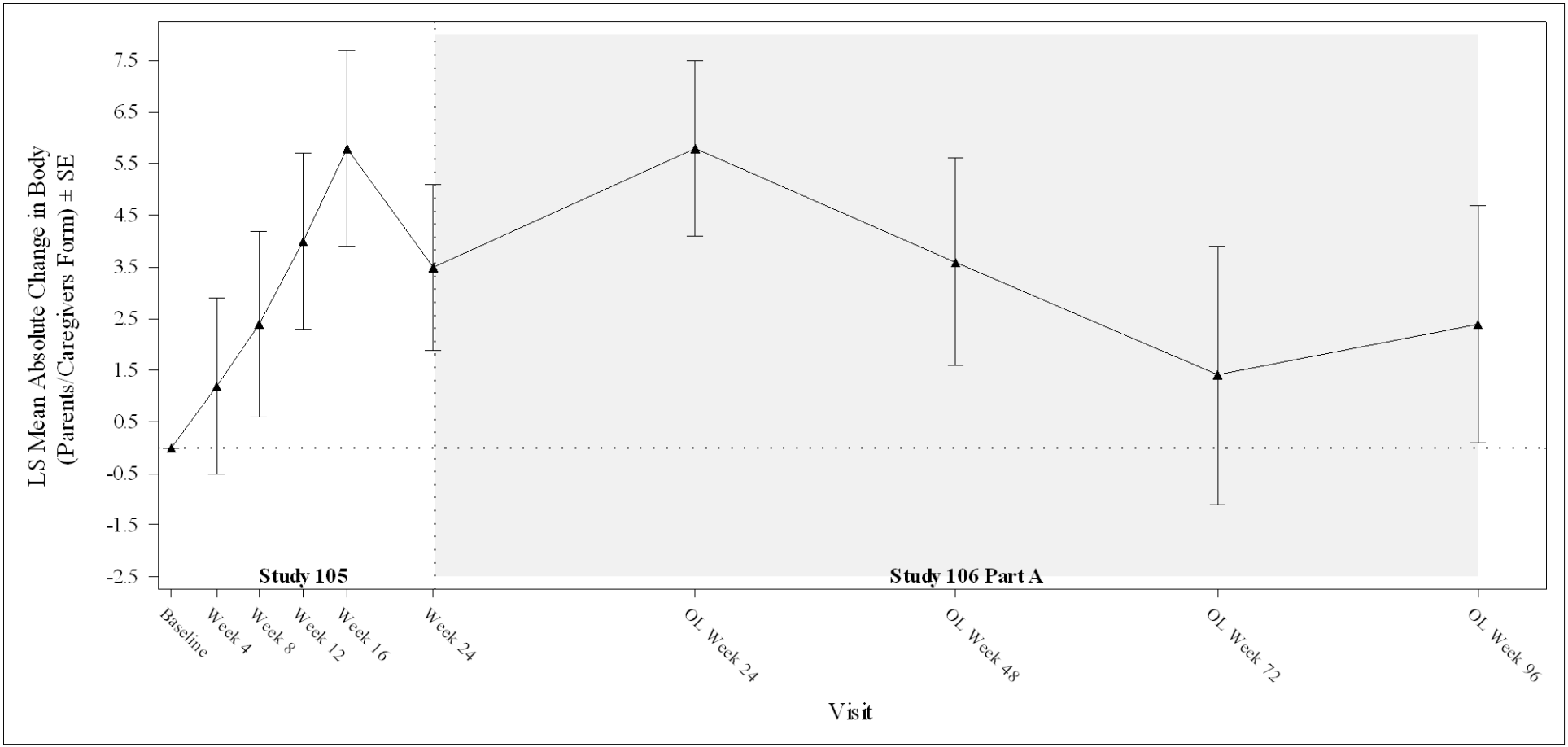
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Parent's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Body (Parents/Caregivers Form)

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Body (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX22-121-106



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Body (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

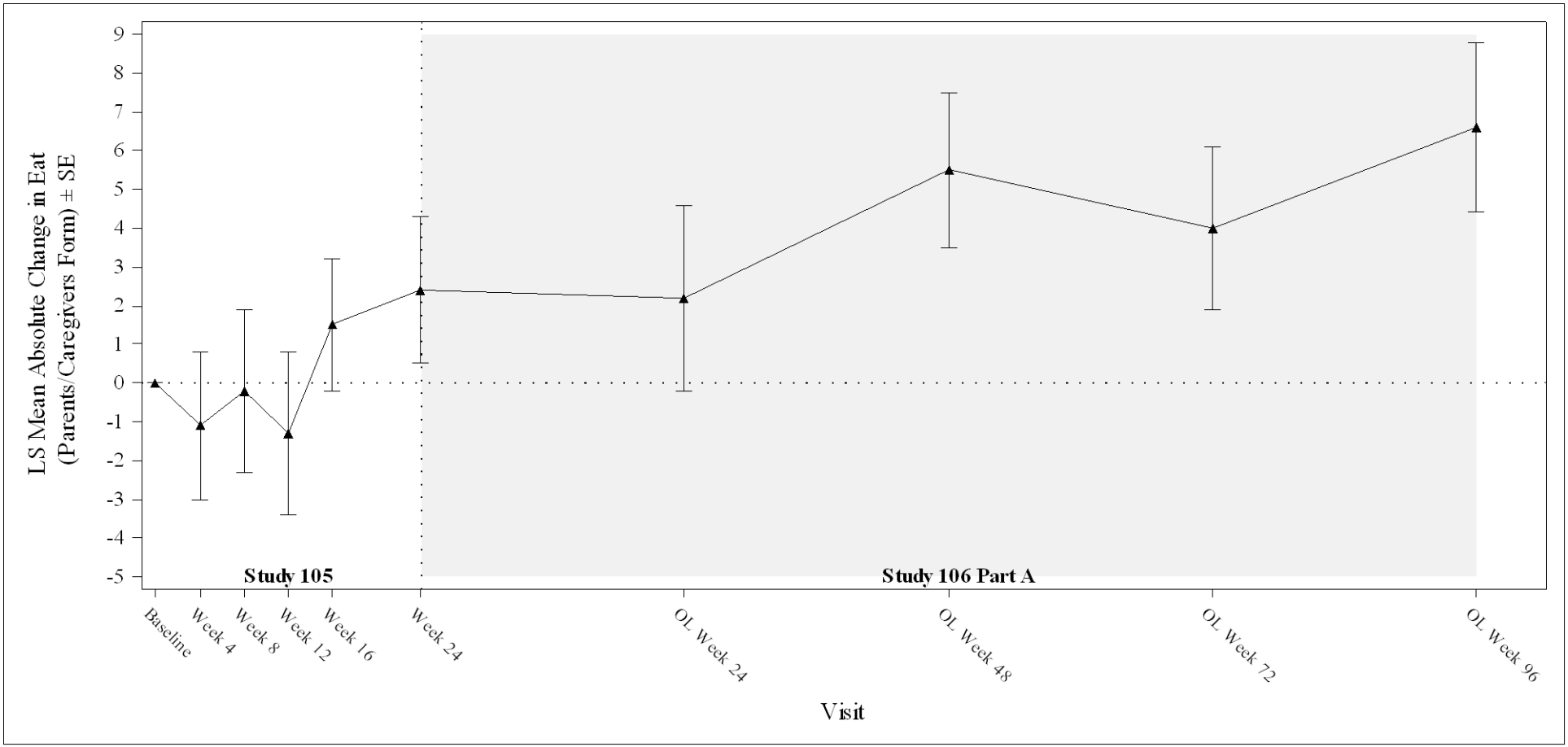
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Parent's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Eat (Parents/Caregivers Form)

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Eat (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

Zusatzanalysen zur Studie VX22-121-106



- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Eat (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

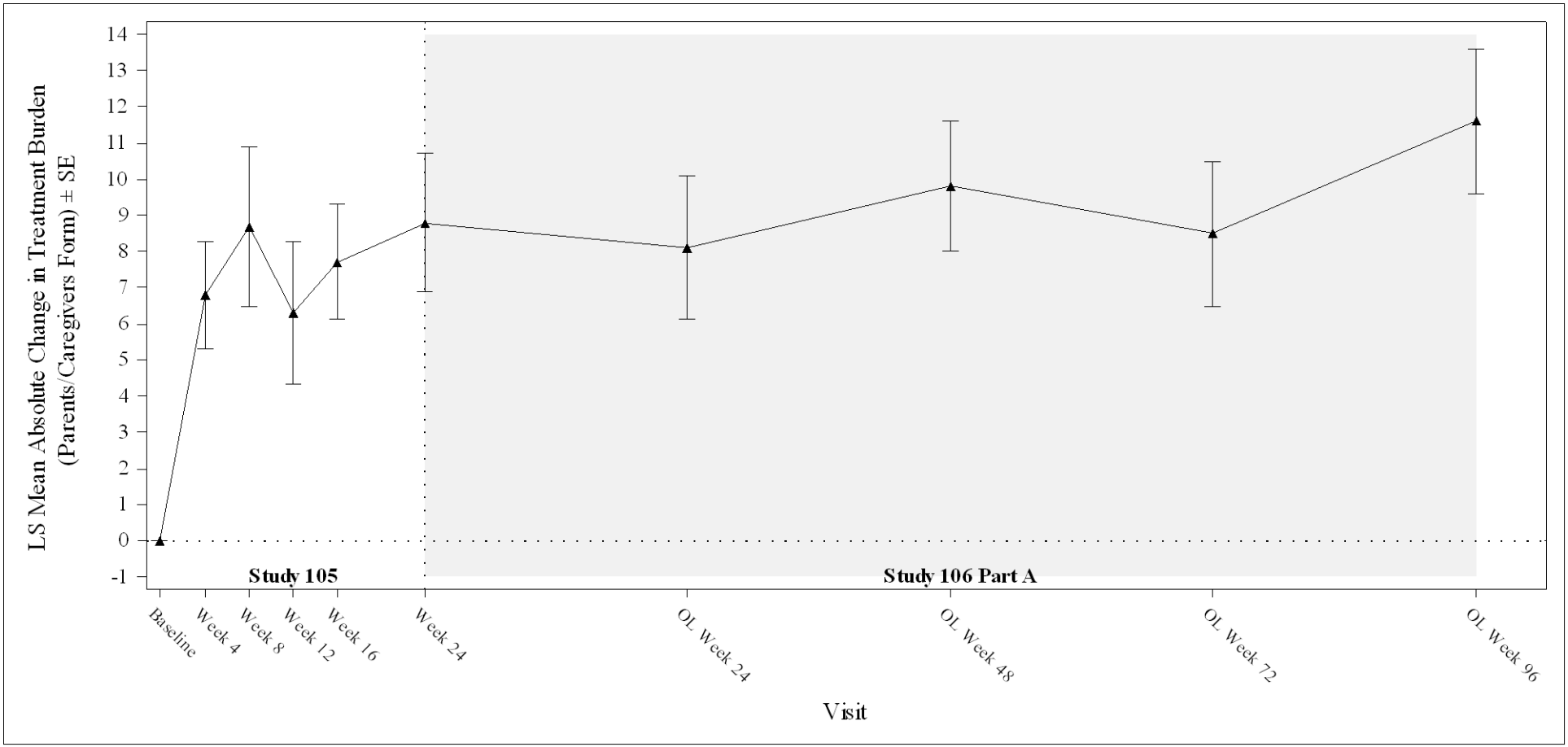
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Parent's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Treatment Burden (Parents/Caregivers Form)

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Treatment Burden (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

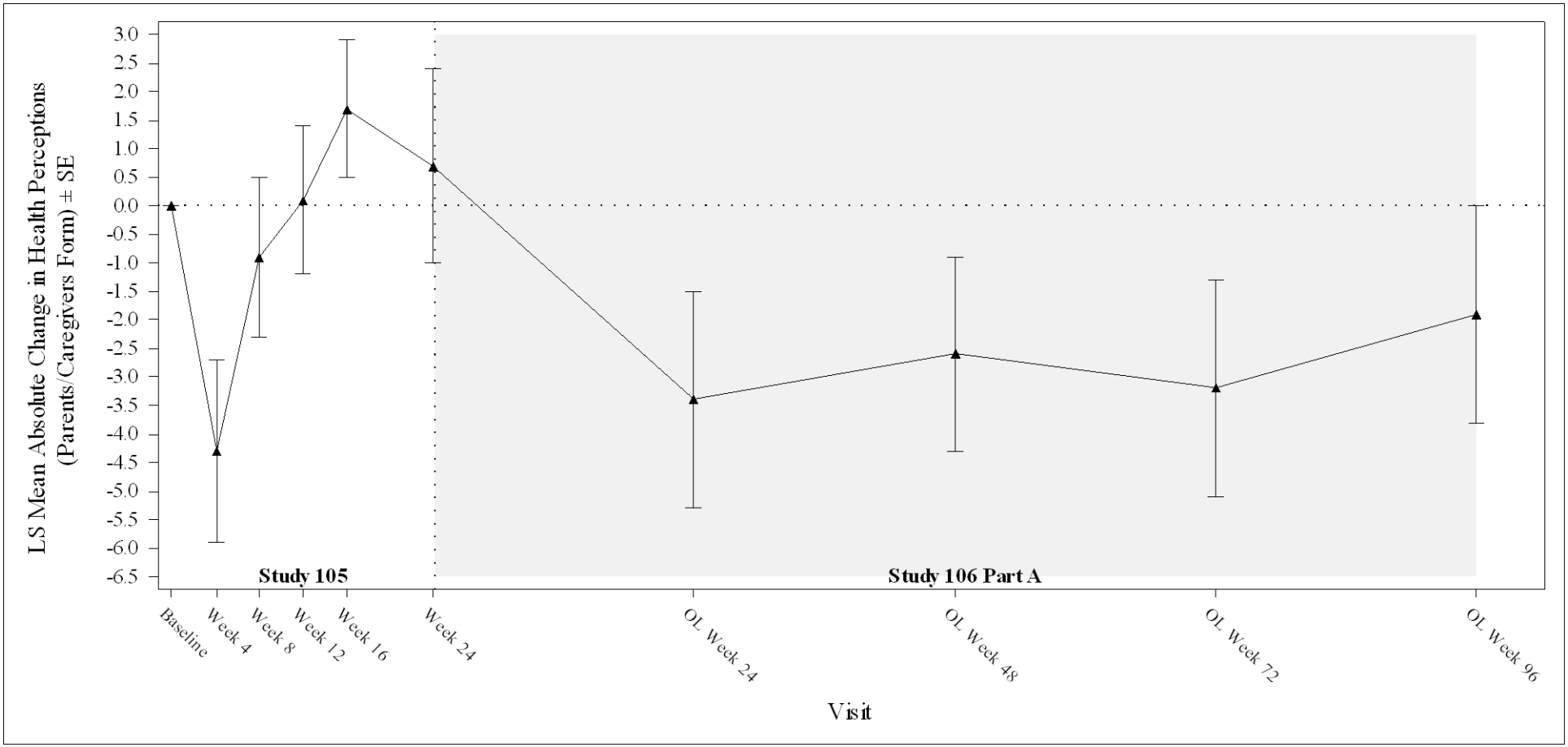
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Parent's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Health Perceptions (Parents/Caregivers Form)

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Health Perceptions (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

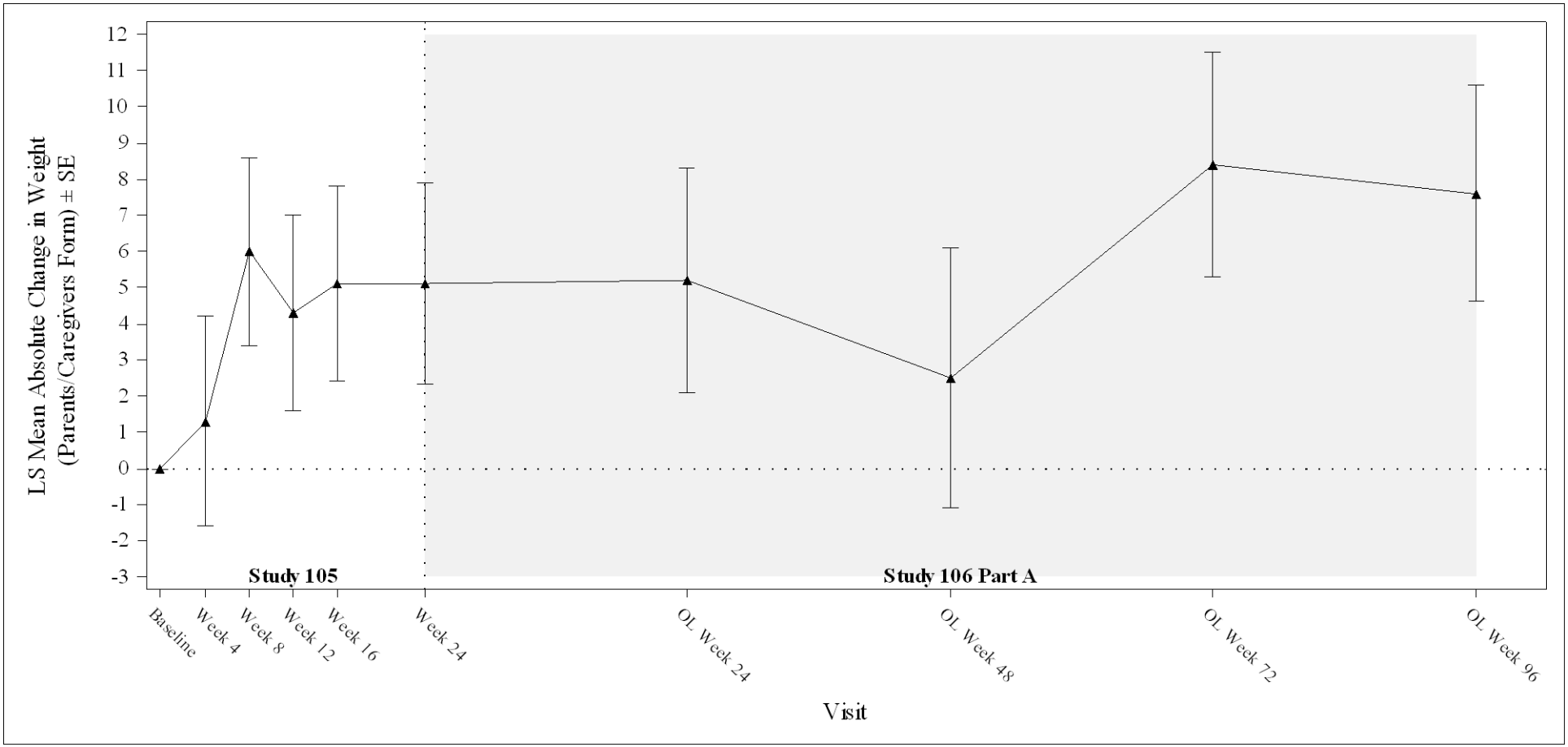
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Parent's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Weight (Parents/Caregivers Form)

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Weight (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Weight (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

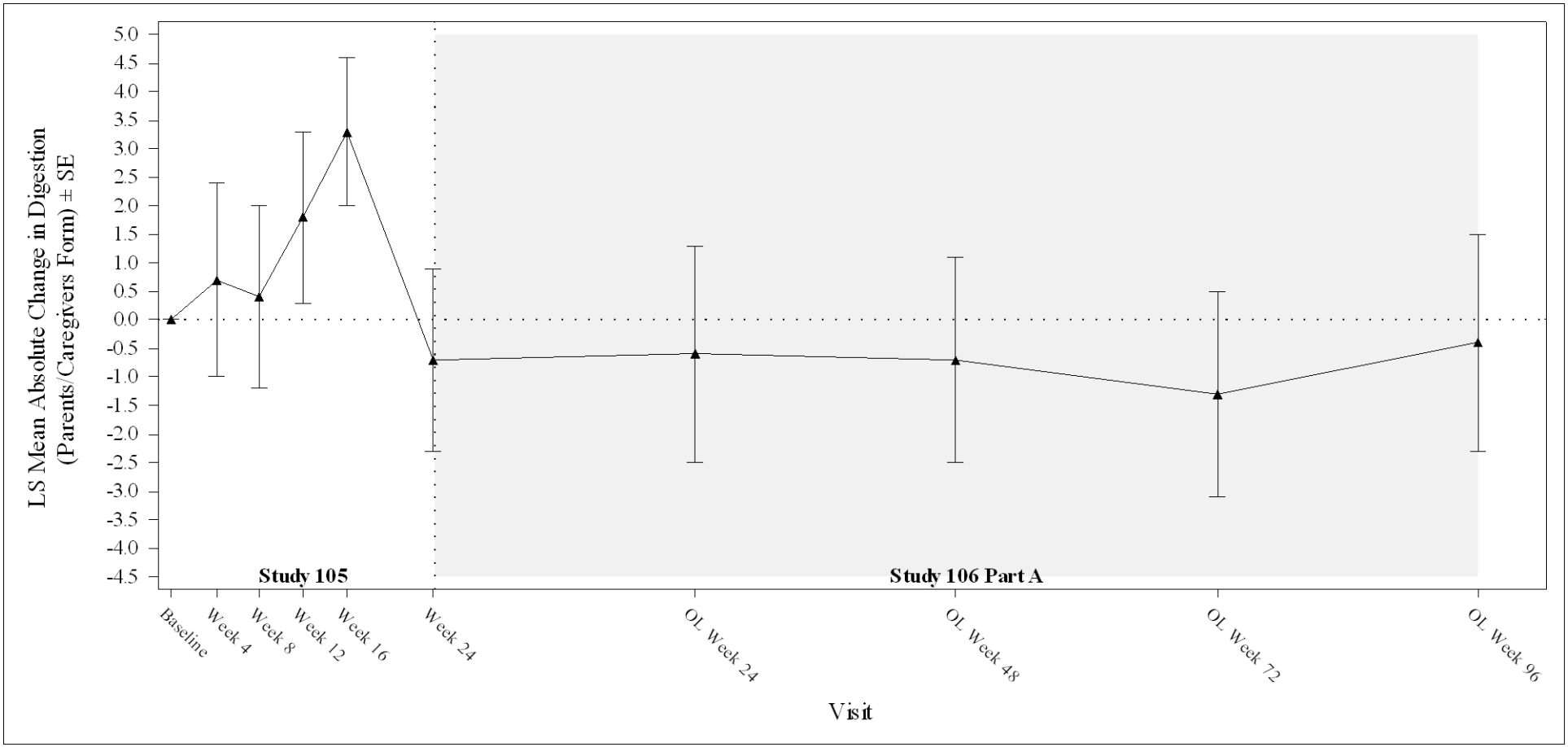
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Figure 14.2.4.2c1a.ph
MMRM Analysis of Absolute Change from Baseline in CFQ-R Domain Score at Each Visit (Parent's Version) - Parent Study Efficacy Period and OL Efficacy Period for Part A
Parent Study Efficacy Analysis Set and OL Full Analysis Set - Cohort 1

Domain: Digestion (Parents/Caregivers Form)

- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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- For the Parent Study Efficacy Period, MMRM is the same as the parent study analysis and is based on the Parent Study Efficacy Analysis Set.
- For the OL Efficacy Period for Part A, MMRM includes data from all available visits and is based on the OL Full Analysis Set for Cohort 1. The model includes fixed categorical effects for genotype (F/F, F/MF, Other) and visit, with baseline CFQ-R Digestion (Parents/Caregivers Form) score as a continuous covariate. Covariance structure=UN, DF=Kenward-Roger.

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